Risk Factors Comparison 2024-02-29 to 2023-03-01 Form: 10-K

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Our business is subject to numerous risks and uncertainties, including those highlighted in the section of this report captioned " Risk Factors. " The following is a summary of the principal risks we face: • We have incurred significant losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future. • We will need to raise additional funding, which may not be available on acceptable terms, if at all. Failure to obtain ~~necessary~~ capital when needed may force us to delay, limit or terminate our product discovery and development programs or commercialization efforts or other operations ~~. • Our business and operations could suffer in the event of an actual or perceived information security incident such as a cybersecurity breach, system failure, or other compromise of our systems or those of a third- party or other contractor or vendor~~ . • Our business substantially depends upon the successful development of XEN1101. If we are unable to obtain regulatory approval for, and successfully commercialize, XEN1101, our business may be materially harmed. • Clinical trials may fail to demonstrate adequately the safety and efficacy of our, or our collaborators', product candidates at any stage of clinical development. Terminating the development of any of our, or our collaborators', product candidates could materially harm our business and the market price of our common shares. • We, or our collaborators, may find it difficult to enroll patients in our clinical trials ~~, including for ultra- orphan, orphan or niche indications,~~ which could delay or prevent **the successful completion of** clinical trials of our product candidates. • We, or our collaborators, may incur unexpected costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our, or our collaborators', product candidates. • The regulatory approval processes of the FDA, EMA and regulators in other foreign jurisdictions are lengthy, time- consuming and inherently unpredictable. If we, or our collaborators, are unable to obtain regulatory approval for our product candidates in a timely manner, or at all, our business ~~will~~ **may** be substantially harmed. • If ~~, in the future,~~ we are unable to establish our own sales, marketing and distribution capabilities or enter into agreements for these purposes, we may not be successful in independently commercializing any future products. • Our prospects for successful development and commercialization of our partnered products and product candidates are dependent upon the research, development and marketing efforts of our collaborators ~~. • We depend on our collaborative relationship with Neurocrine Biosciences Inc., or Neurocrine Biosciences, to further develop and commercialize NBI- 921352, and if our relationship is not successful or is terminated, we may not be able to effectively develop and / or commercialize NBI- 921352~~ . • Our reliance on third parties to manufacture our product candidates may increase the risk that we will not have sufficient quantities of our product candidates, raw materials, APIs or drug products when needed or at an acceptable cost. • We rely on third parties to conduct our pre- clinical studies and clinical trials. If these third parties do not successfully carry out their contractual duties **,** including to comply with applicable laws and regulations or meet expected deadlines, our business could be substantially harmed. • We could be unsuccessful in obtaining or maintaining adequate patent protection for one or more of our products ~~or ,~~ product candidates **or future products** . • We may not be able to protect our intellectual property rights throughout the world **. • Our business and operations could suffer in the event of an actual or perceived information security incident such as a cybersecurity breach, system failure or other compromise of our systems and / or information, including information held by a third-party contractor or vendor** . • The market price of our common shares may be volatile, and purchasers of our common shares could incur substantial losses. • Future sales and issuances of our common shares or securities convertible into or exchangeable for common shares would cause our shareholders to incur dilution and could cause the market price of our common shares to fall. Our Risk Factors are not guarantees that no such conditions exist as of the date of this report and should not be interpreted as an affirmative statement that such risks or conditions have not materialized, in whole or in part. Item 1. Business We are a ~~clinical stage~~ **neuroscience- focused** biopharmaceutical company committed to ~~delivering innovative therapeutics to improve~~ **improving** the lives of ~~patients~~ **people living** with neurological **and psychiatric** disorders. We are advancing a novel product pipeline ~~of neurology- focused therapies~~ to address areas of high unmet medical need, **including** ~~with a focus on~~ epilepsy **and depression** . In addition to our proprietary product candidates, we also have partnered programs with academic and industry collaborators, including Neurocrine Biosciences, Inc., or Neurocrine Biosciences. Our Strategy Our goal is to build a fully-integrated and profitable biopharmaceutical company that discovers, develops, and commercializes innovative therapeutics to ~~improve the health~~ **treat a range** of **neuroscience diseases** ~~patients with epilepsy and other neurological disorders~~ . Key components of our strategy include: • Leveraging our discovery capabilities – which were founded upon our understanding of the genetics of channelopathies combined with proprietary biology and medicinal chemistry assets and know- how – to identify product candidates for development, drug targets and / or new indications for our existing product candidates; • Advancing selected proprietary product candidates through clinical development; • Selectively establishing collaborations that allow us to potentially expand our internal capabilities and / or address broader commercial opportunities than may be possible independently; • Identifying opportunities to further expand our pipeline though indication expansion, acquisition, or in-licensing of external product candidates; and • Commercializing product candidates alone or in collaboration with others. Our Pipeline Our Product Candidates ~~Overview of XEN1101, A Kv7 Potassium Channel Opener~~ XEN1101 is a ~~differentiated~~ **novel, potent** Kv7 potassium channel opener being developed for the treatment of epilepsy **, major depressive disorder, or MDD,** and **potentially** other neurological disorders ~~, including major depressive disorder, or MDD. The Kv7 potassium channel mechanism has been clinically validated with ezogabine, an earlier generation Kv7 opener that was approved by the U. S. Food and Drug Administration, or FDA, as an adjunctive treatment for adults with focal seizures with or without secondary generalization~~ . XEN1101 ~~' s unique composition is chemically designed to improve upon potency, selectivity and~~

~~pharmacokinetics, or~~ **for Epilepsy (** ~~PK, of ezogabine, and we believe XEN1101 does not have ezogabine' s composition- specific tissue pigmentation effects. XEN1101 for~~ Focal Onset Seizures ~~(FOS~~) **Our** ~~In October 2021, we announced positive results from our Phase 2b X- TOLE clinical trial, which evaluated the clinical efficacy, safety and tolerability of XEN1101 administered as an adjunctive treatment for adult patients with focal epilepsy. The topline data showed all primary and secondary seizure reduction endpoints were statistically significant across all dose groups, including the primary endpoint of median percent change, or MPC, from baseline in monthly seizure frequency and in the key secondary endpoint of patients with at least a 50 % reduction in monthly focal seizure frequency from baseline, with p- values of < 0. 001 for both the 20 mg and 25 mg dose groups. For a more detailed description of XEN1101 clinical results, see " Summary of XEN1101 Clinical Results " below. Following the positive results of our Phase 2b X- TOLE clinical trial, we had an End- of- Phase 2 meeting with the FDA and initiated our~~ XEN1101 Phase 3 ~~development~~ **epilepsy** program ~~, which~~ includes two identical Phase 3 clinical trials ~~to be run in parallel~~ , called X- TOLE2 and X- TOLE3, that are designed closely after the Phase 2b X- TOLE clinical trial. These multicenter, randomized, double- blind, placebo- controlled trials ~~will~~ **are** ~~evaluate~~ **evaluating** the clinical efficacy, safety, and tolerability of **15 mg or 25 mg of** XEN1101 administered **with food** as adjunctive treatment in approximately 360 patients per study with focal onset seizures, or FOS. The primary efficacy endpoint is the **median percent change, or** MPC **,** in monthly seizure frequency from baseline through the double- blind period, or DBP, of XEN1101 compared to placebo. **Xenon anticipates patient enrollment in X- TOLE2 will be completed in late 2024 to early 2025.** XEN1101 for **Epilepsy (** Primary Generalized Tonic **-** Clonic Seizures ~~(PGTCS~~) **Our** ~~We have initiated a~~ Phase 3 **X- ACKT** clinical trial **is intended** ~~, called X- ACKT,~~ to support potential regulatory submissions in an additional epilepsy indication of primary generalized tonic **-** clonic seizures, or PGTCS. This multicenter, randomized, double- blind, placebo- controlled study ~~will~~ **is** ~~evaluate~~ **evaluating** the clinical efficacy, safety, and tolerability of **25 mg of** XEN1101 administered **with food** as adjunctive treatment in approximately 160 patients with PGTCS. The primary efficacy endpoint is the MPC in monthly PGTCS frequency from baseline through the DBP of XEN1101 compared to placebo. **XEN1101 for Epilepsy (Open- Label Extension)** Upon completion of the DBP in X- TOLE2, X- TOLE3, or X- ACKT, eligible patients may enter an open- label extension, or OLE, study for up to three years. In addition, the ongoing X- TOLE Phase 2b OLE **, which has been extended from five years to seven years,** continues to generate important long- term data for XEN1101. **Summary of** XEN1101 ~~for Major Depressive Disorder (MDD) Based on promising pre- clinical~~ **Clinical** ~~data with XEN1101 and published clinical data generated using ezogabine, we are evaluating the clinical efficacy, safety and tolerability of XEN1101 administered as monotherapy in approximately 150 patients with MDD in a Phase 2 clinical trial called X- NOVA. Designed as a randomized, double- blind, placebo- controlled, multicenter clinical study, the primary objective is to assess the efficacy of XEN1101 compared to placebo on improvement of depressive symptoms in subjects diagnosed with moderate to severe MDD, using the Montgomery- Åsberg Depression Rating Scale, or MADRS, score change through week six. Topline results~~ **Results** ~~from the X- NOVA study are anticipated~~ in **Epilepsy** ~~the third quarter of 2023. We are also collaborating with the Icahn School of Medicine at Mount Sinai to support an ongoing investigator- sponsored Phase 2 proof- of- concept, randomized, parallel- arm, placebo- controlled multi- site study of XEN1101 for the treatment of MDD in approximately 60 subjects. The primary objective of the study is to investigate the effect of XEN1101 on the brain reward circuit as measured by the change in bilateral ventral striatum activity as assessed by functional MRI, or fMRI. The secondary objectives are to test the effect of XEN1101 compared to placebo on clinical measures of depression and anhedonia using the MADRS and Snaith- Hamilton Pleasure Scale, or SHAPS, respectively.~~ Phase 1: Phase 1 studies conducted in healthy subjects suggested that XEN1101 was generally ~~safe and~~ well tolerated in the doses examined, and its ~~PK~~ **pharmacokinetic** profile supported a once- daily dosing schedule **with food and without the need for titration, which has been utilized in all Phase 2 and Phase 3 trials** . We completed a Phase 1 clinical trial that evaluated the safety, tolerability and ~~PK~~ **pharmacokinetic profile** of both single ascending doses, or SAD, and multiple ascending doses, or MAD, of XEN1101 in healthy subjects. The XEN1101 Phase 1 results include data from six SAD cohorts ranging in dose from 5 to 30 mg (n = 34, placebo = 8), including a crossover food effect cohort (n = 10) with a single 20 mg dose. MAD results included three cohorts ranging in once daily doses from 15 to 25 mg (n = 18, placebo = 6) including two cohorts of 15 mg evaluated in a fasted and fed state over 7 and 10 days, respectively, and one cohort of 25 mg evaluated in a fed state over 10 days. The ~~PK profile of XEN1101 supports a once- per- day dosing schedule without the need for titration. The~~ majority of adverse events, or AEs, were mild or moderate, resolved spontaneously and were consistent with anti- seizure medications, or ASMs. There were no serious adverse events, deaths, or clinically significant delayed ventricular repolarization or laboratory findings. Phase 1 results suggest that XEN1101 is generally ~~safe and~~ well tolerated in the doses examined (single doses of up to 30 mg and multiple doses of up to 25 mg once daily). Phase 1b: Data from a Phase 1b transcranial magnetic stimulation, or TMS, study – which was designed to assess XEN1101' s ability and potency to modulate cortical excitability – demonstrated activity in the target CNS tissue and helped inform dose selection for our Phase 2b clinical trial. This Phase 1b double- blind, placebo- controlled, randomized cross- over TMS study included 20 healthy male subjects. TMS measurements were taken at 2 and 4 hours for all subjects and, due to a prolonged absorption phase displayed by XEN1101, an additional TMS assessment time- point was added at 6 hours for a subset of subjects. Subjects were randomized initially to either a 20 mg dose of XEN1101 or placebo and then, after a one- week wash- out period, crossed over to the other treatment arm. XEN1101 reduced corticospinal excitability, as demonstrated by a concentration dependent elevation in resting motor threshold, or RMT, the key TMS- EMG measure. RMT increased in proportion to XEN1101 plasma concentration showing a mean ± standard error of mean increase of 4. 9 ± 0. 7 % (p < 0. 01) at 6 hours. Active motor threshold, or AMT, also increased in proportion to plasma concentration of XEN1101 with an increase of 2. 0 ± 0. 4 % at 6 hours. In addition, XEN1101 statistically significantly modulated TMS- evoked electroencephalogram, or EEG, potentials, or TEPs, in a pattern consistent with reductions in cortical excitability. Relative to time- matched placebo, at peak plasma levels, XEN1101 decreased the amplitude of TEPs vs placebo at 25, 45 and 180 ms after the TMS pulse. Additional measures of cortical excitability including global mean field power were similarly impacted.

XEN1101 also shifted the power spectra of resting state EEGs toward lower frequencies. This Phase 1b TMS study provided evidence of the CNS effects of a 20 mg dose of XEN1101 as indicated by suppression of cortical and corticospinal excitability, which helped inform dose selection for our XEN1101 Phase 2b clinical trial. Phase 2b X- TOLE Clinical Trial: In October 2021, we announced topline results from the Phase 2b X- TOLE clinical trial, which was designed as a randomized, double- blind, placebo- controlled, multicenter study to evaluate the clinical efficacy, safety, and tolerability of **10 mg, 20 mg, or 25 mg of** XEN1101 administered as once- daily adjunctive treatment **with food** in adult patients with focal epilepsy. The study included a total of 325 randomized and treated subjects in the safety population and 323 subjects in the modified intent- to- treat population for the efficacy analyses. Subjects had an average age of 40. 8 ± 13. 3 years, and 8. 9 %, 40. ~~3~~ **6** %, or 50. ~~8~~ **5** % of the subjects were on and continued taking one, two, or three stable background ASMs throughout the study, respectively, and failed a median of 6 previous ASMs prior to study entry. The median baseline seizure frequency across the study groups was approximately 13. 5 seizures per month. Of the 285 subjects who completed the double- blind period, 96. 5 % entered the OLE to evaluate the long- term safety, tolerability, and effectiveness of XEN1101. Summary of X- TOLE Efficacy Results in the DBP: The X- TOLE trial met its primary efficacy endpoint with XEN1101 demonstrating a statistically significant and dose- dependent reduction from baseline in monthly (defined as 28 days) focal seizure frequency when compared to placebo (monotonic dose response; p < 0. 001). Primary and secondary measures in the topline data set included a pairwise comparison of each active dose to placebo and a responder analysis with the proportion of patients who achieved a 50 % or greater reduction in monthly focal seizure frequency from baseline. XEN1101 demonstrated a statistically significant reduction from baseline in monthly focal seizure frequency in pairwise comparisons to placebo for all three XEN1101 doses. The median percent reduction in monthly focal seizure frequency was 52. 8 % in the XEN1101 25 mg group, 46. 4 % in the XEN1101 20 mg group, and 33. 2 % in the XEN1101 10 mg group compared to 18. 2 % in the placebo group. Statistical significance was achieved for all dose groups compared to placebo with 2- sided p- values of p < 0. 001 for 25 mg vs. placebo, p < 0. 001 for 20 mg vs. placebo, and p = 0. 035 for 10 mg vs. placebo. A prespecified secondary endpoint of the study was a responder analysis, which compared the proportion of study subjects treated with XEN1101 who achieved a ≥ 50 % reduction in monthly focal seizures versus placebo. The percentage of subjects who achieved a ≥ 50 % reduction in monthly focal seizures was 54. 5 % in the XEN1101 25 mg group, 43. 1 % in the XEN1101 20 mg group, and 28. 3 % in the XEN1101 10 mg group compared to 14. 9 % in the placebo group. Statistical significance was achieved for all dose groups compared to placebo with 2- sided p- values of p < 0. 001 for 25 mg vs. placebo, p < 0. 001 for 20 mg vs. placebo, and p = 0. 037 for 10 mg vs placebo. In addition to the topline data, further sub- analyses were presented in December 2021 at the Annual Meeting of the American Epilepsy Society, or AES 2021. These sub- analyses include the proportion of patients with at least a 75 % reduction in monthly focal seizure frequency from baseline along with the proportion of patients who achieved 100 % reduction in monthly seizure frequency from baseline. Efficacy results are summarized in the following table; all p- values are 2- sided comparing the active dose to placebo for the prespecified primary and secondary seizure reduction endpoints: XEN1101 25 mg (N = 112) XEN1101 20 mg (N = 51) XEN1101 10 mg (N = 46) Placebo (N = 114) Median reduction from baseline in monthly focal seizure frequency 52. 8 % (p < 0. 001) 46. 4 % (p < 0. 001) 33. 2 % (p = 0. 035) 18. 2 % Patients with at least a 50 % reduction in monthly focal seizure frequency from baseline 54. 5 % (p < 0. 001) 43. 1 % (p < 0. 001) 28. 3 % (p = 0. 037) 14. 9 % Patients with at least a 75 % reduction in monthly focal seizure frequency from baseline 29. 5 % 29. 4 % 8. 7 % 6. 1 % Patients with 100 % reduction in monthly focal seizure frequency from baseline 6. 3 % 7. 8 % 2. 2 % 1. 8 % Additional sub- analyses were performed in patients with different baseline characteristics given that X- TOLE included a ~~“~~difficult- to- treat ~~”~~patient population as defined by the number of prior failed ASMs, concomitant ASMs on study, and baseline seizure burden. The table below outlines a sub- group analyses of median percent reduction in seizures within the 25 mg dose group, showing that there was a significant increase in seizure reduction in patients with less disease severity at baseline: XEN1101 25 mg Median reduction from baseline in monthly focal seizures ~~frequencyOverall~~ **frequency PlaceboOverall** in X- TOLE **52. 8 %** (N = 112) ~~52~~ **18** . ~~8~~ **2** % **(n = 114)** Prior failed ASMs > 6 43. ~~0~~ **2** % **(n = 45) 14. 2 % (n = 47)** Prior failed ASMs < 6 58. ~~0~~ **3** % **(n = 67) 20. 5 % (n = 67)** Concomitant ASMs = 3 ~~50~~ **51** . ~~8~~ **3** % **(n = 54) 20. 4 % (n = 56)** Concomitant ASMs < 2 ~~60~~ **59** . ~~9~~ **7** % **(n = 58) 14. 4 % (n = 58)** Baseline seizures > 8. 5 per month 50. 8 % **(n = 83) 18. 2 % (n = 84)** Baseline seizures < 8. 5 per month 70. 6 % **(n = 29) 18. 8 % (n = 30)** In addition, an analysis of seizure reduction across seizure subtypes showed a median percent reduction in monthly focal seizure frequency of 86. 9 % **(n = 23)** in ‘ type 4’ focal seizures that lead to generalized tonic clonic seizures in the 25 mg dose group. A time- to- event analysis analyzing the time to reach the baseline monthly focal seizure count during the double- blind period showed a marked dose- dependent decrease in the rate of seizure recurrence when comparing XEN1101 to placebo. These marked reductions in seizures were associated with statistically significant improvements in overall status, as assessed by physicians using the Clinical Global Impression of Change, or CGI- C, and by subject self- reporting using the Patient Global Impression of Change, or PGI- C, scales in the XEN1101 25 mg group, which are shown in the table below ~~with 2- sided p- values~~ : XEN1101 25 mg (N = 112) Placebo (N = 114) CGI- C (Portion of patients much improved or very much improved) 46. 4 % (p < 0. 001) 22. 8 % PGI- C (Portion of patients much improved or very much improved) 42. 9 % (p = 0. 001) 21. 9 % The XEN1101 25 mg group was statistically significant in CGI- C and PGI- C, and the XEN1101 20 mg group was statistically significant in PGI- C, while the XEN1101 20 mg group in CGI- C and the XEN1101 10 mg group for both CGI- C and PGI- C showed numerical improvements over placebo but were not statistically significant. Summary of X- TOLE Safety Results in the DBP: XEN1101 was generally well- tolerated in the DBP with AEs consistent with other ASMs. The incidence of treatment- emergent adverse events, or TEAEs, was higher in the treatment groups as compared to the placebo group, with 62. 3 % of patients in the placebo group, 67. 4 % of patients in the XEN1101 10 mg group, 68. 6 % of patients in the XEN1101 20 mg group, and 85. 1 % of patients in the XEN1101 25 mg group experiencing at least one TEAE. The TEAEs that were greater than or equal to 5 % in all treatment arms were attributed to nervous system disorders; psychiatric disorders; general disorders; gastrointestinal disorders; eye disorders; and infections – with the majority related to the central nervous system, mild or

moderate in severity, and occurring early in the treatment period. Across all XEN1101 dose groups (n = 211), the most common TEAEs were dizziness (n = 52, 24. 6 %), somnolence (n = 33, 15. 6 %), fatigue (n = 23, 10. 9 %), and headache (n = 21, 10. 0 %). The breakdown of subjects with dizziness across dose groups including placebo is as follows: 8 subjects (7. 0 %) in the placebo group, 3 subjects (6. 5 %) in the 10 mg group, 13 subjects (25. 5 %) in the 20 mg group, and 36 subjects (31. 6 %) in the 25 mg group. The incidence of treatment- emergent serious adverse events, or SAEs, was similar in all four arms of the study with 2. 6 % of patients in the placebo group, 4. 3 % of patients in the XEN1101 10 mg group, 3. 9 % of patients in the XEN1101 20 mg group, and 2. 6 % of patients in the XEN1101 25 mg group experiencing at least one treatment- emergent SAE. There were 3. 5 % of subjects in the placebo group, 2. 2 % of subjects in the XEN1101 10 mg group, 13. 7 % of subjects in the XEN1101 20 mg group, and 15. 8 % of subjects in the XEN1101 25 mg group that had an AE leading to treatment discontinuation. Two TEAEs of urinary retention were reported in the active treatment groups, one of which required a dose reduction, and both subjects remained on drug with no other changes or intervention. There was no evidence of urinary retention based upon mean differences across treatment groups in the total or individual items of the American Urological Association Symptom Index. There was no cardiovascular signal of concern based on vital signs from resting or orthostatic tests; there were no safety signals of concern from physical or neurologic exams; and there were no signals of concern from ECGs, safety labs or urinalysis. Weight changes were modest with mean (SD) changes of 0. 2 kg (2. 4) in the placebo group, 0. 6 kg (2. 3) in the 10 mg group, 1. 6 kg (2. 2) in the 20 mg group and 1. 9 kg (2. 9) in the 25 mg group. Additional **Post Hoc** Sub- Analyses of X- TOLE Data and Interim Open Label Extension (OLE) Data: In 2022 **and 2023** , we presented additional sub- group analyses of data from the XEN1101 Phase 2b X- TOLE clinical trial and interim data from the **ongoing** X- TOLE OLE. Additional sub **-** analyses of the X- TOLE data suggest that the rapid onset of efficacy for XEN1101 was associated with starting at an effective, therapeutic ~~and well- tolerated~~ dose. There was a statistically significant reduction in median seizure frequency within ~~1~~ **one** week for all doses compared with placebo. Rapid onset of efficacy of XEN1101 was seen at ~~Week~~ **week** 1, with a dose- dependent reduction from baseline in median weekly seizure frequency of 39. 1 % (~~P~~ **p** < 0. 01, n = 46), 41. 5 % (~~P~~ **p** = 0. 04, n = 50) and 55. 4 % (~~P~~ **p** < 0. 001, n = 110) in the 10 mg, 20 mg, and 25 mg groups, respectively, compared to placebo (20. 2 %, n = 114). ~~Analysis~~ **Analyses** of the interim OLE data ~~shows~~ **show** XEN1101 continues to be generally well- tolerated, yielding long- term efficacy at the 20 mg once- daily dose, with ~~patients experiencing continued seizure reduction during~~ **60 % retention at 24 months in** the OLE **, as** ~~and extended periods~~ of ~~seizure freedom~~ **the analysis cutoff date of September 5, 2023** . During ~~the~~ OLE **study months 18 to 30** , there was a sustained monthly reduction in seizure frequency (~~80~~ **78** % – ~~90~~ **95** % **median percent change** ~~seizure reduction at 12 to 18 months in OLE as measured by MPC~~) from ~~the DBP~~ **double- blind period** baseline, ~~as of~~ **and higher reductions were observed for patients who were receiving one to two ASMs at baseline compared to** ~~the~~ **those receiving three ASMs** ~~analysis cutoff date of September 22, 2022~~ . Seizure freedom for ≥ **3- month, ≥** 6- month **,** and ≥ 12- month consecutive durations was achieved in ~~17~~ **37** . 5 % **, 22. 2 %,** and ~~10~~ **14. 9 % of all patients enrolled in the OLE (n = 275), respectively. Seizure freedom for ≥ 3- month, ≥ 6- month, and ≥ 12- month consecutive durations was achieved in 56. 4 %, 34** . 5 % **and 23. 6 %** of **those** patients **with at least 24 months of treatment in the OLE (n = 165)** , respectively. **At 24 months in the OLE, clinically important improvements in the Quality of Life in Epilepsy Inventory- 31 (QOLIE- 31) subscales of Seizure Worry, Social Functioning, and Medication Effects were seen across all patients (n = 162), with even greater improvements in the seizure- free group (n = 39). In addition, quality- of- life improvements, as measured by the QOLIE- 31, originally reported at year one were maintained or improved at year two of the X- TOLE OLE. No new safety signals were identified, and the clinical data analyzed to date indicates that** XEN1101 continues to be generally well- tolerated in the OLE with AEs consistent with prior results and **AEs seen with** other **anti** ~~ASMs. At the end of the first year in the OLE, patients recorded a mean (SD) weight gain of 1. 1 (5. 9) kg. To date, two AEs of urinary retention occurred in the OLE possibly related to study drug, and both patients continued in the study without requiring intervention. Although not seen to date, we continue to monitor for the emergence of the tissue discoloration that was associated with long-~~ **seizure medications** ~~term exposure to ezogabine~~ . Based on the potential to continue to provide significant benefit to patients, we **have** extended the X- TOLE OLE from ~~three to~~ five **to seven** years ~~. Intellectual Property Related to XEN1101 We have a comprehensive strategy in place to protect and expand the intellectual property portfolio that covers XEN1101. Importantly, two additional U. S. patents were granted in 2021 covering claims related to: (1) distinct crystalline forms of XEN1101 drug substance and pharmaceutical compositions containing the same as compositions- of- matter, along with methods for their preparation and use; and (2) methods of enhancing the bioavailability of XEN1101 by administration with or close to a meal. These U. S. patents are expected to expire in 2040 and 2039, respectively, absent any extensions of patent term. For a more detailed description of our intellectual property portfolio covering our product pipeline, see " — Intellectual Property " below~~ . About Epilepsy and Seizure Types Epilepsy is a chronic neurologic disorder, the hallmark of which is recurrent, unprovoked and unpredictable seizures. Individuals are diagnosed with epilepsy if they have two unprovoked seizures (or one unprovoked seizure with the likelihood of recurrent seizures) that were not caused by a known and reversible medical condition. Seizures are generally described in two major groups: focal onset seizures, or FOS, and generalized onset seizures. FOS are the most common type of seizure experienced by people with epilepsy. FOS are localized within the brain and can either stay localized or spread to the entire brain, which is typically categorized as a secondarily generalized seizure. FOS account for approximately 60 % of seizures in the U. S., which results in a total FOS patient population of approximately 1. 8 million patients. Generalized onset seizures affect both sides of the brain or groups of cells on both sides of the brain at the same time. This term includes primary generalized tonic **-** clonic seizures, or PGTCS, absence seizures, and atonic seizures. Generalized onset seizures account for approximately 30 % of seizures in the U. S., or approximately 0. 9 million patients, of which the majority experience PGTCS. The remaining 10 % of seizures in the U. S. are characterized as unknown onset seizures, which occurs when the beginning of the seizure is unknown. As more information is learned, unknown onset seizures may later be diagnosed as focal onset or generalized onset seizures. Numerous ASMs are available for the

treatment of seizures in the U. S., although there are fewer indicated for PGTCS. The treatment of an individual patient with FOS or PGTCS is currently focused on reduction of seizure frequency, with seizure freedom as the ultimate goal. Early treatment typically begins with monotherapy followed by increasing use of polypharmacy to manage patients with residual seizure burden. Despite the availability of multiple treatment options, ~~approximately~~ **up to** 50 % of patients are considered inadequately managed with initial lines of therapy warranting additional treatment options. For poorly managed patients, physicians increasingly turn to complementary mechanisms used as adjunctive therapy to control seizures. We believe there is a need for new, more effective and tolerable treatments for FOS and PGTCS that have rapid onset of action, unique mechanisms important in polypharmacy, are easy to take (for example, once- daily), and durable. Based on our market research, we believe XEN1101 could offer a compelling value proposition to address FOS and PGTCS, if approved. **XEN1101** ~~Overview of XEN496, a Kv7 Potassium Channel Opener XEN496, a Kv7 potassium channel opener, is a proprietary, pediatric formulation of the active ingredient ezogabine being developed for the treatment of KCNQ2 developmental and epileptic encephalopathy, or~~ **for** ~~KCNQ2~~ **Major Depressive Disorder (MDD) In November 2023, we reported topline results from the randomized, double** ~~-~~ **blind, placebo- controlled,** ~~DEE. The Kv7 potassium channel mechanism has~~ **Phase** ~~been~~ **2 proof- of- concept X- NOVA** ~~clinically --~~ **clinical trial, which** ~~validated~~ **evaluated the clinical efficacy, safety, and tolerability of 10 mg and 20 mg of XEN1101 taken once daily** with **food** ~~ezogabine, an earlier generation Kv7 opener that was approved by the FDA as an adjunctive treatment for adults with focal seizures with or without secondary generalization. Published case reports where physicians have used ezogabine~~ in **168** ~~infants and young children with KCNQ2- DEE suggest that XEN496 may be efficacious in this often hard- to- treat pediatric patient population. We have received Fast Track designation and orphan drug designation, or ODD, for XEN496 for the treatment of seizures associated with KCNQ2- DEE from the FDA, as well as an orphan medicinal product designation from the European Commission. The FDA previously indicated that it is acceptable to study XEN496 in infants and children up to four years old, and that a single, small pivotal trial may be considered adequate in order to demonstrate XEN496' s efficacy in KCNQ2- DEE, provided the study shows evidence of a clinically meaningful benefit in~~ patients with ~~the intended indication~~ **moderate to severe major depressive disorder, or MDD** . ~~Clinical Development~~ **The primary objective was to assess the efficacy** of ~~XEN496~~ **XEN1101 compared to placebo on improvement of depressive symptoms in subjects diagnosed with moderate to severe MDD, using the Montgomery- Åsberg Depression Rating Scale, or MADRS, score change through week 6.** We **anticipate participating in an " end** ~~have developed XEN496 as a proprietary, pediatric - specific, immediate- release formulation~~ of ~~ezogabine -~~ **Phase 2 " meeting with the U** . ~~To~~ **S. Food and Drug Administration, or FDA, in April 2024 to** support the **initiation of our late- stage XEN1101 clinical program in MDD, which will include three** Phase 3 clinical ~~trial~~ **trials ,** ~~of XEN496 in patients~~ with **the first** ~~KCNQ2- DEE, we completed a PK study testing our pediatric formulation in 24 healthy adult volunteers. The PK profile observed for XEN496 was comparable to historical PK data for immediate- release ezogabine tablets, with XEN496 showing similar absorption and elimination curves. We have an ongoing~~ Phase 3 ~~randomized, double- blind, placebo- controlled, parallel group, multicenter clinical trial, called the EPIK~~ study ~~,~~ **expected to begin in the second half of 2024. We are also** evaluating ~~the~~ **other potential indications for the future development of XEN1101. Summary of X- NOVA** ~~efficacy~~ **Efficacy Data** ~~, safety, and tolerability of XEN496 administered as adjunctive treatment~~ in **the DBP:** ~~approximately 40 pediatric patients aged one month to less than 6 years with KCNQ2- DEE.~~ The primary endpoint **of the study was a change in MADRS at week 6. The mean reduction was 13. 90 in the placebo group, 15. 61 in the XEN1101 10 mg group and 16. 94 in the XEN1101 20 mg group. A clear dose response and a clinically meaningful, but not statistically significant, 3. 04 difference between placebo and the XEN1101 20 mg group (p = 0. 135) was observed. Statistical significance was achieved on the pre- specified endpoint of the Hamilton Depression Rating Scale, or HAM- D17, at week 6 with a mean reduction of 10. 18 in the placebo group and 13. 26 in the XEN1101 20 mg group (p = 0. 042). Statistical significance was achieved on the key secondary endpoint of a change in the Snaith- Hamilton Pleasure Scale, or SHAPS, measuring anhedonia at week 6 with a reduction of 5. 30 in the placebo group and 7. 77 in the XEN1101 20 mg group (p = 0. 046). Statistical significance was achieved in MADRS at week 1 with a mean reduction of 4. 88 in the placebo group and 7. 54 in the XEN1101 20 mg group (p = 0. 047) demonstrating early onset of efficacy. Statistical significance was achieved in reporting of at least minimally improved symptoms of depression as assessed by physicians using the Clinical Global Impression of Improvement, or CGI- I, (p = 0. 004) in the XEN1101 20 mg group compared to placebo. Summary of X- NOVA Safety and Tolerability Data in the DBP: XEN1101 was well tolerated with similar rates of adverse events reported across all treatment arms. The most commonly reported TEAEs in the XEN1101 20 mg group included dizziness (17. 9 %), somnolence (10. 7 %), headache (8. 9 %) and disturbance in attention (8. 9 %), as compared to the placebo group which reported dizziness (7. 3 %), somnolence (1. 8 %), headache (12. 7 %) and disturbance in attention (0 %). Rates of discontinuation were similar across all treatment arms and rates of discontinuation due to TEAEs were low with three patients in the XEN1101 20 mg group (5. 4 %), as compared to two patients in the placebo group (3. 6 %). No serious adverse events, or SAEs, were reported in the two XEN1101 treatment groups and there were two patients (3. 6 %) in the placebo group who experienced a treatment- emergent SAE. XEN1101 was not associated with notable weight gain, and patients did not report notable sexual dysfunction. Investigator- Led Phase 2 Proof- of- Concept Study of XEN1101 in MDD We are also collaborating with the Icahn School of Medicine at Mount Sinai to support an ongoing investigator- sponsored Phase 2 proof- of- concept, randomized, parallel- arm, placebo- controlled multi- site study of XEN1101 for the treatment of MDD in approximately 60 subjects. The primary objective of the study** is **to investigate** the ~~percent~~ **effect of XEN1101 on the brain reward circuit as measured by the** change ~~from baseline~~ in **bilateral ventral striatum activity** ~~monthly countable motor seizure frequency during the blinded treatment period,~~ as ~~recorded~~ **assessed** by **functional MRI,** ~~caregivers in a daily seizure diary. Patients may be considered for -~~ **or** ~~an open- label extension if~~ **fMRI. The secondary objectives are to test** ~~they -~~ **the** ~~meet all requirements. We anticipate that~~ **effect of XEN1101 compared to placebo on clinical measures of depression and**

anhedonia using the **MADRS and SHAPS, respectively** ~~EPIK study will be completed in 2024~~. About **Major Depressive Disorder (MDD) MDD** ~~KCNQ2- DEE KCNQ2 developmental and epileptic encephalopathy, or KCNQ2- DEE, otherwise known as EIEE7,~~ is a ~~rare~~ **common** , ~~severe neurodevelopmental~~ **chronic neurological** disorder ~~with a significant seizure burden and profound developmental impairment. KCNQ2- DEE is uniquely~~ characterized by ~~multiple~~ **low mood** , ~~daily~~ **inability to feel pleasure** , ~~refractory seizures presenting within~~ **feelings of guilt and worthlessness, low energy, and other emotional and physical symptoms that last for two weeks or more, and which impairs social, occupational, educational, or other important functioning. MDD is highly prevalent and difficult to treat. According to the National Institutes of Health, an estimated 7. 8 % of U. S. adults (21. 0 million) experience MDD each year, and of** ~~the~~ **them approximately two- thirds had severe impairment associated with their depression. Results of the Sequenced Treatment Alternatives to Relieve Depression, or STAR * D trial, funded by the National Institute of Mental Health, indicate that nearly two- thirds of diagnosed and treated patients do not experience adequate treatment response with** first ~~-~~ ~~week of life~~ **line therapy, and that the majority of these initial failures also fail second- line treatment, highlighting the need for new anti- depressant medications** with **novel mechanisms of action** ~~a prominent tonic component and autonomic signs~~. ~~Seizures~~ **Intellectual Property Related to XEN1101 We have a comprehensive strategy in place to protect and expand the intellectual property portfolio that covers XEN1101. Importantly, two U. S. patents were issued in 2021 with claims covering: (1) distinct crystalline forms of XEN1101 drug substance and related pharmaceutical compositions, along with methods for their preparation and use; and (2) various methods of orally administering XEN1101 with or close to a meal. These U. S. patents** are ~~often accompanied by clonic jerking~~ **expected to expire in 2040 and 2039, respectively, absent any extensions of patent term.** ~~or~~ **For** ~~complex motor behavior. The EEG at onset of the disease shows~~ a **more detailed description of our** ~~burst suppression pattern later evolving into multifocal epileptiform activity. The infants usually develop a severe to profound~~ intellectual **property portfolio covering** ~~disability with axial hypotonia that can be accompanied by limb spasticity. The seizure activity typically decreases with age with some patients becoming seizure free or~~ **our pipeline** ~~experiencing more minor seizure burden by 3 to 5 years~~ of **product candidates** ~~age; however~~ , **see “ —** ~~a survey of patient caregivers indicates that a significant proportion of patients have ongoing seizures beyond this age range. The intellectual~~ **Intellectual Property ” below** ~~disability and other co- morbidities are not reversed or improved with age and patients generally require life- long care. Patients are often non- verbal, and some children may also have autistic features. Seizure- related bradycardia and oxygen desaturation with cyanosis have been observed and are thought to contribute to the significant risk of sudden unexpected death in epilepsy, or SUDEP, in these children. An epidemiology study from Europe examining the incidence and phenotypes of childhood- onset genetic epilepsies reports the incidence of KCNQ2- DEE as approximately 1 per 17, 000 live births~~. New Pipeline Opportunities Given our expertise in drug discovery, our efforts are concentrated on the identification of ion channel targets where we believe novel ~~openers~~ **modulators** might represent significant therapeutic advances ~~, with a particular focus on epilepsy and other CNS- related indications~~. Expansion of our pipeline may come from our internal research efforts and through the acquisition or in- licensing of other external product candidates **. The near- term focus is on internal development candidates targeting Kv7, Nav1. 1 and Nav1. 7. Additional updates will be provided as these pre- clinical drug candidates advance into clinical development** . Our Partnered Programs NBI- 921352, A Clinical Stage, Selective Nav1. 6 Sodium Channel Inhibitor for the Treatment of Epilepsy In December 2019, we entered into a license and collaboration agreement with Neurocrine Biosciences to develop treatments for epilepsy. Neurocrine Biosciences has an exclusive license to XEN901, now known as NBI- 921352, a clinical stage selective Nav1. 6 sodium channel inhibitor, and an exclusive license to pre- clinical compounds for development, including selective Nav1. 6 inhibitors and dual Nav1. 2 / 1. 6 inhibitors. The agreement also included a multi- year research collaboration to discover, identify and develop additional novel Nav1. 6 and Nav1. 2 / 1. 6 inhibitors, which was completed in June 2022. Pursuant to the terms of the agreement, we have the potential to receive certain clinical, regulatory, and commercial milestone payments, as well as future sales royalties. For a more detailed description of the terms of this agreement with Neurocrine Biosciences, see “ — Collaborations, Commercial and License Agreements ” below. NBI- 921352 is ~~a potent, highly selective Nav1. 6 sodium channel inhibitor~~ being developed to treat pediatric patients with SCN8A developmental and epileptic encephalopathy, or SCN8A- DEE ~~, and other potential indications, including adult focal epilepsy~~. **A** ~~Neurocrine Biosciences has received orphan drug and rare pediatric disease designations from the FDA for NBI- 921352 in SCN8A- DEE. Prior to our license and collaboration agreement with Neurocrine Biosciences, we completed a Phase 1 clinical trial in healthy adult subjects, and subsequently developed a pediatric- specific, granule formulation. Neurocrine Biosciences is currently conducting a Phase 2 clinical trial evaluating NBI- 921352 in adult patients with focal- onset seizures, with data expected in the second half of 2023. In addition, a~~ Phase 2 clinical trial is underway evaluating NBI- 921352 in pediatric patients (aged between 2 and 21 years) with SCN8A- DEE. **Neurocrine Biosciences has received orphan drug and rare pediatric disease designations from the FDA for NBI- 921352 in SCN8A- DEE. In November 2023, Neurocrine Biosciences reported that a Phase 2 clinical trial evaluating NBI- 921352 in adult patients with FOS failed to demonstrate meaningful reduction in seizure frequency and that no further development with NBI- 921352 in FOS is planned at this time.** License and Collaboration Agreement with Neurocrine Biosciences, Inc. ~~On~~ **In** December ~~2,~~ 2019 **, as amended in January 2021 and February 2022** , we entered into a license and collaboration agreement, or the Collaboration Agreement, with Neurocrine Biosciences to establish a collaboration under which the parties will identify, research and develop sodium channel inhibitors, including our clinical candidate XEN901, now known as NBI- 921352, and **certain** preclinical candidates ~~XEN393, XPC’ 535~~ **(“ DTCs ”)** and **research compounds** ~~XPC’ 391,~~ which ~~compounds~~ Neurocrine Biosciences will have the exclusive right to further develop and commercialize under the terms and conditions set forth in the Collaboration Agreement. ~~Licenses. Under the terms of the Collaboration Agreement we granted to~~ Neurocrine Biosciences **has** an exclusive, royalty- bearing, sublicensable license to certain of our intellectual property rights for the research, development and commercialization of ~~(i) NBI- 921352; (ii) XEN393, XPC’ 535 and XPC’ 391, collectively referred~~

~~to as the~~ **these** ~~development track candidates, or the DTCs; and (iii) certain research~~ compounds ~~that bind to and inhibit voltage- gated sodium channels Nav1. 2 and Nav1. 6 as their primary mechanism of action, collectively, the Research Compounds and, together with NBI- 921352 and the DTCs, the Compounds,~~ on a worldwide basis for the treatment, cure, diagnosis, prediction or prevention of any human disease or disorder, state, condition and / or malady, subject to certain exceptions set forth in the Collaboration Agreement. We also granted to Neurocrine Biosciences a non- exclusive, non- royalty- bearing, sublicensable license to certain of our intellectual property rights for the screening of compounds for identification as a Select Nav Inhibitor (as defined below) and for the research of certain compounds otherwise expressly excluded from the Collaboration Agreement, or the Excluded Compounds. ~~Exclusivity. During the Research Term (as defined below) and for one year thereafter, other than in accordance with the terms of the Collaboration Agreement, neither Neurocrine Biosciences nor any of its respective affiliates is permitted to directly or indirectly research, develop, manufacture or commercialize any small- molecule Select Nav Inhibitor (as defined below).~~ During the term of the Collaboration Agreement, other than the Excluded Compounds and otherwise in accordance with the terms of the Collaboration Agreement, neither we nor any of our respective affiliates ~~is~~ **are** permitted to directly or indirectly research, develop, manufacture or commercialize a compound that, as its primary mechanism of action, binds to and inhibits voltage- gated sodium channels Nav1. 2 and Nav1. 6, such compound referred to as a Select Nav Inhibitor. ~~Governance. The parties have established a joint steering committee, or JSC, composed of an equal number of representatives from each entity, which will coordinate and oversee the Collaboration Programs (as defined below). The JSC will disband upon the completion or earlier termination of both of the Collaboration Programs. Decisions of the JSC will be made by unanimous vote, provided that in the event of a disagreement on any matter, following a specified dispute resolution procedure, Neurocrine Biosciences will have the right to decide such matter, subject to certain exceptions. Collaboration Programs. We are collaborating with Neurocrine Biosciences on the conduct of two collaboration programs: (i) a joint research collaboration to discover, identify and preclinically develop Research Compounds, or the Research Program, and (ii) a collaborative development program for NBI- 921352 and two DTCs selected by the JSC, or the Initial Development Program and, together with the Research Program, referred to as the Collaboration Programs. The Research Program included the preclinical development of our existing non- clinical Research Compounds and the discovery of new back- up and follow- on Research Compounds to NBI- 921352 and the two DTCs selected by the JSC as clinical development candidates for subsequent development and commercialization by Neurocrine Biosciences. During the term of the Research Program, the parties conducted related activities in accordance with an agreed research plan and budget.~~ Each party ~~was~~ **is** solely responsible for all costs such party ~~incurred~~ **incurs** to conduct its activities under the **development and** research ~~plan~~ **plans**, provided that **, with respect to NBI- 921352 development and research activities,** Neurocrine Biosciences ~~reimbursed~~ **reimburses** us for certain full- time employees and out- of- pocket expenses incurred by us ~~in accordance with the research budget. The Research Program was completed in June 2022. The Initial Development Program includes: (i) completion of any preclinical and clinical studies that were ongoing as the date of the Collaboration Agreement of any NBI- 921352 product and the two DTC products selected by the JSC; (ii) a pharmacokinetic, drug- drug interaction and food effect Phase 1 clinical trial of a NBI- 921352 product to examine the adequacy of a new pediatric formulation; and (iii) all preclinical studies of two DTC products containing the two DTCs selected by the JSC. The parties will use their commercially reasonable efforts to conduct the development activities under the Initial Development Program pursuant to specific development plans. Each party is solely responsible for all costs such party incurs to conduct its activities under these development plans, provided that, with respect to NBI- 921352 development activities, Neurocrine Biosciences reimburses us for certain full- time employees and out- of- pocket expenses incurred by us~~, and with respect to certain development activities related to **certain** ~~the two JSC- selected~~ DTCs, ~~the JSC may determine that~~ Neurocrine Biosciences ~~shall~~ **may** make ~~such~~ **agreed- upon** reimbursements ~~. Development, Regulatory and Manufacturing~~. Except for the activities set forth in the **development** plans ~~for the Collaboration Programs~~, Neurocrine Biosciences is solely responsible, at its sole cost and expense, for all development and manufacturing of the ~~Compounds~~ **compounds** and any pharmaceutical product that contains a ~~Compound~~ **compound**, subject to the Co- Funding Option (as defined below). ~~For~~ **We will have the right to elect to co- fund the development of one product in** the first indication that meets or exceeds a specified prevalence threshold, or a Major Indication, ~~for which Neurocrine Biosciences intends to conduct a Phase 3 clinical trial of a NBI- 921352 product or the first clinical trial of a DTC product following a successful Phase 2 clinical trial for such DTC product, Neurocrine Biosciences will prepare a development plan including an estimated budget and provide such plan to us. We will have the right to elect to co- fund the development of one product in a Major Indication~~ under such development plan and to receive a mid- single digit percentage increase in royalties owed on the net sales as calculated pursuant to the terms of the Collaboration Agreement, or Net Sales, of such products in the U. S., or the Co- Funding Option. If we exercise the Co- Funding Option, the parties will share equally all reasonable and documented costs and expenses that Neurocrine Biosciences incurs in connection with the development of such product in the applicable indication, except costs and expenses that are solely related to the development of such product for regulatory approval outside the U. S ~~.~~. We have not exercised this option as of December 31, ~~2022~~ **2023** ~~. Neurocrine Biosciences will be the regulatory sponsor and is solely responsible for all regulatory activities (except for those delegated to us) under the Collaboration Agreement, including submitting one or more INDs for an NBI- 921352 product. If the FDA grants a Rare Pediatric Disease Priority Review Voucher in connection with the approval of a New Drug Application for a NBI- 921352 product, Neurocrine Biosciences may, at its option, (i) sell it to a third- party and share a specified portion of the proceeds with us; (ii) use it for a product Neurocrine Biosciences is developing outside the Collaboration Agreement and pay us a specified portion of the voucher' s intrinsic value (as calculated pursuant to the terms of the Collaboration Agreement); or (iii) use the voucher for a pharmaceutical product that contains a Compound, in which case no payments would be due to us. If the FDA grants Neurocrine Biosciences a voucher in connection with any other product, Neurocrine Biosciences will retain all rights to such voucher without any payment or other obligations to us. Commercialization. Neurocrine Biosciences has the exclusive right to conduct, and will be solely responsible~~

~~for all aspects of, the commercialization of any pharmaceutical product that contains a Compound. Financial Terms~~ . Neurocrine Biosciences paid us an upfront payment of $ 50. 0 million, which included a $ 30. 0 million payment in cash. For the remainder of the upfront payment, concurrently with the entry into the Collaboration Agreement, the parties entered into the Share Purchase Agreement (as defined below) pursuant to which we issued and sold the Shares (as defined below) to Neurocrine Biosciences for an aggregate purchase price of $ 20. 0 million. Based on the regulatory approval of a clinical trial application in Europe for NBI- 921352 for focal- onset seizures in adults, in September 2021 we received an aggregate milestone payment of $ 10. 0 million in the form of $ 4. 5 million in cash and a $ 5. 5 million in equity investment. In January 2022, we received an aggregate milestone payment of $ 15. 0 million in the form of a $ 6. 75 million payment in cash and a $ 8. 25 million equity investment, based on the FDA' s acceptance of a protocol amendment to expand the study population of a clinical trial in pediatric patients with SCN8A- DEE. The Collaboration Agreement also provides for potential aggregate development and regulatory milestone payments from Neurocrine Biosciences to us of up to $ 325. 0 million for a NBI- 921352 product and up to $ 247. 5 million for each other Compound up to a maximum of three other Compounds. Sales- based milestones of up to $ 150. 0 million for each Compound, including a NBI- 921352 product, will be paid from Neurocrine Biosciences to us upon the achievement of certain Net Sales targets, up to a maximum of four Compounds ~~. Neurocrine Biosciences has further agreed to pay us royalties based on future Net Sales of any pharmaceutical product that contains a Compound. Such royalty percentages, for Net Sales in and outside the U. S., range from (i) for a NBI- 921352 product, a low double- digit percentage to a mid- teen percentage and a high- single digit percentage to low double- digit percentage, respectively; (ii) for each DTC product, a high- single digit percentage to a low double- digit percentage and a mid- single digit percentage to a high- single digit percentage, respectively; and (iii) for each Research Compound product, a mid- single digit percentage to a high- single digit percentage and a tiered mid- single digit percentage, respectively~~ . Neurocrine Biosciences' obligations to pay royalties with respect to a product and country will expire upon the latest of: (i) the expiration of the last to expire valid claim in (a) the parties' joint patent rights filed during the Research Term or a specified period of time thereafter or (b) our patent rights as specified in the Collaboration Agreement, in each case that cover such product; (ii) ten years from the first commercial sale of the product in such country; and (iii) the expiration of regulatory exclusivity for such product in such country, or the Royalty Term. Royalty payments are subject to reduction in specified circumstances, including expiration of patent rights or if average Net Sales decrease by a certain percentage after the introduction of a generic product. ~~Term and Termination.~~ Unless earlier terminated, the term of the Collaboration Agreement will continue on a product- by- product and country- by- country basis until the expiration of the Royalty Term for such product in such country ~~. Upon the expiration of the Royalty Term for a particular product and country, the exclusive license granted by us to Neurocrine Biosciences with respect to such product and country will become fully- paid, royalty free, perpetual and irrevocable~~ . Neurocrine Biosciences may terminate the Collaboration Agreement in its entirety or on a product- by- product or country- by- country basis, for any or no reason, by providing at least 90 days' written notice, provided that such unilateral termination will not be effective (i) with respect to a NBI- 921352 product until Neurocrine Biosciences has used its commercially reasonable efforts to complete one Phase 2 clinical trial for a NBI- 921352 product; (ii) with respect to a DTC product until Neurocrine Biosciences has used its commercially reasonable efforts to complete one Phase 1 clinical trial for a DTC product; and (iii) with respect to the Collaboration Agreement in its entirety until Neurocrine Biosciences has used its commercially reasonable efforts to complete both of these clinical trials. Either party may terminate the Collaboration Agreement in the event of a material breach in whole or in part, subject to specified conditions. If Neurocrine Biosciences is entitled to terminate the Collaboration Agreement due to our uncured material breach, in lieu of termination, Neurocrine Biosciences may elect to reduce all subsequent payments owing from Neurocrine Biosciences to us by half. Upon the termination of the Collaboration Agreement for any reason, all licenses and other rights granted to Neurocrine Biosciences by us shall terminate, provided that if termination is solely with respect to one or more products or countries, then such termination will apply only to the terminated products or countries. Upon termination in certain cases, Neurocrine Biosciences has agreed to grant us licenses to certain Neurocrine Biosciences intellectual property that is reasonably necessary, and that was actually used by Neurocrine Biosciences for the development, manufacturing or commercialization of the terminated products, to research, develop and commercialize the terminated products in the terminated countries. Such license will be royalty- free with respect to any terminated product for which a Phase 2 clinical trial was not completed prior to the effective date of termination, and otherwise will be royalty- bearing ranging from a low- single digit percentage to a high- single digit percentage depending on the stage of development of the applicable product at the effective date of termination. ~~The Collaboration Agreement includes certain other customary terms and conditions, including mutual representations and warranties, indemnification and confidentiality provisions. Amendment. In January 2021, we entered into an amendment with Neurocrine Biosciences pursuant to which we revised certain IND acceptance criteria relating to NBI- 921352 for the potential treatment of SCN8A- DEE. In February 2022, we entered into a second amendment with Neurocrine Biosciences pursuant to which the restrictions imposed on Neurocrine Biosciences prohibiting it from developing, seeking regulatory approval for, marketing or promoting certain early compounds (as the term is defined in the Collaboration Agreement) in the pain field (as the term is defined in the Collaboration Agreement) were removed.~~ Share Purchase Agreements On December 2, 2019, pursuant to the Collaboration Agreement, we entered into a Share Purchase Agreement, or SPA, with Neurocrine Biosciences pursuant to which we issued and sold 1, 408, 847 of our common shares, or Shares, to Neurocrine Biosciences in a private placement for an aggregate purchase price of $ 20. 0 million, or $ 14. 196 per share. The purchase price represented a 20 % premium to the closing price of our common shares on November 29, 2019. ~~In~~ **We entered into additional SPAs in** September 2021 **and** ~~, pursuant to the Collaboration Agreement, as amended in~~ January ~~2021~~ **2022** ~~, we entered into a SPA~~ with Neurocrine Biosciences pursuant to which we issued and sold 275, 337 **and 258, 986, respectively,** of our Shares to Neurocrine Biosciences in ~~a~~ private ~~placement~~ **placements** for ~~an~~ aggregate purchase ~~price~~ **prices** of $ 5. 5 million **(** ~~, or~~ $ 19. 9755 per share **) and $ 8. 25 million ($ 31. 855 per share), respectively** . The purchase price represented a 15 % premium to our 30- day volume- weighted average price immediately

prior to the public ~~announcement~~ **announcements** ~~. In January 2022, pursuant to the Collaboration Agreement, as amended in January 2021, we entered into a SPA with Neurocrine Biosciences pursuant to which we issued and sold 258, 986 of our Shares to Neurocrine in a private placement for an aggregate purchase price of $ 8. 25 million, or $ 31. 855 per share. The purchase price represents a 15 % premium to our 30- day volume- weighted average price immediately prior to the public announcement. The SPAs contain certain other customary terms and conditions, including mutual representations, warranties, and covenants~~ . Asset Purchase Agreement with 1st Order Pharmaceuticals, Inc. In April 2017, we entered into an asset purchase agreement with 1st Order Pharmaceuticals, Inc., or 1st Order, pursuant to which we acquired all rights with respect to XEN1101 (previously known as 1OP2198). 1st Order previously acquired 1OP2198 from Valeant Pharmaceuticals Luxembourg S. a. r. l., an indirect subsidiary of Bausch Health Companies Inc., together with Valeant Pharmaceuticals Ireland Limited, Bausch Health, and assumed certain obligations, including potential milestone and royalty payments. In September 2018, we signed an agreement with Bausch Health to buy out all future milestone payments and royalties owed to Bausch Health with respect to XEN1101, including up to $ 39. 6 million in potential clinical development, regulatory and sales- based milestones and a mid-to- high single digit percentage royalty on commercial sales in exchange for a one- time payment of $ 6. 0 million. In August 2020, we entered into an amendment to the asset purchase agreement to amend certain definitions in the agreement and to modify the payment schedule for certain milestones. Upon execution of the amendment, we made a payment of $ 0. 3 million to 1st Order. In February 2023, an additional $ 1. 4 million was paid for the achievement of clinical and other milestones. We remain responsible for future potential payments of up to $ 6 **. 0** million in regulatory milestones. There are no royalty obligations to 1st Order. As part of our business strategy, we strive to protect the proprietary technologies that we believe are important to our business, including pursuing and maintaining patent protection intended to cover our product candidates and their methods of use and processes for their manufacture, as well as other inventions that are important to our business. We plan to continue to expand our intellectual property estate by filing patent applications directed to compositions, methods of use, treatment and patient selection, formulations and manufacturing processes created or identified from our ongoing development of our product candidates ~~. We generally file applications in the U. S., Canada, the European Union, or EU,~~ and **future products** ~~other commercially significant foreign jurisdictions~~ . We also rely on trade secrets, internal know- how, technological innovations and agreements with third parties to develop, maintain and protect our competitive position. Our ability to be competitive will depend on the success of this strategy. As of December 31, ~~2022~~ **2023** , we owned, co- owned or licensed **16** ~~30 issued~~ U. S. ~~patents and approximately 18 pending U. S. patent applications, including provisional and non- provisional filings. We also owned, co- owned or licensed approximately 363 pending and granted counterpart applications worldwide, including 11 country- specific validations of three European patents. As of December 31, 2022, we owned four issued U. S. patents and six pending U. S. non- provisional patent applications related to XEN1101, and methods of making and using XEN1101 and certain related compounds. Upon issuance, the patents are expected to expire between 2028 and 2042 (absent any extensions of term). In addition, we have approximately 15 foreign~~ issued patents **and 56 patents in foreign jurisdictions** (exclusive of European patent national validations), ~~two~~ **and over 370** pending **patent** ~~PCT international~~ applications **. With regard to XEN1101** , ~~and approximately~~ **as of December 31, 2023, we owned 4 U. S. issued patents,** ~~129~~ - **29** ~~pending applications~~ **issued patents** in ~~various~~ foreign jurisdictions ~~relating to XEN1101 and certain related compounds. As of December 31, 2022, we have filed one U. S. provisional patent application directed to certain of our potassium channel modulators~~ (exclusive of ~~XEN1101~~ **European patent national validations**) ~~, as well as methods of making~~ and **over 200 pending** ~~using the same. Any patents issuing from this application are expected to expire in 2043 (absent any extension in term). As of December 31, 2022, we have filed one U. S. non- provisional~~ patent ~~application and approximately 32 pending~~ applications ~~in various jurisdictions directed to XEN496 (i. e., our pediatric formulation of ezogabine), a genus of related formulations, and methods of making and using the same. Any patents issuing from this application are expected to expire in 2040 (absent any extensions of term). As of December 31, 2022, we owned four issued U. S. patents, one pending U. S. non- provisional patent application, and one U. S. provisional patent application directed to NBI- 921352 (formerly known as XEN901) and methods of making and using this and certain related compounds~~ . The issued patents, along with any patents issuing from these applications, are expected to expire between ~~2037 and 2042~~ - **2028 and 2044** (absent any extensions of term). ~~In addition~~ **With regard to NBI- 921352 (formerly known as XEN901), as of December 31, 2023** , we owned ~~approximately nine foreign~~ **or co- owned 4 U. S.** issued patents **, 12 issued patents in foreign jurisdictions** (exclusive of European patent national validations), ~~two~~ **and over 18** pending ~~PCT international applications, and we have approximately 17 pending corresponding applications in various foreign jurisdictions relating to NBI- 921352 and certain related compounds. Pursuant to our collaboration with Neurocrine Biosciences, Neurocrine Biosciences will oversee the prosecution, maintenance and other matters relating to the patent portfolio for NBI- 921352 and the other selective Nav1. 6 inhibitors and dual Nav1. 2 / 1. 6 inhibitors. As of December 31, 2022, we owned five issued U. S. patents, and two U. S. non- provisional~~ patent applications ~~directed to certain of our selective inhibitors of Nav1. 6 and / or Nav1. 2 (exclusive of NBI- 921352), as well as methods of making and using the same~~ . The issued patents, along with any patents issuing from these applications **, are expected to expire between 2037 and 2044 (absent any extensions of term). With regard to our selective inhibitors of Nav1. 6 and / or Nav1. 2 (exclusive of NBI- 921352), as of December 31, 2023, we owned 6 U. S. issued patents, 15 issued patents in foreign jurisdictions (exclusive of European patent national validations), and over 90 pending patent applications. The issued patents, along with any patents issuing from these applications,** are expected to expire between 2037 and 2039 (absent any extensions of term). ~~In addition~~ **Pursuant to our collaboration with Neurocrine Biosciences, Neurocrine Biosciences controls the prosecution, maintenance and other matters relating to the patent portfolio for NBI- 921352 and the other selective Nav1. 6 inhibitors and dual Nav1. 2 / 1. 6 inhibitors, although we have a right to comment. With regard to our development programs, including targets related to Kv7 (exclusive of XEN1101), Nav1. 1 and Nav1. 7, as of December 31, 2023** , we owned ~~approximately seven foreign~~ **1 U. S. issued patent and over 20 pending patent applications. The** issued patents ~~and approximately 97 pending corresponding~~ **,**

along with any patents issuing from these applications ~~in various foreign jurisdictions (exclusive of European patent national validations) relating to our selective inhibitors of Nav1. 6 and / or Nav1. 2 (exclusive of NBI- 921352) .~~ **are** ~~as well as methods of making and using the same. As of December 31, 2022, we co- owned one issued U. S. patent directed to Nav1. 7 inhibitors, as well as methods of making and using the same. The issued patent is~~ expected to expire ~~in~~ **between** 2036 **and 2044** (absent any extensions of term). Competition The biotechnology and pharmaceutical industries are highly competitive and are characterized by rapidly advancing technologies and a strong emphasis on proprietary products. While we believe that our technology, development experience, scientific knowledge and drug discovery approach provide us with certain advantages, we face potential competition in our discovery and product **candidate** development efforts from many different approaches and sources, including pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions. Any product candidates or products that we, or our collaborators, successfully develop and commercialize will compete with existing products and new products that may become available in the future. Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, pre- clinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we, or our collaborators, do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early- stage companies may also prove to be significant competitors, particularly through collaboration arrangements with large and established companies. Our commercial opportunities could be reduced or eliminated if our competitors develop and commercialize products or therapies that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA, European Medicines Agency, or EMA, or other foreign regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third- party payers. Aside from the product marketplace, our competitors also compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites, recruiting patients for clinical trials, and by acquiring technologies complementary to, or necessary for, our programs. The key competitive factors affecting the success of all of our product candidates, if approved, are likely to be their efficacy, safety, convenience, price, the effectiveness of alternative products, the level of competition and the availability of coverage, and adequate reimbursement from government and other third- party payers. Our product candidates that are in clinical development may compete with various therapies and drugs, both in the marketplace and currently under development. ~~ASMs for the Treatment of Epilepsy~~ If one or more of our proprietary or partnered ~~products~~ **product candidates** were approved for the treatment of epilepsy, we anticipate that they could potentially compete with other ASMs or one another. **These** ~~Currently~~ **currently commonly** prescribed ASMs, among others, include ~~phenytoin, levetiracetam,~~ brivaracetam, carbamazepine, cenobamate, clobazam ~~, lamotrigine, valproate, oxcarbazepine, topiramate, lacosamide, ethosuximide, perampanel, cannabidiol~~ , eslicarbazepine acetate, **ethosuximide,** gabapentin **, lacosamide, lamotrigine, levetiracetam, oxcarbazepine, perampanel, phenytoin, topiramate,** and **valproate** ~~fenfluramine. The FDA has not yet approved any drug products specifically for KCNQ2- DEE or for SCN8A- DEE~~ . There are other ASMs in ~~clinical~~ development that could potentially compete with our products, including ~~products~~ **product candidates** in development from ~~Angelini Pharma,~~ Biohaven Ltd **.** , Cerevel Therapeutics Holdings, Inc., ~~Eliem~~ **Equilibre Biopharmaceuticals Corp., Johnson & Johnson Innovative Medicine, Neurona** Therapeutics ~~,~~ Inc. ~~, Eisai Co., Ltd., Epygenix Therapeutics, Inc., Janssen Pharmaceuticals, Inc., Jazz Pharmaceuticals plc, Longboard Pharmaceuticals Inc., Marinus Pharmaceuticals, Inc., Neurocrine Biosciences~~ , Praxis Precision Medicines, Inc., ~~QurAlis Corporation~~ **Rapport Therapeutics, Inc.** , SK Life Science Inc., ~~Stoke~~ **Supernus Pharmaceuticals, Inc., and Zhimeng Biopharma, Inc. If one or more of our proprietary product candidates were approved for the treatment of MDD, we anticipate that they could potentially compete with other anti- depressant medications, or ADs. Patients with MDD are typically treated with a variety of ADs, which include selective serotonin reuptake inhibitors, or SSRIs, benzodiazepines, serotonin / norepinephrine reuptake inhibitors, or SNRIs, norepinephrine and dopamine reuptake inhibitors, or NDRIs, N- methyl- D- aspartate, or NMDA, receptor agonists and atypical antipsychotics. Currently prescribed antidepressants include benzodiazepines, brexpiprazole, bupropion, bupropion / dextromethorphan, cariprazine, citalopram, duloxetine, escitalopram, esketamine, fluoxetine, ketamine, sertraline, trazodone, tricyclic agents, venlafaxine, vilazodone and vortioxetine. We are aware of several companies developing product candidates for the treatment of MDD including AbbVie Inc., Biohaven Ltd., Intra- Cellular Therapies, Inc., Johnson & Johnson Innovative Medicine, Neumora** Therapeutics **,** Inc., **Relmada Therapeutics** ~~Takeda Pharmaceutical Company Ltd.~~ , **Inc., Sage Therapeutics, Inc.** and ~~UCB~~ **Sumitomo Pharma America** , Inc. Government Regulation We are developing small- molecule product candidates, which are regulated as drugs by the FDA and equivalent regulatory authorities outside the U. S. Within the FDA, the Center for Drug Evaluation and Research, or CDER, regulates drugs. Drugs are subject to regulation under the Federal Food, Drug, and Cosmetic Act, or FD & C Act, and other federal, provincial, state, local and foreign statutes and regulations. The FD & C Act and corresponding regulations govern, among other things, the testing, manufacturing, safety, efficacy, labeling, packaging, storage, record keeping, distribution, import, export, reporting, advertising and other promotional practices involving drugs. FDA approval of an **investigational new drug application, or** IND ~~application~~ **,** must be obtained before clinical testing of drugs is initiated, and each clinical study protocol for such product candidates is reviewed by the FDA and **an institutional review board, or** IRB **,** prior to initiation in the U. S. FDA approval also must be obtained before marketing of drugs in the U. S. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, provincial, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources **,** and we may not be able to obtain the required regulatory approvals ~~possible civil or criminal sanctions~~ .Failure to comply with the applicable U.S. **regulatory** requirements at any time during the

product development process,approval process or after approval ~~,~~may subject an applicant **and /** or ~~manufacturer~~ **sponsor** to **a variety of** administrative or judicial ~~civil or criminal~~ sanctions ~~and adverse publicity~~ . ~~FDA~~ **These** sanctions could include **,among other actions,FDA' s** refusal to approve pending applications,withdrawal of an approval, **imposition of a** clinical hold, **issuance of** warning or untitled **letters and other types of enforcement- related** letters,product recalls,product seizures **,relabeling or repackaging** ,total or partial suspension of production or distribution,injunctions,fines,refusals of government contracts, ~~mandated corrective advertising or communications with doctors,debarment,~~ restitution,disgorgement of profits,or civil or criminal **investigations and** penalties ~~.Any agency~~ **brought by FDA and the Department of Justice** or ~~judicial enforcement action could have a material adverse effect on us.Drug manufacturers and~~ other **governmental** entities ~~involved in~~ . U. S. Drug Development Process The process required by the FDA before a drug product may be marketed in the U. S. generally involves the following: • completion of nonclinical laboratory tests and animal studies according to **good laboratory practices, or** GLPs **,** and applicable requirements for the humane use of laboratory animals ~~or~~ **and** other applicable regulations; • submission to the FDA of an application for an IND, which must become effective before human clinical studies may begin; • performance of adequate and well- controlled human clinical studies according to the FDA' s regulations commonly referred to as good clinical practices, or GCPs, and any additional requirements for the protection of human research subjects and their health information, to establish the safety and efficacy of the proposed product for its intended use; • submission to the FDA of an NDA for drug products for marketing approval that includes substantial evidence of safety and efficacy **, which is usually** based on large **-** scale ~~phase~~ **Phase** 3 clinical studies; • satisfactory completion of an FDA **pre- approval** inspection of the manufacturing facility or facilities where the product is produced to assess compliance with good manufacturing practices, or GMP, to assure that the facilities, methods and controls are adequate to consistently manufacture the product pursuant to regulatory requirements; • potential FDA ~~audit~~ **inspection** of the nonclinical and clinical study sites that generated the data in support of the NDA; and • **payment of applicable user fees and** FDA review and approval of the NDA **. The data required to support an NDA is generated in two distinct development stages: pre- clinical and clinical. For new chemical entities, the pre- clinical development stage generally involves synthesizing the active component, developing the formulation and determining the manufacturing process, evaluating purity and stability, as well as carrying out non- human toxicology, pharmacology and drug metabolism studies in the laboratory, which support subsequent clinical testing. The conduct of the pre- clinical tests must comply with federal regulations, including GLPs and the U. S. Department of Agriculture' s Animal Welfare Act. The sponsor must submit the results of the pre- clinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. An IND is a request for authorization from the FDA to administer an investigational drug product to humans. The central focus of an IND submission is on the general investigational plan and the protocol (s) for human trials. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA raises concerns or questions regarding the proposed clinical trials and places the IND on clinical hold within that 30- day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns or questions before the clinical trial can begin. Some long- term pre- clinical testing, such as animal tests of reproductive AEs and carcinogenicity, may continue after the IND is submitted. The FDA may also impose clinical holds on a drug candidate at any time before or during clinical trials due to safety concerns or non- compliance. Accordingly, submission of an IND does not guarantee the FDA will allow clinical trials to begin, or that, once begun, issues will not arise that could cause the trial to be suspended or terminated. If the FDA accepts the IND, the drug can then be studied in human clinical trials to determine if the drug is safe and effective. The clinical stage of development involves the administration of the drug product to human subjects, including patients, under the supervision of qualified investigators in accordance with GCPs, which establish standards for conducting, recording data from, and reporting the results of clinical trials, and also include the requirement that all research subjects provide their informed consent in writing for their participation in any clinical trial** . Human clinical studies are typically conducted in three sequential phases that may overlap or be combined: • Phase 1. The drug is initially introduced into healthy human subjects and tested for safety. In the case of some products for severe or life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients that have the condition or disease being studied. • Phase 2. The drug is evaluated in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine a dose range and dosing schedule. • Phase 3. Clinical studies are undertaken to further evaluate dosing and dosing schedule, clinical efficacy, and safety in an expanded patient population at geographically dispersed clinical study sites. These clinical studies are intended to establish the overall risk / benefit ratio of the product and provide an adequate basis for product labeling. Post- approval clinical studies, sometimes referred to as Phase 4 clinical studies, may be conducted after initial marketing approval. These clinical studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication, particularly for long- term safety follow- up. **In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA.** During all phases of clinical development, regulatory agencies require extensive monitoring and auditing of all clinical activities, clinical data ~~,~~and clinical study investigators. Concurrent with clinical studies, companies usually complete additional animal studies and must also develop additional information about the physical characteristics of the drug as well as finalize a process for manufacturing the product in commercial quantities in accordance with GMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other requirements, the sponsor must develop methods for ensuring the quality, identity, strength ~~,~~and purity of the final drug. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug ~~candidate~~ does not undergo unacceptable deterioration over its labeled shelf life. Further, **due to disasters and public health emergencies** ~~as a result of the COVID- 19 pandemic~~ , we may be required to develop and implement additional clinical

trial policies and procedures designed to help protect subjects ~~from the COVID- 19 virus~~ . For example, the FDA has issued guidance on conducting clinical trials during ~~the pandemic~~ **major disruptions due to disasters and public health emergencies** , which describes a number of considerations for sponsors of clinical trials impacted by ~~the~~ **these** ~~pandemic~~ **events** , ~~including certain reporting requirements, and additional guidance on the good manufacturing practice considerations for responding~~ to **ensure** ~~COVID- 19 infection and other~~ -- **the** ~~topics~~ **safety of trial participants, maintaining GCP compliance, and minimizing risks to trial integrity** . We may be required to make further adjustments to our clinical trials or business operations based on current or future guidance and regulatory requirements as a result of ~~the COVID- 19 pandemic~~ **major disruptions due to disasters and public health emergencies** . U. S. Review and Approval Processes After the completion of clinical studies of a drug, FDA approval of an NDA must be obtained before commercial marketing of the drug **can begin** . The NDA must include results of product development, laboratory and animal studies, human studies, information on the manufacture and composition of the product, proposed labeling and other relevant information. In addition, under the Pediatric Research Equity Act, or PREA, an NDA or supplement to an NDA must contain data to assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers. Unless otherwise required by regulation, PREA does not apply to any drug for an indication for which orphan designation has been granted. The testing and approval processes require substantial time and effort **,** and there can be no assurance that the FDA will accept the NDA for filing and, even if filed, that any approval will be granted on a timely basis, if at all. Under the Prescription Drug User Fee Act, or PDUFA, as amended, each NDA must be accompanied by a substantial user fee. PDUFA also imposes an annual product fee for drugs and an annual establishment fee on facilities used to manufacture prescription drugs. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business. Additionally, no user fees are assessed on NDAs for products designated as orphan drugs, unless the product also includes a non- orphan indication. Within 60 days following submission of the application, the FDA reviews the NDA to determine if it is substantially complete before the agency accepts it for filing. The FDA may refuse to file any marketing application that it deems incomplete or not properly reviewable at the time of submission and may request additional information, including additional clinical data. In this event, the NDA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in- depth substantive review of the NDA. The FDA reviews the application to determine, among other things, whether the proposed product is safe and effective for its intended use, and whether the product is being manufactured in accordance with GMPs. The FDA may refer applications for novel products or products that present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. During the product approval process, the FDA also will determine whether a Risk Evaluation and Mitigation Strategy, or REMS, is necessary to assure the safe use of the product. If the FDA concludes a REMS is needed, the sponsor of the NDA must submit a proposed REMS; the FDA will not approve the application without a REMS, if required. Notwithstanding the submission of relevant data and information, the FDA may ultimately decide that the NDA does not satisfy its regulatory criteria for approval and deny approval. Data obtained from clinical studies are not always conclusive and the FDA may interpret data differently than we interpret the same data. If the agency decides not to approve the marketing application, the FDA will issue a ~~Complete~~ **complete** ~~Response~~ **response** letter ~~that usually~~ **, which typically** describes all of the specific deficiencies in the application identified by the FDA. The deficiencies identified may be minor ~~, for example~~ **(e. g.** , requiring labeling changes ~~,~~ **)** or major ~~, for example~~ **(e. g.** , requiring additional clinical studies **)** . Additionally, the ~~Complete~~ **complete** ~~Response~~ **response** letter may include recommended actions that the applicant might take to place the application in a condition for approval. If a ~~Complete~~ **complete** ~~Response~~ **response** letter is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, or withdraw the application. If a product receives regulatory approval, the approval will be limited to the specific diseases and dosages studied in clinical trials ~~or~~ **, and** the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling. The FDA may impose restrictions and conditions on product distribution, prescribing ~~,~~ or dispensing pursuant to a REMS request, or otherwise limit the scope of any approval **. Drug approvals may be withdrawn for non- compliance with regulatory standards or if problems occur following initial marketing** . One of the performance goals agreed to by the FDA under the PDUFA is to complete its review of 90 % of standard new molecular entity, or NME, NDAs within ten months from the filing date and 90 % of priority NME NDAs within six months from the filing date, whereupon a review decision is to be made. The FDA does not always meet its PDUFA goal dates **,** and its review goals are subject to change from time to time. The review process and the PDUFA goal date may be extended by three months if **, within the last three months before the PDUFA goal date,** the FDA requests **(** or the application sponsor otherwise provides ~~),or a new analysis or major reanalysis of studies previously submitted to the pending application~~ .Post- Approval Requirements Rigorous and extensive FDA regulation of drug continues after approval,particularly with respect to GMP.We will rely,and expect to continue to rely,on third parties for the production of clinical and commercial quantities of any products that we may commercialize.Manufacturers of our products **are** ~~will be~~ required to comply with applicable requirements in the GMP regulations,including quality control and quality assurance and maintenance of records and documentation.Other post- approval requirements applicable to drug manufacturers,include reporting of GMP deviations that may affect the safety,efficacy or quality of a distributed product,record- keeping requirements,reporting of adverse effects,reporting updated safety and efficacy information,and complying with electronic record and signature requirements.We also must comply with the FDA' s advertising and promotion requirements,such as those related to direct- to- consumer

advertising,the prohibition on promoting products for uses or in patient populations that are not described in or are otherwise inconsistent with the product' s approved labeling (known as " off- label use "),and industry- sponsored scientific and educational activities.Discovery of previously unknown problems or the failure to comply with the applicable regulatory requirements may result in restrictions on the marketing of a product or withdrawal of the product from the market as well as possible civil or criminal sanctions.Failure to comply with the applicable U.S.requirements at any time during the product development process,approval process or after approval,may subject an applicant or manufacturer to administrative or judicial civil or criminal sanctions and adverse publicity.FDA sanctions could include refusal to approve pending applications,withdrawal of an approval,clinical hold,warning or untitled letters,product recalls,product seizures,total or partial suspension of production or distribution,injunctions,fines,refusals of government contracts,mandated corrective advertising or communications with doctors,debarment,restitution,disgorgement of profits,or civil or criminal penalties. ~~An~~ **Any** agency or judicial enforcement action could have a material adverse effect on us.Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies,and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with GMPs and other laws.Accordingly,manufacturers must continue to expend time,money,and effort in the area of production and quality control to maintain GMP compliance.Discovery of problems with a product after approval may result in restrictions on a product,manufacturer **,** or holder of an approved NDA,including withdrawal of the product from the market.In addition,changes to the manufacturing process or facility generally require prior FDA approval before being implemented and other types of changes to the approved product,such as **adding new indications and additional labeling claims,are also subject to further FDA review and approval** additional **labeling claims, are also subject to further FDA review and approval** ~~information or clarification regarding information already provided in the submission within the last three months before the PDUFA goal date~~ . Fast Track Designation **, Priority Review, Breakthrough Therapy Designation and Accelerated Approval** The FDA has various programs, including ~~Fast~~ **fast** ~~Track~~ **track designation, priority review, breakthrough therapy designation and accelerated approval** , which are intended to expedite **or simplify** the process for the development and **FDA** review of drugs. Even if a drug qualifies for one or more of these programs, the FDA may later decide that the drug no longer meets the conditions for qualification. Generally, drugs that are eligible for these programs are those for serious or life- threatening conditions, those with the potential to address unmet medical needs ~~,~~ and those that offer meaningful benefits over existing treatments. ~~For example~~ **While these pathways can reduce the time it takes for the FDA to review an NDA** , **they do not guarantee that a product will receive FDA approval. To be eligible for a** ~~Fast~~ **fast** ~~Track~~ **track designation, the FDA must determine, based on the request of a sponsor, that a drug** is **intended to treat** a ~~process~~ **serious or life threatening disease or condition for which there is no effective treatment and demonstrates the potential to address an unmet medical need for the disease or condition. Under the fast track program, the sponsor of a drug candidate may request the FDA to** ~~designed~~ **designate the product for a specific indication as a fast track product concurrent with or after the filing of the IND for the drug candidate. The FDA must make a fast track designation determination within 60 days after receipt of the sponsor' s request. In addition** to ~~expedite~~ **other benefits, such as the ability to use surrogate endpoints and have greater interactions with the FDA, the FDA may initiate review of sections of a fast track product' s NDA before the application is complete. This rolling review is available if the applicant provides, and the FDA approves, a schedule for the submission of the remaining information and the applicant pays applicable user fees. However,** the FDA' s **time period goal for reviewing a fast track application does not begin until the last section of the NDA is submitted. A fast track drug also may be eligible for accelerated approval and priority** review ~~of drugs~~ **. In addition, the fast track designation may be withdrawn by the FDA if it believes** that ~~treat serious or life- threatening diseases or conditions and fill unmet medical needs. Under~~ the ~~Fast Track~~ **designation is no longer supported by data emerging in the clinical trial** process ~~,~~ **. The FDA may give a priority review designation to** drugs that offer major advances in treatment **,** or provide a treatment where no adequate therapy exists **. A** ~~, may also receive~~ priority review ~~by~~ **means that the goal for** the FDA **to** ~~, or~~ review ~~within~~ **an application is** six months ~~of~~ **, rather than** the **standard** ~~filing of an NDA compared to a traditional~~ review ~~time~~ of ten months **under current PDUFA guidelines** . ~~Although~~ **These six- and ten- month review periods are measured from the " filing " date rather than the receipt date for NDAs for new molecular entities, which typically adds approximately two months to the timeline for review and decision from the date of submission. Most products that are eligible for** ~~Fast~~ **fast** ~~Track~~ **track** ~~and~~ **designation are also likely to be considered appropriate to receive a** priority review **. Under** ~~do not affect~~ the ~~standards~~ **provisions of the new Food and Drug Administration Safety and Innovation Act,** ~~for~~ **or** ~~approval~~ **FDASIA, enacted by Congress in 2012, a sponsor can request designation** of a drug **candidate as** ~~, and may not result in~~ a ~~faster approval~~ **" breakthrough therapy** , **" typically by** ~~if approval is granted, for Fast Track designated drugs,~~ the **end** ~~FDA will also attempt to facilitate early and frequent meetings with a sponsor~~ of **the** ~~a Fast Track designated drug, to expedite such~~ drug' s **Phase II trials. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life- threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Drugs designated as breakthrough therapies are also eligible for accelerated approval. For breakthrough therapies, the FDA may take certain actions, such as intensive and early guidance on the drug development program, that are intended to expedite the development and** review **of** ~~and~~ **an application for approval. FDASIA also codified and expanded on FDA' s accelerated approval regulations, under which FDA may approve a drug for a serious or life threatening illness that provides meaningful therapeutic benefit over existing treatments based on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on an intermediate clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit.**

A surrogate endpoint is a marker that does not itself measure clinical benefit but is believed to predict clinical benefit. This determination takes into account the severity, rarity or prevalence of the disease or condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require a sponsor of a drug receiving accelerated approval to perform Phase IV or post marketing studies to verify and describe the predicted effect on irreversible morbidity or mortality or other clinical endpoint, and the drug may be subject to accelerated withdrawal procedures. All promotional materials for drug candidates approved under accelerated regulations are subject to prior review by the FDA. Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for the FDA review or approval will not be shortened. Furthermore, fast track designation, priority review, accelerated approval and breakthrough therapy designation, do not change the standards for approval and may not ultimately expedite the development **or approval process** . Orphan Drug Designation Under the Orphan Drug Act, the FDA may grant orphan designation to a drug intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200, 000 individuals in the U. S., or more than 200, 000 individuals in the U. S. and for which there is no reasonable expectation that the cost of developing and making a drug available in the U. S. for this type of disease or condition will be recovered from sales of the product. ~~We have received orphan~~ **Orphan** drug ~~designation from the FDA for XEN496 (active ingredient ezogabine), a drug we are evaluating in a Phase 3 clinical trial for the treatment of KCNQ2- DEE. Orphan product~~ designation must be requested before submitting an NDA. After the FDA grants orphan ~~product~~ **drug** designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan ~~product~~ **drug** designation does not convey any advantage in or shorten the duration of the regulatory review and approval process. Orphan drug products may also be eligible for **rare pediatric disease, or** RPD **,** designation if greater than 50 % of patients living with the disease are under age 19 and the condition affects fewer than 200, 000 individuals in the U. S. A priority review voucher will be given to the sponsor of a product with an RPD designation at the time of product approval that ~~is~~ **can be redeemed to receive a priority review of a subsequent marketing application for a different product. Such vouchers are** transferable to another company. If a product **candidate** that has orphan designation subsequently receives the first FDA approval for such drug for the disease or condition for which it has such designation, the product is entitled to orphan ~~product~~ **drug** exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity. Competitors, however, may receive approval of different products for the same indication for which the orphan ~~product~~ **drug** has exclusivity or obtain approval for the same product but for a different indication for which the orphan ~~product~~ **drug** has exclusivity. Orphan ~~product~~ **drug** exclusivity also could block the approval of one of our ~~products~~ **product candidates** for seven years if a competitor obtains approval of the same product for the same orphan indication as defined by the FDA, or if our product candidate is determined to be contained within the competitor' s product for the same orphan indication or disease. If a ~~drug~~ **product candidate** designated as an orphan ~~product~~ **drug** receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan ~~product~~ **drug** exclusivity. Orphan drug status in the EU has similar, but not identical, benefits, including up to ten years of exclusivity. In Catalyst Pharms., Inc. v. Becerra, 14 F. 4th 1299 (11th Cir. 2021), the court disagreed with the FDA' s longstanding position that the orphan drug exclusivity only applies to the approved use or indication within an eligible disease, and not to all uses or indications within the entire disease or condition. In particular, the circuit court held that the orphan ~~–~~drug exclusivity for Catalyst' s drug blocked the FDA' s approval of another drug for all uses or indications within the same orphan- designated disease, ~~or~~ Lambert- Eaton myasthenic syndrome (LEMS), even though Catalyst' s drug was approved at that time only for use in the treatment of LEMS in adults. Accordingly, the court ordered the FDA to set aside the approval of a drug indicated for LEMS in children. This decision created uncertainty in the application of ~~the~~ orphan drug exclusivity. On January 24, 2023, the FDA published a notice in the Federal Register to clarify that while the agency ~~complies~~ **complied** with the court' s order in Catalyst, the FDA intends to continue to apply its longstanding interpretation of the regulations to matters outside of the scope of the Catalyst order – that is, the agency will continue tying the scope of orphan ~~–~~drug exclusivity to the uses or indications for which a drug is approved, which permits other sponsors to obtain approval of a drug for new uses or indications within the same orphan **-** designated disease or condition that have not yet been approved. It is unclear how future litigation, legislation, agency decisions ~~,~~and administrative actions will impact the scope of ~~the~~ orphan drug exclusivity . Post- Approval Requirements Rigorous and..... subject to further FDA review and approval . Controlled Substance Regulation The United States Controlled Substances Act, or CSA, establishes registration, security, recordkeeping, reporting, storage, distribution and other requirements administered by the Drug Enforcement Administration, or DEA. The DEA is concerned with the control of handlers of controlled substances, and with the equipment and raw materials used in their manufacture and packaging, in order to prevent loss and diversion into illicit channels of commerce. The DEA regulates controlled substances as Schedule I, II, III, IV or V substances. Schedule I substances by definition have a high potential for abuse, have no established medicinal use, and may not be marketed or sold in the U. S. ~~–~~A pharmaceutical product may be listed as Schedule II, III, IV or V, with Schedule II substances considered to present the highest risk of abuse and Schedule V substances the lowest relative risk of abuse among such substances. Annual registration is required for any facility that manufactures, distributes, dispenses, imports or exports any controlled substance. The registration is specific to the particular location, activity and controlled substance schedule. For example, separate registrations are needed for import and manufacturing, and each registration will specify which schedules of controlled substances are authorized. The DEA typically inspects a facility to review its security measures prior to issuing a registration. Security requirements vary by controlled substance schedule, with the most stringent requirements applying to Schedule I and Schedule II substances. Required security measures include background checks on employees and physical control of inventory through measures such as cages, surveillance cameras and inventory reconciliations. Records must be maintained for the handling of all controlled substances, and periodic reports made to the DEA. Reports must also be made for

thefts or losses of any controlled substance, and to obtain authorization to destroy any controlled substance. In addition, special authorization and notification requirements apply to imports and exports. The DEA conducts periodic inspections of certain registered establishments that handle controlled substances. Failure to maintain compliance with applicable requirements, particularly as manifested in loss or diversion, can result in enforcement action that could have a material adverse effect on our business, results of operations and financial condition. The DEA may seek civil penalties, refuse to renew necessary registrations, or initiate proceedings to restrict, suspend or revoke those registrations. In certain circumstances, violations could result in criminal proceedings. Individual states also regulate controlled substances, and we and our contract manufacturers will be subject to state regulation on distribution of these products, including licensing, recordkeeping and security. Controlled substances are also regulated pursuant to several international drug control treaties. These treaties are enforced by the United National Commission on Narcotic Drugs. The U. S. is a signatory to these treaties and thus must conform its laws and regulations to the international requirements, which generally include licensing, recordkeeping and reporting requirements. Any change in the international treaties regarding classification of these products could affect regulation of these substances in the U. S. and in other countries. Further, marketing approval and controlled substance classification procedures vary among countries, can involve additional testing and administrative review periods ~~,~~ and may be otherwise complicated if our product candidates contain ingredients already classified as controlled substances in the countries where we develop them, which could make such product candidates subject to applicable controlled substances laws prior to commercialization. Foreign regulation of controlled substances can differ significantly from U. S. DEA and state regulations. The time required to obtain marketing approval and controlled substance classification in other countries may differ from and be longer than that required to obtain FDA approval and DEA classification in the U. S. U. S. Patent Term ~~Restoration~~ **Extension** and Marketing Exclusivity Depending upon the timing, duration and specifics of the FDA approval of the use of our product candidates, some of our U. S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch- Waxman ~~Amendments~~ **Act** . The Hatch- Waxman ~~Amendments~~ **Act** ~~permit~~ **permits** a patent ~~restoration~~ term **extension** of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. ~~However, patent~~ **Patent** term ~~restoration~~ **extension** cannot extend the remaining term of a patent beyond a total of 14 years from the product' s approval date. Only one patent applicable to an approved product is eligible for ~~the~~ extension and the application for the **patent term** extension must be submitted **within 60 days** ~~prior to the expiration~~ of ~~the patent~~ **receipt of FDA approval** . The U. S. Patent and Trademark Office, in consultation with the FDA, reviews and approves the application for any patent term extension ~~or restoration~~ . Under the Hatch- Waxman ~~Amendments~~ **Act** , a drug product containing a new chemical entity as its active ingredient is entitled to five years of market exclusivity **. A drug product is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety** , **which is defined as the molecule or ion responsible for the activity of the drug substance, excluding those appended portions of the molecule that cause the drug to be** ~~and~~ - **an ester, salt, or other noncovalent derivative. During this exclusivity period, the FDA may not approve an abbreviated new drug application, or ANDA, or** a **505 (b) (2) NDA submitted by another company that contains the previously approved active moiety. However, an ANDA or 505 (b) (2) NDA may be submitted after four years if it contains a certification of patent invalidity or non- infringement. A drug** product whose active ingredient was previously FDA **-** approved, and for which the sponsor is required to generate new clinical ~~data~~ **investigations such as to support new indications, dosages, strengths or dosage forms,** is entitled to three years of market exclusivity. **This three- year exclusivity covers only the conditions of use associated with the new clinical investigations and, as a general matter, does not prohibit the FDA from approving ANDAs or 505 (b) (2) NDAs for generic versions of the original unmodified drug product, although the approval of such an application may not be effective until, at the earliest, after the full five years of market exclusivity has expired.** A drug **product** can also obtain pediatric market exclusivity in the U. S. and, if granted, adds six months to existing **marketing** ~~exclusivity~~ **exclusivities** ~~periods~~ and **any Orange Book- listed** patent ~~terms~~ - **term (s)** . This six- month exclusivity, which runs from the end of other exclusivity ~~protection~~ **periods and /** or patent term **(s)** , may be granted based on the timely, voluntary, and as- agreed upon completion of a pediatric study in accordance with an FDA- issued " Written Request " for such a study **, even if the data do not show that the drug product was effective in the pediatric population studied** . Additional Regulation **Manufacturing, sales, promotion and other activities following drug approval are also subject to regulation by numerous regulatory authorities in addition to the FDA, including, in the United States, the Centers for Medicare & Medicaid Services, other divisions of the Department of Health and Human Services, the Drug Enforcement Administration for controlled substances, the Consumer Product Safety Commission, the Federal Trade Commission, the Occupational Safety & Health Administration, the Environmental Protection Agency and state and local governments. In the United States, the activities of pharmaceutical manufacturers are subject to federal and state laws designed to prevent " fraud and abuse " in the healthcare industry. The laws generally limit financial interactions between manufacturers and health care providers or other participants in the healthcare industry and / or require disclosure to the government and public of such interactions. Many of these laws and regulations contain ambiguous requirements or require administrative guidance for implementation. Pharmaceutical manufacturers are also required to provide discounts or rebates under government healthcare programs or to certain government and private purchasers in order to obtain coverage under federal healthcare programs such as Medicaid. Participation in such programs may require tracking and reporting of certain drug prices. Manufacturers are subject to fines and other penalties if such prices are not reported accurately. The handling of any controlled substances must comply with the U. S. Controlled Substances Act and Controlled Substances Import and Export Act. Drugs must meet applicable child- resistant packaging requirements under the U. S. Poison Prevention Packaging Act. Manufacturing, sales, promotion and other activities are also potentially subject to federal and state consumer protection and unfair competition laws. The failure to comply with regulatory requirements**

subjects manufacturers to possible legal or regulatory action. Depending on the circumstances, failure to meet applicable regulatory requirements can result in criminal prosecution, fines or other penalties, injunctions, recall or seizure of drugs, total or partial suspension of production, denial or withdrawal of product approvals, exclusion from participation in government healthcare programs or refusal to allow a firm to enter into supply contracts, including government contracts. In addition ~~to~~ **, even if a firm complies with FDA and** ~~the~~ **other** ~~foregoing~~ **requirements** , **new information** ~~provincial, state and federal U. S. and Canadian laws~~ regarding ~~environmental protection and hazardous substances~~ **the safety or efficacy of a product could lead the FDA to modify or withdraw product approval. Prohibitions or restrictions on sales or withdrawal of future products marketed by us could materially** affect our business **in** ~~. These and~~ **an** ~~other laws govern~~ **adverse way. Changes in regulations, statutes** ~~our~~ **or the interpretation** ~~use, handling and disposal~~ of **existing regulations could impact our business** ~~various biological, chemical and radioactive substances used~~ in **the future** ~~, and wastes generated~~ by **requiring** , **for example: (i) changes to our manufacturing arrangements; (ii) additions** ~~our~~ **or** ~~operations~~ **modifications to product labeling; (iii) the recall or discontinuation of our products; or (iv) additional record- keeping requirements** . If ~~our operations result in contamination of~~ **any such changes were to be imposed,** ~~the~~ **they** ~~environment or expose individuals to hazardous substances, we~~ could ~~be liable for damages and governmental fines. We believe that we are in material compliance with applicable environmental laws and that continued compliance therewith will not have a material adverse~~ **adversely** ~~effect~~ **affect** ~~on~~ **the operation of** our business ~~. We cannot predict, however, how changes in these laws may affect our future operations~~ . Global Anti- Corruption Laws The U. S. Foreign Corrupt Practices Act and the Canadian Corruption of Foreign Public Officials Act, the U. S. Travel Act, the OECD Anti- Bribery Convention, Title 18 United States Code section 201, and any other applicable domestic or foreign anti- corruption or anti- bribery laws to which we are subject prohibit corporations and individuals from engaging in certain activities to obtain or retain business or to influence a person working in an official capacity. It is illegal to pay, offer to pay or authorize the payment of anything of value to any foreign government official, government staff member, political party or political candidate in an attempt to obtain or retain business or to otherwise influence a person working in an official capacity. We may also be held liable for the acts of our third- party agents under the U. S. Foreign Corrupt Practices Act, Canadian Corruption of Foreign Public Officials Act, and other applicable anti- corruption and anti- bribery laws. Noncompliance with these laws could subject us to investigations, sanctions, settlements, prosecution, other enforcement actions, disgorgement of profits, significant fines, damages, other civil and criminal penalties or injunctions, suspension or debarment from contracting with certain persons, the loss of export privileges, whistleblower complaints, reputational harm, adverse media coverage ~~,~~ and other collateral consequences. Any investigations, actions or sanctions or other previously mentioned harm could have a material negative effect on our business, operating results and financial condition. Government Regulation Outside of the U. S. In addition to regulations in the U. S., we will be subject to a variety of regulations in other jurisdictions governing, among other things, research, development, testing, manufacture, quality control, controlled substances, approval, labeling, packaging, storage, record- keeping, promotion, advertising, distribution, post- approval monitoring and reporting, marketing and export and import of drugs, and reimbursement requirements. Generally, before a new drug can be marketed, considerable data demonstrating its quality, safety and efficacy must be obtained, organized into a format specific for each regulatory authority, submitted for review and approved by the regulatory authority. Whether or not we obtain FDA approval for a product **candidate** , we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical studies or marketing of the product **candidate** in those countries. Certain countries outside of the U. S. have a similar process that requires the submission of a clinical study application much like the IND prior to the commencement of human clinical studies. ~~In the EU, for example, a CTA must be submitted to each country' s national health authority and an independent ethics committee, much like the FDA and the IRB, respectively. Once the CTA is approved in accordance with a country' s requirements, clinical study development may proceed. Similar requirements regarding a CTA and ethics approval exist in Canada.~~ The requirements and ~~process~~ **processes** governing the conduct of clinical studies, product licensing, coverage, pricing and reimbursement vary from country to country. In all cases, the clinical studies are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki ~~. The EU clinical trials legislation currently is undergoing a transition process mainly aimed at harmonizing and streamlining clinical- trial authorization, simplifying adverse- event reporting procedures, improving the supervision of clinical trials and increasing their transparency~~ . The Clinical Trials Regulation EU No 536 / 2014, **or the CTR,** which replaced the Clinical Trials Directive, entered into application on January 31, 2022, ~~is intended to~~ **harmonizes the procedures for the submission, assessment and monitoring of clinical drug trials in the EU, thus** ~~simplify~~ **simplifying** the current rules for clinical trial authorization and standards of performance. ~~For instance,~~ **The CTR requires a clinical trial sponsor to obtain approval from** ~~there~~ **the national competent authority (NCA) of each** ~~will be a streamlined application procedure via a single- entry point, a~~ European Union **member state in which the clinical trial is to be conducted. Furthermore, the sponsor can only start a clinical trial at a specific study site after the local research ethics committee, or REC, has issued a favorable opinion. Subject to the transition arrangement referenced below, a sponsor submits a single application for a clinical trial authorization, or CTA, through a centralized EU clinical trials** portal **called the Clinical Trials Information System, or CTIS. One NCA (the reporting EU member state selected by the sponsor) takes the lead in validating and evaluating the application, as well as consulting and coordinating with the other concerned member states in which the clinical trial is to be conducted. If** ~~and~~ **an** ~~database~~ **application is rejected, it may be amended and resubmitted through CTIS. A concerned member state may in limited circumstances declare an " opt- out " from an approval and prevent the clinical trial from being conducted in that member state. The CTR foresees a three- year transition period. As of January 31, 2023, all new CTA applications had to be submitted via CTIS and be made pursuant to the CTR. From and after January 31, 2025, any trials approved under the Clinical Trial Directive (now replaced by the CTR) which are still ongoing will need to comply with the CTR**

and be recorded in CTIS. In the UK, clinical trials of medicinal products for human use are primarily governed by the Medicines for Human Use (Clinical Trials) Regulations 2004 (as amended). Similar to the EU, before a clinical trial can be initiated in the UK, a CTA must be obtained from the Medicines and Healthcare products Regulatory Agency, or MHRA, as well as a positive opinion from a REC . To obtain regulatory approval of an investigational drug under EU regulatory systems, we must submit a marketing authorization application, or MAA **. There are two types of marketing authorizations: • The centralized MA is issued by the European Commission through the centralized procedure, based on the opinion of the Committee for Medicinal Products for Human Use, or the CHMP, of the EMA, and is valid throughout the entire territory of the EEA. The centralized procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, advanced- therapy medicinal products (gene- therapy, somatic cell- therapy or tissue- engineered medicines) and medicinal products containing a new active substance indicated for the treatment of human immunodeficiency virus, acquired immunodeficiency syndrome, cancer, neurodegenerative disorders, diabetes, auto- immune and other immune dysfunctions and viral diseases. The centralized procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU. Under the centralized procedure, the maximum timeframe for the evaluation of a MA application by the EMA is 210 days, excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP. Clock stops may extend the timeframe of evaluation of a MA application considerably beyond 210 days. Where the CHMP gives a positive opinion, the EMA provides the opinion together with supporting documentation to the European Commission, who makes the final decision to grant a MA, which is ordinarily issued within 67 days of receipt of the EMA' s recommendation. Accelerated assessment might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of a major public health interest, particularly from the point of view of therapeutic innovation. The timeframe for the evaluation of a MA application under the accelerated assessment procedure is 150 days, excluding clock stops, but it is possible that the CHMP may revert to the standard time limit for the centralized procedure if it determines that the application is no longer appropriate to conduct an accelerated assessment. • National MAs, which are issued by the NCAs of the EEA member states and only cover their respective territory, are available for products not falling within the mandatory scope of the centralized procedure. Where a product has already been authorized for marketing in a member state of the EEA, this national MA can be progressively recognized in other EEA member states through the mutual recognition procedure. If the product has not received a national MA in any EEA member state at the time of application, it can be approved simultaneously in various EEA member states through the decentralized procedure. Under the decentralized procedure, an identical dossier is submitted to the NCAs of each of the EEA member states in which the MA is sought, one of which is selected by the applicant as the Reference Member State (the RMS). The competent authority of the RMS prepares a draft assessment report, a draft summary of the product characteristics (SmPC), and a draft of the labeling and package leaflet, which are sent to the other EEA member states, referred to as the Concerned Member States, for their approval. If the Concerned Member States raise no objections, based on a potential serious risk to public health, to the assessment, SmPC, labeling, or packaging proposed by the RMS, the product is subsequently granted a national MA in all EEA member states to which an application was submitted. In relation to the UK, until the end of 2024, under the Northern Ireland Protocol which is contained in the Agreement on the withdrawal of the United Kingdom of Great Britain and Northern Ireland from the European Union and the European Atomic Energy Community, centralized MAs continue to provide a valid basis for commercializing medicinal products in Northern Ireland. However, centralized MAs no longer provide a valid basis for the commercialization of medicinal products in Great Britain. Pursuant to the Windsor Framework (which is a political declaration by the European Commission and the UK Government to correct the post-Brexit restrictions of movements of goods including medicines), from January 1, 2025, all new medicinal products for the UK market will be authorized by the MHRA which will grant on behalf of the UK Licensing Authority a single UK-wide MA for all medicinal products intended for sale in the UK, enabling medicinal products to be sold in a single pack and under a single authorization throughout the UK, including Northern Ireland, but the UK packaging must carry a clearly legible ' UK only' to be allowed onto the UK market. Since leaving the EU, the MHRA has introduced changes to national licensing procedures, including procedures to prioritize access to new medicines that will benefit patients, an accelerated assessment procedure, and new routes of evaluation for novel products and biotechnological products. There is no wholesale recognition of EU pharmaceutical legislation between the jurisdictions, and EU MAs do not automatically provide a valid basis for the commercialization of medicinal products in Great Britain, From January 1, 2024, companies are able to request the MHRA to recognize MAs granted by acceptable Reference Regulators in foreign jurisdictions (including the EU) under a new International Recognition Procedure, or IRP. IRP allows the MHRA to take into account the expertise and decision- making of trusted regulatory authorities to conduct targeted assessments of IRP applications while retaining the authority to reject applications if the evidence provided is considered insufficiently robust** . The application used to file the NDA in the U. S. is similar to that required in the EU, with the exception of, among other things, country- specific document requirements. Reimbursement approval for the drug by regulatory authorities is also required before a drug may be commercialized. The EU also provides opportunities for **data and** market exclusivity. For example, in the EU, upon receiving marketing authorization, ~~new chemical entities generally~~ **innovative medicinal products (including both small molecules and biological medicinal products) approved on the basis of a complete independent data package consisting of quality, preclinical testing results, and clinical trial data** receive eight years of data exclusivity **upon grant of an MA,** and an additional two years of ~~market~~ **marketing** exclusivity. If granted, data exclusivity prevents **generic or biosimilar applicants** ~~regulatory authorities in the EU~~ from **cross-** referencing the innovator' s **preclinical and**

clinical trial data ~~to assess~~ **contained in the dossier of the reference medicinal product when applying for** a generic ~~application. During~~ **or biosimilar MA until** the **data exclusivity** ~~additional two- year~~ period ~~of market exclusivity,~~ **has expired. Even if** a generic ~~marketing authorization can be submitted,~~ and **a biosimilar** ~~the innovator' s data may be referenced, but no generic~~ product **is approved, it** can be marketed **only** until the expiration of the **full ten- year exclusivity period. The overall ten- year period can be extended to a maximum of 11 years if, during the first eight years of those ten years, the MA holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are determined to bring a significant clinical benefit in comparison with currently approved therapies. The UK domestic law follows the same formula of regulatory data and** ~~market~~ **marketing** exclusivity. However, there is no guarantee that a product will be considered by the EU' s regulatory authorities to be a new chemical entity **or new active substance** , and products may not qualify for data exclusivity. Products receiving orphan designation in the EU can receive ten years of market exclusivity, ~~during which~~ **provided that the orphan designation is maintained at the** time **of grant of the marketing authorization. During the ten- year orphan market exclusivity period,** no **application for a** similar medicinal product for the same indication may be ~~placed on~~ **accepted by any regulatory authority in** the ~~market~~ **EU for approval** . An orphan product can also obtain an additional two years of market exclusivity in the EU for **completing** pediatric studies **in compliance with an agreed Pediatric Investigation Plan even though the data do not lead to approval of a pediatric indication** . No extension to any supplementary protection certificate can be granted on the basis of pediatric studies for orphan indications. The criteria for designating an " orphan medicinal product " in the EU are similar in principle **but not identical** to those in the U. S. Under Article 3 of Regulation (EC) 141 / 2000, a medicinal product may be designated as orphan if (1) it is intended for the diagnosis, prevention or treatment of a life- threatening or chronically debilitating condition; (2) either (a) such condition affects no more than five in 10, 000 persons in the EU when the application is made, or (b) the product, without the benefits derived from orphan status, would not generate sufficient return in the EU to justify investment; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the EU, or if such a method exists, the product will be of significant benefit to those affected by the condition, as defined in Regulation (EC) 847 / 2000. **The criteria for orphan designation must be re- assessed and confirmed at the time when a marketing authorization is granted in order to benefit from a period of 10 years orphan market exclusivity. The MHRA conducts an equivalent assessment, against the criteria specific to the UK. In the EEA, orphan drug designation must be requested before submitting an application for MA. The EMA' s Committee for** Orphan **Medicinal Products (COMP) is required to re- assess the granted orphan designation at the time of MA grant to ensure that it continues to meet the criteria for the designation to be maintained. Otherwise, the orphan designation can be revoked. In contrast, the MHRA does not grant orphan designations during the development of the medicinal product. Instead, the MHRA will decide whether the criteria are satisfied at the point of grant of an MA. In the EEA and the UK, orphan** medicinal products are eligible for financial incentives such as reduction of fees or fee waivers and are, upon grant of a marketing authorization, entitled to ten years of market exclusivity for the approved therapeutic indication ~~. The application for orphan drug designation must be submitted before the application for marketing authorization~~ . The applicant will receive a fee reduction for the marketing authorization application if the orphan drug designation has been granted, but not if the designation is still pending at the time the marketing authorization is submitted. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. The 10- year market exclusivity may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan designation, for example, if the product is sufficiently profitable not to justify maintenance of market exclusivity. Additionally, marketing authorization may be granted to a similar **medicinal** product for the same **therapeutic** indication at any time if: • the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior; • the applicant consents to a second orphan medicinal product application; or • the applicant cannot supply enough orphan medicinal product **. A " similar medicinal product " is defined as a medicinal product containing a similar active substance or substances as contained in an authorized orphan medicinal product, and which is intended for the same therapeutic indication. In the EEA, companies developing a new medicinal product must agree upon a pediatric investigation plan (" PIP"), with the EMA' s Pediatric Committee (the" PDCO"), and must conduct pediatric clinical trials in accordance with that PIP, unless a waiver applies. The PIP sets out the timing and measures proposed to generate data to support a pediatric indication of the drug for which MA is being sought. The PDCO can grant a deferral of the obligation to implement some or all of the measures of the PIP until there are sufficient data to demonstrate the efficacy and safety of the product in adults. Further, the obligation to provide pediatric clinical trial data can be waived by the PDCO when this data is not needed or appropriate because the product is likely to be ineffective or unsafe in children, the disease or condition for which the product is intended occurs only in adult populations, or when the product does not represent a significant therapeutic benefit over existing treatments for pediatric patients. Products that are granted a MA with the results of the pediatric clinical trials conducted in accordance with the PIP (even where such results are negative) are eligible for six months' supplementary protection certificate extension (if any is in effect at the time of approval). In the case of orphan medicinal products, a two- year extension of the orphan market exclusivity may be available. This pediatric reward is subject to specific conditions and is not automatically available when data in compliance with the PIP are developed and submitted. According to local law requirements, the UK MHRA adopts a similar approach to the EEA to facilitate the development of medicinal products for the pediatric population** . For other countries outside of the EU, such as Canada and countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical studies, product and establishment licensing, coverage, data protection, pricing and reimbursement vary from country to country. In all cases, again, the clinical studies are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. If we fail to comply with applicable foreign regulatory requirements, we may be

subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, inability to import or export, seizure of products, operating restrictions and criminal prosecution. Pharmaceutical Coverage, Pricing and Reimbursement Significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which we obtain regulatory approval. In the U. S. and markets in other countries, sales of any products for which we receive regulatory approval for commercial sale will depend, in part, on the availability of coverage and adequate reimbursement from third- party payers. Third- party payers include government programs such as Medicare or Medicaid, **and private payers such as private health insurance and** managed care plans, ~~private health insurers,~~ and other organizations. These third- party payers may deny **or limit** coverage or reimbursement for a product **. Within the U. S., coverage and reimbursement** ~~or~~ **for** ~~therapy in whole or in~~ **drug products can differ significantly from payer to payer. One third-** ~~part~~ **party** ~~if they determine~~ **payer' s decision to cover a particular drug product or service does not ensure** that **other payers will also provide coverage for** the product or ~~therapy was not medically appropriate or necessary~~ **will provide coverage at an adequate reimbursement rate** . Third- party payers may attempt to control costs by limiting coverage **(e. g.,** to specific drug products on an approved list, or formulary, which might not include all of the FDA- approved drug products for a particular indication **)** , **by controlling utilization (e. g., requiring pre- approval or prior authorization for new or innovative drug therapies before they will provide coverage for specific patients)** and by limiting the amount of reimbursement for ~~particular procedures or drug~~ **drugs** ~~treatments~~ . The cost of pharmaceuticals continues to generate substantial governmental and third- party payer interest. We expect that the pharmaceutical industry will experience pricing pressures due to the trend toward managed healthcare, the increasing influence of managed care organizations and additional legislative proposals. Third- party payers are increasingly challenging the price and examining the medical necessity and cost- effectiveness of medical products and services, in addition to their safety and efficacy. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain the FDA approvals. Our product candidates may not be considered medically necessary or cost- effective. A payer' s decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Adequate third- party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development. ~~Some third- party payers also require pre- approval or prior authorization of coverage for new or innovative drug therapies before they will reimburse healthcare providers who prescribe such therapies or patients who use such prescription drugs.~~ While we cannot predict **what** ~~whether any proposed~~ cost- containment measures will be adopted or otherwise implemented in the future, ~~these requirements~~ **new measures** or any announcement ~~or adoption~~ of ~~such proposals~~ **proposed measures** could have a material adverse effect on our ability to obtain adequate prices for our product candidates and to operate profitably. In international markets, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. There can be no assurance that our products will be considered medically reasonable and necessary for a specific indication, that our products will be considered cost- effective by third- party payers, that coverage or an adequate level of reimbursement will be available or that the third- party payers' reimbursement policies will not adversely affect our ability to sell our products profitably. In addition, in many foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing and reimbursement vary widely from country to country. For example, the EU provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, products launched in the EU do not follow price structures of the U. S. and generally prices tend to be significantly lower. Healthcare Reform In the U. S. and foreign jurisdictions, there have been a number of legislative and regulatory changes to the healthcare system that could affect our future results of operations. In particular, there have been and continue to be a number of initiatives at the U. S. federal and state levels that seek to reduce healthcare costs **generally and drug costs specifically** . In the U. S., ~~the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or~~ **for example** ~~the Medicare Modernization Act, changed the way Medicare covers and pays for pharmaceutical products. The Medicare Modernization Act expanded Medicare coverage for drug purchases by the elderly by establishing Medicare Part D and introduced a new reimbursement methodology based on average sales prices for physician administered drugs under Medicare Part B. In addition, this legislation provided authority for limiting the number of drugs that will be covered in any therapeutic class under the new Medicare Part D program. Cost reduction initiatives and other provisions of this legislation could decrease the coverage and reimbursement rate that our customers receive for any of our approved products. While the Medicare Modernization Act applies only to drug benefits for Medicare beneficiaries, private payers often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the Medicare Modernization Act may result in a similar reduction in payments from private payers. Enacted in March 2010~~ , the Patient Protection and Affordable Care Act, as amended, or PPACA, is a sweeping law ~~intended to broaden access to~~ **enacted in March 2010 that expanded health care coverage through Medicaid expansion and the implementation of the individual mandate for** health insurance ~~, reduce or constrain the growth of healthcare spending, enhance remedies against healthcare fraud and abuse, add new transparency requirements for healthcare and health insurance industries, impose new taxes and fees on pharmaceutical and medical device manufacturers and impose additional health policy reforms. Among other things, PPACA revises the definition of " average~~ **coverage and** ~~manufacturer price " for reporting purposes,~~ which **included changes** ~~could increase the amount of Medicaid drug rebates~~ to ~~states. Further,~~ the **coverage and reimbursement of** ~~PPACA also imposes a significant annual fee on companies that manufacture or import branded prescription~~ drug products **under government healthcare programs** . ~~Since its enactment~~ **Beyond the PPACA** , there

~~remain judicial and Congressional challenges to certain aspects of the PPACA, and we expect there will be additional challenges and amendments to the PPACA in the future. Any changes to the PPACA~~ are ~~likely to~~ **ongoing and widespread health care reform efforts, a number of which** have **focused** ~~an impact~~ on **regulation of prices** ~~our -~~ **or payment for drug products** ~~results of operations, and may have a material adverse effect on our business~~ . ~~In particular~~ **Drug pricing and payment reform was a focus of the Trump Administration and has been a focus of the Biden Administration. For example** , **federal legislation enacted** in ~~June~~ 2021 **eliminates a** ~~the U. S. Supreme Court held that Texas and other challengers had no legal standing to challenge the PPACA, dismissing the case on procedural grounds without specifically ruling on the constitutionality of the PPACA. Thus, the PPACA will remain in effect in its current form. We cannot predict how this decision or future litigation will impact our business, or what other healthcare measures and regulations will ultimately be implemented at the federal or state level or their effect on our business. Under the American Rescue Plan Act of 2021, effective January 1, 2024, the~~ statutory cap on Medicaid ~~Drug~~ **drug** ~~Rebate~~ **rebate** ~~Program~~ **program** rebates **effective January 1** ~~that manufacturers pay to state Medicaid programs will be eliminated. Elimination of this cap may require a pharmaceutical manufacturer to pay more in rebates than it receives on the sale of products~~ , ~~which could have a material impact on our business. In August 2022~~ **2024 . As another example** , ~~Congress passed~~ the Inflation Reduction Act **(IRA)** of 2022 **contains various** ~~, which includes prescription~~ drug **price negotiation, inflationary rebate, and pricing** provisions **with varying implementation dates. The IRA allows** ~~that have significant implications for the pharmaceutical industry and Medicare beneficiaries, including allowing~~ the federal government to negotiate a maximum fair price for certain high- priced single **-** source Medicare drugs, ~~imposing~~ **imposes** penalties and excise tax for manufacturers that fail to comply with the drug price negotiation requirements, ~~requiring~~ **requires** inflation rebates for all Medicare Part B and Part D drugs ~~,~~ **(** with limited exceptions ~~,~~ **)** if their drug prices increase faster than inflation, and ~~redesigning~~ **redesigns** Medicare Part D to reduce out- of- pocket prescription drug costs for beneficiaries, among other changes. The impact of ~~these~~ -- **the** ~~legislative, executive,~~ **IRA on our business** and ~~administrative actions and any future healthcare measures and agency rules implemented by~~ **the broader pharmaceutical industry remains uncertain as implementation is ongoing. As another example, in 2022, subsequent to the enactment of the IRA,** the Biden administration **released an executive order directing the HHS to report** on **how** ~~us and~~ the ~~pharmaceutical industry~~ **Center for Medicare and Medicaid Innovation (" CMMI ") could be leveraged to test new models for lowering drug costs for Medicare and Medicaid beneficiaries. The report** ~~as~~ **was** ~~a whole~~ **issued in 2023 and proposed various models that CMMI** is ~~unclear. The implementation of~~ **currently developing which seek to lower the** cost ~~containment measures~~ **of drugs, promote accessibility and improve quality of care. These changes** or other ~~healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our product candidates if approved. Complying with any new legislation and regulatory~~ changes could ~~be time- intensive and expensive, resulting in a material adverse effect~~ **affect the market conditions for our products. We expect continued scrutiny** on ~~our business~~ **drug pricing and government price reporting from Congress, agencies, and other bodies** . At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. For example, **on January 5, 2024, the FDA approved Florida' s Section 804 Importation Program, or SIP, proposal to import certain drugs from Canada for specific state healthcare programs. It is unclear how this program will be implemented, including which drugs will be chosen, and whether it will be subject to legal challenges in the United States or Canada. Other states have also submitted SIP proposals that are pending review by the FDA. Any such approved importation plans, when implemented, may result in lower drug prices for products covered by those programs. Additionally,** a number of states ~~are considering or~~ have ~~recently~~ enacted state drug price transparency and reporting laws that could substantially increase our compliance burdens and expose us to greater liability under such state laws ~~once~~ **if and when** we **have marketed** ~~begin commercialization after obtaining regulatory approval for any of our~~ products. ~~Implementation of cost containment measures or other healthcare~~ **Healthcare** ~~reforms~~ - **reform efforts have been and may continue to be subject to scrutiny and legal challenge. For example, with respect to the PPACA, tax reform legislation was enacted** that ~~affect~~ **eliminated** the ~~pricing and /~~ **tax penalty established** ~~or~~ **for** ~~availability~~ **individuals who do not maintain mandated health insurance coverage beginning in 2019 and, in 2021, the U. S. Supreme Court dismissed the latest judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality** of **the PPACA. As another example, revisions to regulations under the federal anti- kickback statute would remove protection for traditional Medicare Part D discounts offered by pharmaceutical manufacturers to pharmacy benefit managers and health plans. Pursuant to court order, the removal was delayed and recent legislation imposed a moratorium on implementation of the rule until January 2032. As another example, the IRA** drug **price negotiation program has been challenged** ~~products may impact our ability to generate revenue, attain or maintain profitability, or commercialize products for which we may receive regulatory approval~~ in ~~the future~~ **litigation filed by various pharmaceutical manufacturers and industry groups** . We expect that ~~PPACA, as well as other~~ healthcare reform measures that have been ~~and~~ **or in the future** may be adopted ~~in the future~~ , may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product, and could seriously harm ~~our~~ **any** future revenue **generation** . Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payers. ~~The implementation of cost containment measures~~ **Complying with any new legislation and regulatory changes could be time- intensive and expensive, resulting in a material adverse effect on** ~~or~~ **our business** ~~other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our products~~ . Legislative and regulatory proposals have been made to expand post- approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on

the regulatory approvals **, if any,** of our product candidates ~~, if any,~~ may be. In addition, increased scrutiny by Congress of the FDA' s approval process may significantly delay or prevent regulatory approval, as well as subject us to more stringent product labeling and post- marketing testing and other requirements. In addition, different pricing and reimbursement schemes exist in other countries. In the European Community, governments influence the price of pharmaceutical products through their pricing and reimbursement rules and control of national healthcare systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may be marketed only once a reimbursement price has been agreed upon. Some of these countries may require, as **a** condition of obtaining reimbursement or pricing approval, the completion of clinical trials that compare the cost- effectiveness of a particular product ~~candidate~~ to ~~currently~~ **other then-** available therapies. Other member states allow companies to fix their own prices for medicines, but monitor and control company profits. The downward pressure on healthcare costs in general, particularly prescription drugs, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross- border imports from low- priced markets exert a commercial pressure on pricing within a country. **On May 1, 2021, the EU and UK trade and cooperation agreement, or TCA, entered into application. The TCA includes specific provisions concerning pharmaceuticals, which include the mutual recognition of the outcomes of GMP inspections. Applicants and MA holders may submit GMP certificates issued by the MHRA for sites located outside the EU / EEA as supporting information for EU regulatory submissions. However, the TCA does not foresee wholesale mutual recognition of UK and EU pharmaceutical regulations. The regulatory regime in Great Britain currently broadly aligns with EU regulations. However, it is possible that these regimes may diverge in the future, given proposed legislative changes such as the European Commission' s proposals for the entire overhaul of the pharmaceutical regulatory regime.** Other Healthcare Laws and Compliance Requirements In the **United States** ~~U. S.~~ , **pharmaceutical** ~~the research, manufacturing~~ **manufacturers** ~~, distribution, sale and promotion of drug products that we are developing~~ are subject to **numerous other federal, state and local laws designed to, for example, prevent fraud and abuse; promote transparency in interactions with others in the healthcare industry;** ~~regulation~~ **regulate pricing of drugs and protect the privacy of individual information. These laws are enforced** by various federal ~~,~~ **and** state **enforcement** ~~and local~~ authorities ~~in addition to the FDA~~ , including **but not limited to, the U. S. Department of Justice, and individual U. S. Attorney offices within the Department of Justice, the U. S. Department of Health and Human Services, or HHS, HHS' various divisions, including but not limited to,** the Centers for Medicare & Medicaid Services, **or CMS** ~~other divisions of the U. S. Department of Health and Human Services (e. g.~~ , **and** the Office of Inspector General ~~)~~ , **and** ~~the U. S. Department of Justice,~~ state ~~Attorneys General,~~ **boards of pharmacy. We may be subject to various federal** and ~~other~~ state **laws pertaining to** ~~and local government agencies. For example, sales, marketing and scientific / educational grant programs must comply with applicable~~ health care **"** fraud and abuse **, " including anti kickback** laws, **and false claims laws, for activities related to past and future sales of any products reimbursable by third party payers** such as ~~the~~ federal **health care programs (including Medicare and Medicaid) or, in some cases, commercial health plans.** Anti- ~~Kickback~~ **kickback** ~~Statute~~ **laws generally prohibit a pharmaceutical manufacturer from soliciting** , **offering, receiving, or paying anything of value to generate business, including the purchase, prescription or use of a particular drug. False claims laws generally prohibit anyone from knowingly and willingly presenting, or causing to be presented, any claims for payment for reimbursed drugs or services to third- party payers that are false or fraudulent. Although the specific provisions of these laws vary, their scope is generally broad and there may not be regulations, guidance or court decisions that apply the laws to particular industry practices. There is therefore a possibility that our practices might be challenged under such laws. Laws and regulations have also been enacted by** the federal ~~False Claims Act, Stark~~ **government and various states to regulate the sales and marketing practices of pharmaceutical manufacturers with marketed products. The** ~~law~~ **laws** ~~,~~ and ~~implementing~~ regulations ~~,~~ **generally limit financial interactions between manufacturers** and ~~similar state~~ **health care providers; require manufacturers to adopt certain compliance standards; require disclosure to the government and public of financial interactions; require disclosure of marketing expenditures or pricing information, regulate drug pricing and / or require the registration of pharmaceutical sales representatives. Many of these** laws ~~. Pricing~~ and ~~rebate~~ **regulations contain ambiguous requirements or require administrative guidance for implementation. Given the lack of clarity in laws and their implementation, any future activities (if we obtain approval and / or reimbursement from federal healthcare** programs ~~must comply with~~ **for our product candidates) could be subject to challenge. Federal laws, including** the Medicaid Drug Rebate Program **, require pharmaceutical manufacturers to report certain calculated product prices to the government or provide certain discounts or rebates to government authorities or private entities, often as a condition of reimbursement under government healthcare programs. These laws are complex and the failure to calculate reported prices correctly or provide appropriate prices and rebates can expose a manufacturer to penalties and other sanctions. The distribution of drugs and biological products is subject to additional** requirements ~~of the Omnibus Budget Reconciliation Act of 1990, as amended,~~ and **regulations** ~~the Veterans Health Care Act of 1992~~ , ~~as amended. If~~ **including extensive record- keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical** products **.** ~~are made available to authorized users of the~~ Federal ~~Supply Schedule of the General Services Administration, additional laws and requirements apply. Other laws and regulations that may apply to prescription drug manufacturers include the Sunshine Act, prescription drug price reporting requirements, and various state transparency and reporting laws. All business activities of prescription drug manufacturers are also potentially subject to federal~~ and state consumer protection and unfair competition laws ~~. The federal Anti- Kickback Statute prohibits any person, including a prescription drug manufacturer (or a party acting on its behalf), from knowingly and willfully soliciting, receiving, offering or providing remuneration, directly or indirectly, to induce or reward either the referral of an~~ **and regulations** ~~individual, or the furnishing, recommending, or arranging for a good or service, for which payment may be made under a federal healthcare program such as the Medicare and Medicaid programs. This~~

~~statute can be applied~~ broadly **regulate marketplace activities and that potentially harm consumers and could apply** to ~~include arrangements between~~ **the activities of** pharmaceutical manufacturers ~~on one~~ **. We may be subject to data privacy** ~~hand -~~ **and security laws in** ~~and any referral source on~~ the **various jurisdictions in which we operate, obtain or store personally identifiable information. Numerous U. S. federal and state laws govern the collection, use, disclosure and storage of personal information. Various foreign countries also have, or are developing, laws governing the collection, use, disclosure and storage of personal information. Globally,** ~~other -~~ **there** ~~, including prescribers, purchasers, and formulary managers. The term " remuneration " has been broadly interpreted to include anything of value, including, for example, gifts, discounts, the furnishing of supplies or equipment, credit arrangements, payments of cash, waivers of payments, ownership interests, and service fees, unless expressly exempted or protected by a safe harbor. Further, the statute has been interpreted to cover any arrangement where one purpose of the remuneration was to obtain remuneration in exchange for referral or to induce further referrals for~~ an **increasing focus on privacy** ~~item or service. Although there are a number of statutory exemptions~~ and **data** ~~regulatory safe harbors protecting -~~ **protection** ~~certain legitimate~~ **issues that may affect our** business **. Efforts to ensure** ~~arrangements from prosecution, the exemptions and safe harbors are drawn narrowly, and practices~~ that ~~involve remuneration intended to induce prescribing, purchasing or~~ **our** ~~recommending may be subject to scrutiny if they do not qualify for an exemption or safe harbor. Our practices may not in all cases meet all of the criteria of an applicable safe harbor for protection from liability under the federal Anti- Kickback Statute. The reach of the Anti- Kickback Statute was broadened by PPACA, which, among other things, amends the intent requirement of the federal Anti- Kickback Statute such that the government does not need to prove that a person had the intent to specifically violate the statute in order to find a violation. In addition, the PPACA provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti- Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act (discussed below) or the civil monetary penalties statute, which imposes fines against any person who is determined to have presented or caused to be presented claims to a federal healthcare program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent. Additionally, many states have adopted laws similar to the federal Anti- Kickback Statute, and some of these state prohibitions apply to referral of patients for healthcare items or services reimbursed by any third- party payer, not only the Medicare and Medicaid programs in at least some cases, and do not expressly provide for certain safe harbors or impose different requirements for safe harbor protection under applicable state laws. The federal False Claims Act imposes liability on any person or entity that, among other things, knowingly presents, or causes to be presented, a false or fraudulent claim for payment by a federal healthcare program. The qui tam provisions of the False Claims Act allow a private individual to bring civil actions on behalf of the federal government alleging that the defendant has submitted or cause to be submitted a false claim to the federal government, and to share in any monetary recovery. In recent years, the number of suits brought by private individuals has increased dramatically. In addition, various states have enacted false claims laws analogous to the False Claims Act. Many of these state laws apply where a claim is submitted to any third- party payer and not merely a federal healthcare program. There are many potential bases for liability under the False Claims Act. Liability arises, primarily, when an entity knowingly submits, or causes another to submit, a false claim for reimbursement to the federal government. The False Claims Act has been used to assert liability on the basis of inadequate care, kickbacks and other improper referrals, improperly reported government pricing metrics such as Best Price or Average Manufacturer Price, improper use of Medicare numbers when detailing the provider of services, improper promotion of off- label uses (i. e., uses not expressly approved by FDA in a drug' s label), and allegations as to misrepresentations with respect to the services rendered. Our future~~ activities ~~relating to the reporting of discount and rebate information and other information affecting federal, provincial, state and third- party reimbursement of our products, and the sale and marketing of our products and our service arrangements or data purchases, among other activities, may be subject to scrutiny under these laws. We are unable to predict whether we would be subject to actions under the False Claims Act or a similar state law, or the impact of such actions. However, the cost of defending such claims, as well as any sanctions imposed, could adversely affect our financial performance. Also, the Health Insurance Portability and Accountability Act of 1996, or HIPAA, created several new federal crimes, including healthcare fraud, and false statements relating to healthcare matters. The healthcare fraud statute prohibits knowingly and willfully executing a scheme to defraud any healthcare benefit program, including private third- party payers. The false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. In addition, we may be subject to, or our marketing activities may be limited by, data privacy and security regulation in the U. S. and foreign jurisdictions in which we conduct our business, including jurisdictions in which we conduct our clinical trials. For example, HIPAA and its implementing regulations established uniform federal standards for certain " covered entities " (healthcare providers, health plans and healthcare clearinghouses) governing the conduct of certain electronic healthcare transactions and protecting the security and privacy of protected health information. The American Recovery and Reinvestment Act of 2009 included expansion of HIPAA' s privacy and security standards called the Health Information Technology for Economic and Clinical Health Act, or HITECH. Among other things, HITECH makes HIPAA' s privacy and security standards directly applicable to " business associates " — independent contractors or agents of covered entities that create, receive, maintain, or transmit protected health information in connection with providing a service for or on behalf of a covered entity. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney' s fees and costs associated with pursuing federal civil actions. In addition, in May 2016, the EU formally adopted the General Data Protection Regulation, or GDPR, which applies to all EU member states from May 25, 2018 and replaced the European Union Data Protection Directive. The GDPR has imposed many new or additional requirements including, but not limited to, obtaining consent of the individuals to whom the personal data~~

~~relates, the nature and scope of notifications provided to the individuals, the security and confidentiality of the personal data, data breach notification and using third- party processors in connection with the processing of the personal data. Failure to~~ comply with **applicable healthcare** ~~the GDPR could subject us to regulatory sanctions, delays in clinical trials, criminal prosecution and / or civil fines or penalties. Additionally, GDPR creates a direct cause of action by individual data subjects. The GDPR is a complex law~~ **laws** and ~~the regulatory~~ **regulations will involve substantial costs. Given the breadth of the laws and regulations, limited** guidance ~~is still~~ **for certain laws and regulations and** evolving **government interpretations** ~~, including with respect to how the GDPR should be applied in the context~~ of ~~clinical trials or other~~ -- **the** ~~transactions from~~ **laws and regulations, governmental authorities may possibly conclude** that ~~we may gain access to personal data. In 2021, the UK became a " third country " under the GDPR. These changes in the law will increase our costs of compliance and result in greater legal risks. Other countries maintain different privacy laws that we are subject to. The Physician Payment Sunshine Act, or~~ **our business** ~~the Sunshine Act, requires applicable manufacturers and certain distributors of prescription drugs, among other products, that are available for coverage by Medicare, Medicaid or the Children' s Health Insurance Program to report annually to the Secretary of HHS: (i) payments or other transfers of value made by that entity, or by a third- party as directed by that entity, to covered recipients, such as physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain non- physician healthcare professionals (such as physician assistants and nurse practitioners, among others), and teaching hospitals or to third parties on behalf of such physicians, non- physician healthcare professionals or teaching hospitals; and (ii) physician ownership (including immediate family member' s ownership) and investment interests in the entity. There are also an increasing number of state and local " sunshine " or transparency and reporting laws that require applicable manufacturers to make reports to states on pricing and marketing information. The U. S. federal government discloses the reported information on a publicly available website. Several states have enacted legislation requiring pharmaceutical companies to, among other things, establish marketing compliance programs, file periodic reports with the state, make periodic public disclosures on sales, marketing, pricing, clinical trials and other activities, and / or register their sales representatives, as well as to prohibit pharmacies and other healthcare entities from providing certain physician prescribing data to pharmaceutical companies for use in sales and marketing, and to prohibit certain other sales and marketing~~ practices ~~. These federal, state, and local laws~~ may **not** ~~affect our sales, marketing, and other promotional activities by imposing administrative and compliance burdens on us. If we fail to track and report as required by these laws or otherwise~~ comply with ~~these laws, we could be subject to the penalty provisions of the pertinent state and federal authorities. Because of the breadth of these health care laws and the narrowness of available statutory and regulatory exemptions, it is possible that some of our business activities could be subject to challenge under one or more of~~ such laws. If our operations are found to be in violation of any of ~~the~~ **these** ~~federal and state~~ laws ~~described above~~ or any other governmental regulations that **may** apply to us, we may be subject to ~~penalties, including criminal and~~ significant civil ~~monetary~~ **, criminal and administrative** penalties, damages, fines ~~, imprisonment~~ , exclusion from ~~participation in~~ government **funded** healthcare programs, ~~injunctions~~ **such as Medicare and Medicaid** , ~~recall~~ **and the curtailment or restructuring of** ~~or~~ **our** ~~seizure of products~~ **operations. Further** , **defending against any such** ~~total or partial suspension of production, denial or withdrawal of pre- marketing product approvals, private qui tam~~ actions **can be costly, time- consuming and may require significant personnel resources. Therefore, even if we are successful in defending against any such actions that may be** brought **against** ~~by individual whistleblowers in the name of the government or refusal to allow~~ us ~~to enter into supply contracts~~ , ~~including government contracts, the curtailment or restructuring of our operations, and corporate integrity agreement, which impose certain compliance, certification and reporting obligations, any of which could adversely affect our ability to operate~~ our business **may be impaired** ~~and our results of operations~~ . To the extent that any of our products are sold in a foreign country or if we contract with vendors or independent contractors outside of the U. S., we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post- approval requirements, including safety surveillance, anti- corruption / anti- bribery laws, anti- kickback laws, healthcare fraud and abuse laws, and implementation of corporate compliance programs and reporting of payments or transfers of value to healthcare professionals. While we are not aware of any current issues, we are unable to predict whether we will be subject to actions under applicable healthcare laws, or the impact of such actions on our business. However, the costs of defending such actions or claims, as well as any sanctions imposed, could result in a material adverse effect on our business or financial condition. Environmental Matters Our operations require the use of hazardous materials (including biological materials) which subject us to a variety of federal, provincial and local environmental and safety laws and regulations. Some of the regulations under the current regulatory structure provide for strict liability, holding a party potentially liable without regard to fault or negligence. We could be held liable for damages and fines as a result of our, or someone else' s, business operations should contamination of the environment or individual exposure to hazardous substances occur. We **believe that we are in material compliance with applicable environmental laws and that continued compliance therewith will not have a material adverse effect on our business. We** cannot predict **, however,** how changes in laws or development of new regulations will affect our business operations or the cost of compliance. Human Capital Our board of directors and management recognize that creating long- term enterprise value is advanced by considering the interests and concerns of many stakeholders, including those of our employees. As of December 31, ~~2022~~ **2023** , we had ~~213~~ **259** employees, including ~~203~~ **251** full- time and part- time permanent employees, of which ~~157~~ **179** are located in Canada and ~~46~~ **72** are located in the U. S. ~~.~~ Of our employees, ~~159~~ **190** were primarily engaged in research and development, ~~62~~ **78** of whom hold a Ph. D. or M. D. (or equivalent) degree **, and 69 were engaged in general and administrative or commercial activities** . None of our employees are represented by a labor union. We have not experienced any work stoppages and we consider our relations with our employees to be good. As competition for qualified personnel in the biotechnology and pharmaceutical field is intense, attracting and retaining qualified employees at all levels is critical to our business. We continuously strive to ensure that employee morale remains strong, and conduct employee engagement surveys to identify areas of focus and monitor employee turnover rates. **As of December 31, 2023, and for the last several years, our company turnover rate was and has been**

lower than the industry market average. We have established comprehensive and competitive compensation ~~, leave~~ and benefits programs to attract and retain ~~the~~ highly qualified personnel ~~essential~~ **and** to ~~our business~~ **incentivize and reward strong performance** . In addition to providing our employees with competitive salaries, we believe that employees should share in the potential financial gains resulting from the advancement of our programs ~~. Our practice is~~ **by way of annual bonuses** to **permanent employees based on the achievement of corporate and / or personal objectives. To align the interests of our employees with those of our shareholders, we** award stock options to **all** permanent employees, both upon initial hiring and annually thereafter ~~, and pay annual bonuses to permanent employees based on the achievement of corporate and / or personal objectives~~ . Our leave programs include paid vacation, personal, sick, disability and other paid and unpaid leaves. Our health and wellness programs include medical, dental, vision care, retirement savings, employee assistance programs **, flexible work schedules** and other benefits. As a biopharmaceutical company with highly educated employees, we believe that our employees must stay current with advances in our industry and continue to grow in their careers. We ~~offer~~ **support our employees' further development through** a variety of internal training ~~and development opportunities as well as dedicated resources for colleagues to attend conferences~~ and external professional development ~~programs~~ **opportunities, including conference attendance and tuition reimbursement** . We are committed to diversity, equity ~~and~~ **,** inclusion **and accessibility** , or ~~DEI~~ **DEIA** , at all levels of our company, and we have established a joint management / employee ~~DEI Committee~~ **committee** to progress ~~this~~ **these** important ~~issue~~ **issues** . We will continue to focus on measuring and extending our diversity and inclusion initiatives across our entire workforce. We recruit the best ~~-~~ qualified employees regardless of sex, gender, ethnicity, race, religion, or other protected traits, and it is our policy to comply with all applicable laws related to discrimination in the workplace. We currently rely, and expect to continue to rely, on ~~collaborators, either directly or through~~ third- party contract manufacturers, or CMOs, to manufacture **(or produce sufficient quantities of materials required for the manufacture of) our product candidates for pre- clinical testing and clinical trials, and we intend to do so for the commercial manufacture of our products. Similarly, we may rely on collaborators to manufacture, either directly or through CMOs,** product candidates licensed to them ~~or work with multiple CMOs to produce sufficient quantities of materials required for the manufacture of our product candidates for pre- clinical testing and clinical trials and intend to do so for the commercial manufacture of our products~~ . Accordingly, we have not internally developed any manufacturing facilities or hired related personnel. To date, we have obtained materials for our product candidates from multiple third- party manufacturers **and suppliers** . We believe that all of the materials required for the manufacture of our product candidates can be obtained from more than one source. However, the manufacturing processes for each of our product candidates vary and sourcing adequate supplies may be made more difficult depending on the type of product candidate involved. Our product candidates generally can be manufactured in reliable and reproducible synthetic processes from readily available starting materials, excipients and packaging components. ~~The drug substance chemistry generally is amenable to scale- up and does not require unusual equipment in the manufacturing processes.~~ Corporate Information We were incorporated in the Province of British Columbia on November 5, 1996 under the predecessor to the Business Corporations Act (British Columbia) under the name " Xenon Bioresearch Inc. " We continued from British Columbia to the federal jurisdiction pursuant to Section 187 of the Canada Business Corporations Act, or the CBCA, on May 17, 2000 and concurrently changed our name to " Xenon Genetics Inc. " We registered as an extra- provincial company in British Columbia on July 10, 2000 and changed our name to " Xenon Pharmaceuticals Inc. " on August 24, 2004. We ~~have~~ **had** one wholly- owned subsidiary as of December 31, ~~2022~~ **2023** , Xenon Pharmaceuticals USA Inc., which was incorporated in Delaware on December 2, 2016. Our principal executive offices are located at ~~200 —~~3650 Gilmore Way, Burnaby, British Columbia, Canada V5G 4W8, and our telephone number is (604) 484- 3300. We are a reporting issuer in British Columbia, Alberta and Ontario, but our shares are not listed on any recognized Canadian stock exchange. Our common shares trade on the Nasdaq Global Market under the symbol " XENE. " Where You Can Find Additional Information We make available free of charge through our investor relations website, http: / / investor. xenon- pharma. com, our annual reports, quarterly reports, current reports, proxy statements and all amendments to those reports as soon as reasonably practicable after such material is electronically filed or furnished with the U. S. Securities and Exchange Commission, or SEC. These reports may also be obtained without charge by contacting Investor Relations, Xenon Pharmaceuticals Inc., ~~200 —~~3650 Gilmore Way, Burnaby, British Columbia, Canada V5G 4W8, e- mail: investors @ xenon- pharma. com. Our website and the information contained therein or incorporated therein are not intended to be incorporated into this Annual Report on Form 10- K. The SEC maintains a website that contains reports, proxy and information statements, and other information regarding reports that we file or furnish electronically with them at www. sec. gov. Additional information related to Xenon is also available on SEDAR at www. sedar. com. Item 1A. Risk Factors You should carefully consider the following risk factors, in addition to the other information contained in this report, including the section of this report captioned " Management' s Discussion and Analysis of Financial Condition and Results of Operations " and our financial statements and related notes. If any of the events described in the following risk factors and the risks described elsewhere in this report occurs, our business, operating results and financial condition could be seriously harmed. This report on Form 10- K also contains forward- looking statements that involve risks and uncertainties. Our actual results could differ materially from those anticipated in the forward- looking statements as a result of factors that are described below and elsewhere in this report. Our Risk Factors are not guarantees that no such conditions exist as of the date of this report and should not be interpreted as an affirmative statement that such risks or conditions have not materialized, in whole or in part. Risks Related to Our Financial Condition and Capital Requirements Investment in biopharmaceutical product development is highly speculative because it entails substantial capital expenditures and significant risk that a ~~potential~~ product candidate may fail to demonstrate adequate efficacy or an acceptable safety profile, gain regulatory approval and become commercially viable. We have no products approved for commercial sale and have not generated any revenue from product sales to date, and we will continue to incur significant research and development and other expenses related to our clinical development and ongoing operations. As a result, we are not profitable and have incurred losses in each period since our inception. Since our inception,

we have devoted substantially all of our financial resources and efforts to research and development, including pre- clinical studies, manufacturing of investigational drug and our clinical trials. Our financial condition and operating results, including net losses, may fluctuate significantly from quarter to quarter and year to year. Accordingly, you should not rely upon the results of any quarterly or annual periods as indications of future operating performance. We do not expect to have sustained profitability for the foreseeable future. We had net losses of $ ~~125~~ **182** . 4 million, $ **125. 4 million and $** 78. 9 ~~million and $ 28. 8~~ million for the years ended December 31, **2023,** 2022 ~~,~~ **and** 2021 ~~and 2020~~ , respectively, and an accumulated deficit of $ ~~482~~ **665** . ~~7~~ **1** million as of December 31, ~~2022~~ **2023** , which were driven by expenses incurred in connection with our research and development programs and from general and administrative costs associated with our operations. We expect to continue to incur significant losses for the foreseeable future, and we expect these losses to increase as we continue our research and development of, and seek regulatory approvals for our product candidates. We expect to incur significant expenses and increasing operating losses for the foreseeable future as we: • continue our research and pre- clinical and clinical development of our product candidates; • conduct additional pre- clinical, clinical or other studies for our product candidates; • manufacture **, label, serialize and distribute** drug substance and drug product for clinical trials and commercialization; • seek regulatory and marketing approvals for any of our product candidates that successfully complete clinical trials; • hire and retain additional personnel, such as clinical, quality assurance, regulatory, scientific, commercial and administrative personnel; • seek to identify and validate additional product candidates; • acquire or in- license other product candidates and technologies; • make milestone or other payments under our in- license or other agreements, including, without limitation, payments to 1st Order Pharmaceuticals, Inc. and other third parties; • maintain, protect and expand our intellectual property portfolio; • establish sales, marketing, distribution and other commercial infrastructure to commercialize any products for which we may obtain marketing approval; • create additional infrastructure and incur additional costs to support our operations and our product development and planned future commercialization efforts; and • experience any delays or encounter **adverse** issues with **respect to** any of the above. Our expenses could increase beyond expectations for a variety of reasons, including if we are required by the U. S. Food and Drug Administration, or FDA, the European Medicines Agency, or EMA, or other regulatory authorities to perform clinical and other studies including post- approval commitments in addition to those that we currently anticipate, or if there are any delays in establishing appropriate manufacturing arrangements to support our clinical trials, the development of any of our product candidates or commercialization. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our shareholders' equity and working capital. We do not generate any revenue from product sales and may never become profitable. Our ability to generate revenue and achieve profitability depends on our ability, alone or with collaborators, to successfully complete the development of, and obtain the regulatory approvals necessary to commercialize, our product candidates. Successful commercialization will require achievement of many key milestones, including demonstrating safety and efficacy in clinical trials, obtaining regulatory, including marketing, approval for these product candidates, manufacturing, marketing and selling those products for which we, or any of our existing or future collaborators, may obtain regulatory approval, satisfying any post- marketing requirements and obtaining reimbursement for our products from private insurance or government ~~payors~~ **payers** . Because of the uncertainties and risks associated with these activities, we are unable to accurately and precisely predict the timing and amount of revenues, the extent of any further losses or if or when we might achieve profitability. We and our existing or future collaborators may never succeed in these activities and, even if we ~~do, or any existing or future collaborators~~ do, we may never generate revenues that are large enough for us to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Additionally, our expenses could increase if we are required by the FDA, EMA or other regulatory authorities to perform clinical trials in addition to those currently expected, or if there are any delays in completing our clinical trials or the development of any of our product candidates. If any of our product candidates fail in clinical trials or do not gain regulatory approval, or if any of our future products, if any, once approved, fail to achieve market acceptance or adequate market share, we may never become profitable. If we are unable to ~~achieve~~ **generate** sufficient revenue to become profitable and remain so, our financial condition and operating results will be negatively impacted, and the market price of our common shares might be adversely impacted. Since our inception, we have dedicated most of our resources to the discovery and development of our pre- clinical and clinical product candidates. We expect to continue to spend substantial amounts of resources to continue the pre- clinical and clinical development of our current and future programs. If we are able to gain marketing approval for product candidates that we develop, we will require significant additional amounts of capital in order to launch and commercialize such product candidates to the extent that such launch and commercialization are not the responsibility of a collaborator. In addition, other unanticipated costs may arise in the course of our development efforts. Because the design and outcome of our planned and anticipated clinical trials is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of any product candidate we develop. Our future capital requirements depend on many factors, including but not limited to: • the scope, progress, results and costs of researching and developing our current product candidates, as well as ~~other~~ additional product candidates we may develop and pursue in the future; • the timing of, and the costs involved in, obtaining marketing approvals for our product candidates and any ~~other~~ additional product candidates we may develop and pursue in the future; • the number of future product candidates that we may pursue and their development requirements; • if approved, the costs of commercialization activities for any product candidate that receives regulatory approval to the extent such costs are not the responsibility of an existing or future collaborator, including the costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities; • subject to the receipt of regulatory approval, revenue, if any, received from commercial sales of our product candidates and any ~~other~~ additional product candidates we may develop and pursue in the future; • whether our existing collaborations generate substantial milestone payments and, ultimately, royalties on future approved products for us; • our ability to maintain existing collaborations and to establish new collaborations, licensing or other arrangements and the financial terms of such ~~agreements~~ **arrangements; • the costs**

associated with any transactions to acquire or in- license other product candidates and technologies ; • our headcount growth and associated costs as we expand our research and development efforts and initiate pre- commercial activities; • the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing patents, including litigation costs and the outcome of such litigation; and • the ongoing costs of operating as a public company. Based on our research and development plans and our timing expectations related to the progress of our programs, we expect that our existing cash and cash equivalents and marketable securities as of the date of this report, will enable us to fund our operating expenses and capital expenditure requirements for at least the next 12 months. Our operating plan may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned. Raising funds in the future may present additional challenges and future financing may not be available in sufficient amounts or on terms acceptable to us, if at all. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, reduce or terminate our product development programs or plans for commercialization. We may allocate our limited resources to pursue a particular product candidate or indication and fail to capitalize on other product candidates or indications that may be more profitable or for which there is a greater likelihood of success. Because we have limited financial and management resources, we focus on a limited number of research programs and product candidates. As a result, we may forgo or delay pursuit of opportunities with other product candidates or for **our current product candidates in** other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial drugs or profitable market opportunities. Our spend on current and future research and development programs and product candidates for specific indications may not yield any commercially viable drugs. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights. Raising additional capital may cause dilution to our existing shareholders, restrict our operations or require us to relinquish rights to our technologies or product candidates. We expect our expenses to increase in connection with our planned operations. Unless and until we can generate a substantial amount of revenue from any approved product candidates, we expect to finance our future cash needs through public or private equity offerings, debt financings, royalty- based financing, collaborations, licensing arrangements or other sources, or any combination of the foregoing. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans. The terms of any financing arrangements we enter into may adversely affect the holdings or the rights of our shareholders and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our common shares to decline. The sale of additional equity or convertible securities also would dilute all of our shareholders. Historically, we have also financed our operations through the incurrence of debt. Any future incurrence of indebtedness would result in increased fixed payment obligations and, potentially, the imposition of restrictive covenants. Such covenants could include limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. We could also be required to seek funds through collaborations or marketing, distribution or licensing arrangements, or royalty- based financings with third parties, and we may have to relinquish valuable rights to our technologies, future revenue streams or product candidates, or grant licenses on terms that may not be favorable to us. If we are unable to raise additional capital when needed, we may be required to delay, reduce or terminate our product discovery and development programs, commercialization efforts, or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. In addition, any additional fundraising efforts may divert our management from their day- to- day activities, which may adversely affect our ability to develop and commercialize our product candidates. We are subject to risks associated with currency fluctuations which could impact our results of operations. As of December 31, ~~2022~~ **2023** , approximately ~~6~~ **3** % of our cash and cash equivalents and marketable securities were denominated in Canadian dollars. We incur significant expenses in Canadian dollars in connection with our operations in Canada. We do not currently engage in foreign currency hedging arrangements for our Canadian dollar expenditures, and, consequently, foreign currency fluctuations may adversely affect our earnings; however, in the future, we may engage in exchange rate hedging activities in an effort to mitigate the impact of exchange rate fluctuations. Any hedging technique we implement may fail to be effective. If our hedging activities are not effective, changes in currency exchange rates may have a more significant impact on the market price of our common shares. Risks Related to Our Business and Industry We and our collaborators face substantial competition in the markets for our product candidates, which may result in others discovering, developing or commercializing products before us or doing so more successfully than we, or our collaborators, do. The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. We face potential competition in drug discovery and product development from many different approaches and sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions, governmental agencies, as well as public and private research institutions. Any product candidates that we, or our collaborators, successfully develop and commercialize will compete with existing products and any new products that may become available in the future. The key competitive factors affecting the success of all of our product candidates, if approved, are likely to be their efficacy, safety and / or tolerability, convenience and ease of administration, price, the potential advantages of alternative products, the level of generic competition, and the availability of coverage and adequate reimbursement from government and other third- party payers. Our commercial opportunities could be reduced or eliminated if our competitors develop and commercialize products or therapies that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA, EMA or other foreign regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, our

ability to compete may be affected by decisions made by insurers or other third- party payers. If **one or** more ~~than one~~ of our proprietary or partnered products were approved for the treatment of epilepsy, we anticipate that they could potentially compete with **other anti- seizure medications, or ASMs, or** one another ~~and~~ **. In addition, if one or more of our proprietary products were approved for the treatment of major depressive disorder, or MDD, we anticipate that they could potentially compete with** other anti- ~~seizure~~ **depressant** medications, or **ADs** ~~ASMs. To the extent that we are unable to compete effectively against one or more of our competitors in these areas, our business will not grow and our financial condition, results of operations and the market price of our common shares may suffer~~ . We have no marketed proprietary products and have not yet completed clinical development beyond Phase 2 clinical trials, which makes it difficult to assess our ability to develop our future product candidates and commercialize any resulting products independently. As a company, we have no previous experience in completing a Phase 3 clinical trial ~~or in completing clinical trials in pediatric or orphan drug indications,~~ and related regulatory requirements including a New Drug Application, or NDA, or equivalent submission, or the commercialization of products. We have not yet demonstrated our ability to independently and repeatedly conduct clinical development after Phase 2, obtain regulatory approval, manufacture **drug substance or** drug product on a registrational and commercial scale or arrange for a third- party to do so on our behalf, and commercialize therapeutic products. We will need to develop such abilities if we are to execute on our business strategy to develop and independently commercialize product candidates. To execute on our business plan for the development of independent programs, we will need to successfully: • reach agreement with multiple regulatory agencies on clinical and pre- clinical studies required for registration; • execute our clinical development and manufacturing plans for later- stage product candidates; • obtain required regulatory approvals in each jurisdiction in which we will seek to commercialize products; • build and maintain appropriate pre- commercialization capabilities as well as commercial sales, distribution and marketing capabilities; • build and implement effective market access strategy and gain market acceptance for our future products, if any; and • manage our spending as costs and expenses increase due to clinical trials, regulatory approvals and commercialization activities. If we are unsuccessful in accomplishing these objectives, we will not be able to develop and commercialize any future product candidates independently and could fail to realize the potential advantages of doing so. If we are not successful in discovering, developing and commercializing additional product candidates, our ability to expand our business and achieve our strategic objectives may be impaired. We have built a product development pipeline by identifying product candidates either from our internal research efforts or through acquiring or in- licensing other product candidates or technologies ~~. To date, our internal discovery efforts have yielded multiple development candidates, including XEN901, which we licensed to Neurocrine Biosciences and is now known as NBI- 921352~~ . Both our internal discovery efforts and our assessment of potential acquisition or in- licensing opportunities require substantial technical, financial and human resources, regardless of whether we identify any viable product candidates. If we are unable to identify additional product candidates suitable for clinical development and commercialization either from our internal research efforts or through acquiring or in- licensing other product candidates or technologies, we may not be able to obtain product revenue in future periods, which likely would result in significant harm to our financial position and adversely impact the market price of our common shares. If we fail to attract and retain our executive officers and key personnel, we may be unable to successfully develop our product candidates, perform our obligations under our collaboration agreements, conduct our clinical trials and commercialize our product candidates. Our success depends in part on our continued ability to attract, retain and motivate highly qualified management, clinical and scientific personnel. Our industry has experienced a high rate of turnover of management personnel in recent years. Replacing executive officers or other key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to develop, gain regulatory approval of and commercialize products successfully. We are highly dependent upon our executive officers, including Mr. Ian Mortimer, our President and Chief Executive Officer. The loss of services of one or more of our executive officers could materially delay or even prevent the successful development of our product candidates. In addition, we will need to hire additional personnel as we expand our clinical development activities and develop commercial capabilities, including a sales infrastructure to support our independent commercialization efforts. We may not be able to attract and retain personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for individuals with similar skill sets. The inability to recruit or loss of the services of any executive or key employee may impede the progress of our research, development and commercialization objectives. Our employees, collaborators and other personnel may engage in misconduct or other improper activities, including non- compliance with legal and regulatory standards and requirements, which could cause significant liability for us and harm our reputation. We are exposed to the risk of fraud or other misconduct by our employees, collaborators, vendors, investigational site staff, consultants, commercial partners and other personnel. Misconduct by those parties could include intentional, reckless and / or negligent conduct or disclosure of unauthorized activities to us that violates: • the regulations of the FDA, EMA and other foreign regulators, including those laws requiring the reporting of true, complete and accurate information to such authorities; • manufacturing standards; • insider trading laws; • data privacy, data protection and security; • federal and state healthcare fraud and abuse laws and regulations in the U. S. and abroad; and • laws that require the reporting of financial information or data accurately. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self- dealing and other abusive practices. Additionally, we are subject to applicable foreign, federal and state data privacy and security laws. For additional information, see " Risk Factors ~~-~~ We are subject to evolving global laws and regulations relating to privacy, data protection and information security, which may require us to incur substantial compliance costs, and any failure or perceived failure by us to comply with such laws and regulations may harm our business and operations. " Various laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Any misconduct could also involve the improper use or misrepresentation of information obtained in the course of clinical trials or creating fraudulent data

in our pre- clinical studies or clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of conduct applicable to all of our employees, officers, directors, agents and representatives, including consultants, but it is not always possible to identify and deter misconduct, and the precautions we take to detect and prevent misconduct may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or claims, demands, or lawsuits stemming from an actual or alleged failure to comply with these laws and regulations. Additionally, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves, achieving a favorable settlement or otherwise asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, disgorgement, integrity oversight and reporting obligations, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations. Additionally, 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. We may encounter difficulties in managing our growth, including headcount, and expanding our operations successfully. Our business strategy involves continued development and, where development is successful, commercialization of select product candidates. In order to execute on this strategy, we will need to build out a regulatory, sales, manufacturing, supply chain and marketing infrastructure and expand our development capabilities or contract with third parties to provide these capabilities and infrastructure for us. To achieve this, we will need to identify, hire and integrate personnel, compensate our employees on adequate terms in an increasingly competitive, inflationary market and continue to implement and improve our managerial, operational and financial systems. As our operations expand, we expect that we will need to manage additional relationships with various strategic collaborators, suppliers and other third parties. Future growth will impose significant added responsibilities on members of management including the need to identify, recruit, maintain, motivate and integrate additional employees. Also, our management may need to divert a disproportionate amount of its attention away from our day- to- day activities and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our business, give rise to operational errors, loss of business opportunities, loss of employees and reduced productivity amongst remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of existing and additional product candidates. If we are unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate and grow revenue could be reduced, and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize product candidates and compete effectively will depend, in part, on our ability to effectively manage any future growth. In the ordinary course of business, we process personal data and other sensitive information, including our proprietary and confidential business data, trade secrets, intellectual property, data about trial participants collected in connection with clinical trials, and other sensitive data. Our data processing activities subject us to numerous data privacy and security obligations, such as various laws, regulations, guidance, industry standards, external and internal privacy and security policies, contracts, and other obligations that govern the processing of personal data by us and on our behalf. In the U. S., federal, state, and local governments have enacted numerous data privacy and security laws, including data breach notification laws, personal data privacy laws, and consumer protection laws. For example, the U. S. federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, imposes specific requirements relating to the privacy, security, and transmission of individually identifiable health information **that apply to most U. S. health care providers with which we interact, such as our U. S. clinical trial sites** . At the state level, the California Consumer Privacy Act of 2018, or CCPA, as amended and supplemented by the California Privacy Rights Act, imposes obligations on businesses to which it applies. The CCPA allows for statutory fines for noncompliance. Although the CCPA exempts some data processed in the context of clinical trials, the CCPA, to the extent applicable to our business and operations, may increase compliance costs and potential liability with respect to other personal information we maintain about California residents. Other states have also enacted data privacy laws. Additional data privacy and security laws have been proposed at the federal, state, and local levels in recent years, which could further complicate compliance efforts. Outside the U. S., the European Union' s **General Data Protection Regulation, or EU** GDPR **,** and the United Kingdom' s GDPR, or UK GDPR, impose strict requirements for processing the personal data of individuals. For example, under the EU GDPR, government regulators may impose temporary or definitive bans on data processing, as well as fines of up to 20 million euros or 4 % of annual global revenue, whichever is greater. Further, individuals may initiate litigation related to our processing of their personal data. Certain foreign jurisdictions have enacted data localization laws and cross- border personal data transfer laws, which could make it more difficult to transfer information across jurisdictions, such as transferring or receiving personal data that originates in the **European Union, or** EU **. Additional jurisdictions continue to enact and modify their data privacy laws, which increases the complexity of the data privacy landscape** . Although we endeavor to comply with all applicable data privacy and security obligations, these obligations are quickly changing in an increasingly stringent fashion, creating some uncertainty as to how to comply, and potentially requiring us to modify our policies and practices, which may be costly and may divert the attention of management and technical personnel. Further, we may at times fail, or be perceived to have failed, to have complied and could face significant consequences. These consequences may include, but are not limited to, government enforcement actions, investigations and other proceedings; additional reporting requirements and / or oversight; bans on processing personal data; orders to destroy or not use personal data; and imprisonment of company officials. Any of these events could have a material adverse effect on our reputation, business, or financial condition, including but not limited to: interruptions or stoppages in our business operations, including our clinical trials; inability to process personal data or to operate in certain

jurisdictions; limited ability to develop or commercialize our products; expenditure of time and resources to defend any claim or inquiry; adverse publicity; or revision or restructuring of our operations. **Our business and operations could suffer in the event of an actual or perceived information security incident such as a cybersecurity breach, system failure, or other compromise of our systems and / or information, including information held by a third- party contractor or vendor.** We rely on both internal information technology systems and networks, and those of third **- party** ~~parties and their~~ vendors and contractors, to **acquire,** transmit, store and otherwise process information in connection with our business activities. **Our** ~~We are increasingly dependent upon our technology systems to operate our business and our~~ ability to effectively manage our business depends on the security, reliability and adequacy of our and our third- party ~~or other~~ contractors' ~~or~~ **and** vendors' technology systems **. Any incident, whether hostile or inadvertent, that adversely impacts the confidentiality, integrity or availability of our systems** and **/ or** data **,** ~~. Any cyberattack~~ including phishing, business email compromise, social engineering, ransomware or other malware, or any security breach, security incident ~~,~~ or other destruction, loss, or unauthorized use or other processing of data maintained or otherwise processed by us or on our behalf could result in a loss of intellectual property or misappropriation of trade secrets, disruptions to our business and operations, subject us to increased costs and require us to expend time and resources to address the matter, may subject us to claims, demands, and proceedings by private parties, regulatory investigations and other proceedings, and fines, penalties, and other liability and have a material adverse effect on our business. In addition, the loss, alteration or other damage to or other unavailability of pre- clinical data or clinical trial data from completed or ongoing clinical trials for our product candidates could result in delays in our development and regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Any cyber- attack, security breach or incident, or other destruction, loss or unauthorized processing of data maintained or otherwise processed by us or on our behalf, or the perception any such matter has occurred, could result in actual or alleged violations of applicable U. S. and international privacy, data protection, information security and other laws and regulations, harm our reputation and subject us to litigation and governmental investigations and proceedings by federal, state and local regulatory entities in the U. S. and by international regulatory entities, resulting in exposure to material civil and / or criminal proceedings and liability. In addition, we may incur significant additional expense to implement further measures relating to privacy, data protection and information security, whether in response to an actual or perceived security breach or incident or otherwise. To date, we have not experienced any material impact to our business, financial position or operations resulting from cyberattacks or other information security incidents; however, because of frequently changing attack techniques, along with the increased volume and sophistication of such attacks, our business, financial position or operations could be adversely impacted in the future. Moreover, the **increasingly distributed nature of computing, including** prevalent use of mobile devices ~~that~~ **to** access confidential information ~~,~~ **and** widespread use of cloud- based applications ~~with~~ **hosted in** remote data centers, ~~and ability to work remotely all increase~~ **increases** the risk of security breaches and incidents. These risks may be heightened due to the increasing number of our and our **third- party** vendors' and contractors' personnel working remotely. As cyber threats continue to evolve, we may be required to expend significant additional resources to continue to modify or enhance our protective measures or to investigate and remediate information security vulnerabilities **, threats and incidents** . While we have implemented **layered** security measures, our computer systems and the external systems and services used by our third- party contract manufacturers, or CMOs, and contract research organizations, or CROs, and their vendors and contractors remain potentially vulnerable to these events and there can be no assurance that we will be successful in preventing cyber- attacks or successfully mitigating their effects. Our liability insurance may not be sufficient in type or amount to cover us against claims related to security breaches, cyberattacks and other related breaches. ~~In addition, regulators are considering new cybersecurity regulations. For example, the SEC has proposed amendments to its disclosure rules regarding cybersecurity risk management, strategy, governance and incident reporting by public companies. These proposed regulations may impact the manner in which we operate.~~ A variety of risks associated with international operations could materially harm our business. We must dedicate additional resources to comply with numerous laws and regulations in each jurisdiction in which we operate and plan to operate outside the U. S., including those countries outside the U. S. in which we are conducting clinical trials. As we engage in significant cross- border and international activities, we will be subject to risks related to international operations, including: • different regulatory requirements for ~~initiating~~ **conducting** clinical trials, registering and maintaining approval of **, manufacturing and advertising** drugs in foreign countries; • reduced protection for intellectual property rights in certain countries; • unexpected changes in tariffs, trade barriers and regulatory requirements; • economic weakness, including inflation, political instability or open conflict in particular foreign economies and markets; • differing and multiple ~~payor~~ **payer** reimbursement regimes, government payers or patient self- pay systems; • compliance with tax, employment, immigration and labor laws for employees living or traveling abroad; • foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations of doing business in another country; • workforce uncertainty in countries where labor unrest is more common than in North America ~~; • different controlled substance legislation between countries and legislation in certain countries that may restrict, limit, or delay our ability to manufacture and / or transport our product candidates~~ ; • potential or actual violations of domestic and international anti- corruption laws, such as the U. S. Foreign Corrupt Practices Act and the U. K. Bribery Act, or of U. S. and international import, export and re- export control and sanctions laws and regulations, the likelihood of which may increase with an increase of operations in foreign jurisdictions, directly or indirectly through third parties (whose corrupt or other illegal conduct may subject us to liability), which may involve interactions with government agencies or government- affiliated hospitals, universities and other organizations, such as conducting clinical trials, selling our products, and obtaining necessary permits, licenses, patent registrations, and other regulatory approvals; • tighter restrictions on privacy and data protection, and more burdensome obligations associated with the collection, use and retention of data, including clinical data and genetic material, may apply in jurisdictions outside of North America; • production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; • business interruptions resulting from geopolitical actions, including war,

civil and political unrest ~~(such as the ongoing conflict between Russia and Ukraine)~~ and terrorism, or natural disasters including earthquakes, typhoons, floods and fires; and • supply and other disruptions resulting from the impact of public health pandemics or epidemics ~~, including the COVID- 19 pandemic,~~ on our strategic partners, third- party manufacturers, suppliers and other third parties upon which we rely. If we are unable to successfully manage these risks associated with cross- border and international activities, our business could be materially harmed ~~. Health pandemics or epidemics, including the COVID- 19 pandemic and other public health crises, may materially and adversely affect our business, financial condition and results of operations. The COVID- 19 pandemic and other public health crises may materially and adversely affect our business, financial condition and results of operations in several ways. For example, because our supply chain for raw materials, drug substance and drug product is worldwide, it could be subject to significant disruptions. There may be related restrictions on the export, import or shipment of raw materials, drug substance or drug product that could materially delay our business or clinical trials. In addition, our ability to initiate clinical sites and enroll patients globally may be negatively impacted by the COVID- 19 pandemic and other public health crises. With each additional COVID- 19 variant, there is a risk that COVID- 19 infections could affect a sizable number of employees at the same time, which could in turn significantly affect our operations. Additionally, if any of our critical vendors are impacted, our business could be affected if we become unable to timely procure essential equipment, clinical trial drug product, supplies or services. There continues to be uncertainty around the ultimate impact of the COVID- 19 pandemic on public health, business operations and the overall economy; therefore, the negative impact on our financial position, operating results and liquidity cannot be reasonably estimated at this time, but the impact may be material~~ . U. S. holders of our common shares may suffer adverse tax consequences if we are characterized as a passive foreign investment company. Generally, for any taxable year in which 75 % or more of our gross income is passive income, or at least 50 % of the average percentage of our assets (as determined under applicable Treasury Regulations, which may be determined in part by the market value of our common shares, which is subject to change) are held for the production of, or produce, passive income, we would be characterized as a passive foreign investment company, or PFIC, for U. S. federal income tax purposes. Based on ~~the price of our common shares and the composition of~~ our gross income and gross assets, we **are deemed** ~~do not believe we were~~ a PFIC for the taxable year ~~ended~~ **ending** December 31, ~~2022~~ **2023 and may** ~~but we could~~ be a PFIC ~~in~~ **for** subsequent **taxable** years. Our status as a PFIC is a fact- intensive determination made on an annual basis, and we cannot provide any assurance regarding our PFIC status for the current taxable year or future taxable years. If we are a PFIC for any year, U. S. holders of our common shares may suffer adverse tax consequences. Gains realized by non- corporate U. S. holders on the sale of our common shares would be taxed as ordinary income, rather than as capital gain, and the preferential tax rate applicable to dividends received on our common shares would be lost. Interest charges would also be added to taxes on gains and dividends realized by all U. S. holders. U. S. holders should consult their own tax advisors with respect to their particular circumstances. A U. S. holder may avoid these adverse tax consequences by timely making a qualified electing fund election. For each year that we would meet the PFIC gross income or asset test, an electing U. S. holder would be required to include in gross income its pro rata share of our net ordinary income and net capital gains, if any. A U. S. holder may make a qualified electing fund election only if we commit to provide U. S. holders with their pro rata share of our net ordinary income and net capital gains. We will provide, upon request, our U. S. holders with the information that is necessary in order for them to make a qualified electing fund election and to report their pro rata shares of ordinary earnings and net capital gains for each year we believe we were a PFIC. U. S. holders should consult their own tax advisors with respect to making this election and the related reporting requirements. A U. S. holder may also mitigate the adverse tax consequences by timely making a mark- to- market election. Generally, for each year that we meet the PFIC gross income or asset test, an electing U. S. holder would include in gross income the increase in the value of its common shares during each of its taxable years and deduct from gross income the decrease in the value of such shares during each of its taxable years. A mark- to- market election may be made and maintained only if our common shares are regularly traded on a qualified exchange, including the Nasdaq Global Market, or Nasdaq. Whether our common shares are regularly traded on a qualified exchange is an annual determination based on facts that, in part, are beyond our control. Accordingly, a U. S. holder might not be eligible to make a mark- to- market election to mitigate the adverse tax consequences if we are characterized as a PFIC. U. S. holders should consult their own tax advisors with respect to the possibility of making this election. In addition, if we are or become a PFIC (or our PFIC status is uncertain), it may deter certain U. S. investors from purchasing our common shares, which could have an adverse impact on the market price of our common shares. Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited. **We have significant** ~~At December 31, 2022 we had~~ Canadian federal net operating loss carryforwards ~~totaling $ 338. 0 million~~ which **are limited** ~~will begin to expire~~ in **life** ~~2026. In addition~~ , ~~we had~~ Canadian federal investment tax credit carryforwards ~~of $ 27. 3 million~~ and provincial investment tax credit carryforwards ~~of $ 8. 4 million~~ which ~~will begin to expire in 2023. The net operating losses which are limited in life and tax credit carryforwards~~ could expire unused and be unavailable to offset future income tax liabilities. The rules dealing with Canadian and U. S. federal, provincial, state, and local income taxation are constantly under review by persons involved in the legislative process and by the ~~Canadian~~ -- **Canada** Revenue Agency, Internal Revenue Service and the U. S. Treasury Department. Changes to tax laws, or changes in interpretations of existing laws (which changes may have retroactive application), including with respect to net operating losses and tax credits, could adversely affect us or holders of our common shares. In recent years, many such changes have been made and changes are likely to continue to occur in the future. Future changes in tax laws could have a material adverse effect on our business, cash flow, financial condition or results of operations. We may become subject to income tax in jurisdictions in which we are organized or operate, which would reduce our future earnings. There is a risk that we may become subject to income tax in jurisdictions outside of Canada and the U. S., if under the laws of any such jurisdiction, we are considered to be carrying on a trade or business there or earn income that is considered to be sourced there and we do not qualify for an exemption. In jurisdictions where we do not believe we are subject to tax, we can provide no certainty that tax authorities in those jurisdictions

will not subject one or more tax years to examination. Tax examinations are often complex as tax authorities may disagree with the treatment of items reported by us, the result of which could have a material adverse effect on our operating results and financial condition. Acquisitions or other strategic transactions could disrupt our business, cause dilution to our shareholders and otherwise harm our business. We actively evaluate various strategic transactions on an ongoing basis, including the acquisition of other businesses, products or technologies as well as pursuing strategic alliances, licensing transactions or investments in complementary businesses. Any of these transactions could be material to our financial condition and operating results and expose us to many risks, including: • disruption in our relationships with collaborators or suppliers as a result of such a transaction; • unanticipated liabilities related to acquired companies; • difficulties integrating acquired personnel, technologies and operations into our existing business; • retention of key employees; • diversion of management time and focus from operating our business to pursuing strategic transactions and managing any such strategic alliances, joint ventures or acquisition integration challenges; • dilution to our shareholders if we issue equity in connection with such transactions; • increases in our expenses and reductions in our cash available for operations and other uses; and • possible write- offs or impairment charges relating to acquired businesses. Foreign acquisitions involve unique risks in addition to those mentioned above, including those related to integration of operations across different cultures and languages, currency risks and the particular economic, political and regulatory risks associated with specific countries. Also, the anticipated benefit of any strategic alliance or acquisition may not materialize. Future acquisitions or dispositions could result in potentially dilutive issuances of our equity securities, the incurrence of debt, contingent liabilities or amortization expenses or write- offs of goodwill, any of which could harm our financial condition. We cannot predict the number, timing or size of future acquisitions, or the effect that any such transactions might have on our operating results. Our current and future operations in the U. S. and elsewhere will be subject, directly or indirectly, to applicable federal and state anti- kickback, fraud and abuse, false claims, transparency, health information privacy and security, and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, administrative burdens, and diminished profits and future earnings. Healthcare providers and third-party payers in the U. S. and elsewhere play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our ~~current~~ arrangements with ~~health~~ **healthcare** ~~care~~ providers **, ~~and our future arrangements with~~** third- party payers **, patients** and ~~customers~~ **other parties within the healthcare industry** may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations ~~, including, without limitation, the federal Anti-Kickback Statute and the federal False Claims Act and similar laws in foreign jurisdictions in which we conduct business,~~ that may constrain the business or financial arrangements and relationships through which we market, sell **,** and distribute any products for which we obtain marketing approval. ~~In addition~~ **Restrictions under applicable healthcare and data privacy laws and regulations include the following** , **some of which will apply only if and when** we **have a marketed product** ~~may be subject to transparency laws and patient privacy regulation by the federal government and by the U. S. states and foreign jurisdictions in which we conduct our business. The applicable federal, state and foreign healthcare laws and regulations that may affect our ability to operate include the following~~ : • the federal Anti- Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward 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 and state healthcare programs such as Medicare and Medicaid; • federal civil and criminal false claims laws, including the federal False Claims Act, which can be enforced through civil whistleblower, or qui tam actions, as well as civil monetary penalty laws can impose criminal and civil penalties, assessment, and exclusion from participation for various forms of fraud and abuse involving the federal ~~health~~ **healthcare** ~~care~~ programs, such as Medicare and Medicaid; • **the federal Health Insurance Portability and Accountability Act of 1996, or** HIPAA, ~~including its~~ **as amended, which imposes** criminal and civil liability ~~provisions~~ **for executing a scheme to defraud any healthcare benefit program** and **also establishes requirements related to the** privacy **~~and~~ ,** security ~~obligations imposed on covered entities~~ , and ~~business associates~~ **transmission of individually identifiable health information which apply to many healthcare providers, physicians, and third- party payers with whom we interact** ; • the **FDCA, which, among other things, strictly regulates drug product and medical device marketing, prohibits manufacturers from marketing such products for off- label use and regulates the distribution of samples; •** federal **laws that require pharmaceutical manufacturers** ~~Physicians Payment Sunshine Act, also referred~~ to **report certain calculated product prices to the government or provide certain discounts or rebates to government authorities or private entities, often** as **a condition of reimbursement under governmental healthcare programs; •** the ~~CMS~~ **so- called federal" sunshine law" or** Open Payments ~~,~~ which requires ~~applicable~~ manufacturers of ~~certain~~ drugs, devices, biologics **,** and medical supplies **to report to the Centers** for ~~which payment is available under~~ Medicare ~~,~~ **&** Medicaid **Services** ~~or the Children' s Health Insurance Program (with certain exceptions) to report annually to CMS,~~ information related to ~~: certain~~ payments ~~or~~ **and** other transfers of value ~~made~~ to ~~physicians (defined to include doctors of medicine and osteopathy, dentists, podiatrists, optometrists and licensed chiropractors), certain non- physician healthcare professionals (such as physician assistants and nurse practitioners among others), and~~ teaching hospitals **, physicians, and other healthcare practitioners,** as well as ~~information regarding~~ ownership ~~or~~ **and** investment interests held by physicians and their immediate family members; **• federal and state consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;** and • analogous state and foreign laws and regulations, such as state anti- kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third- party payers, including private insurers; state and foreign laws that **limit financial interactions between manufacturers** ~~require pharmaceutical companies to comply with the pharmaceutical industry' s voluntary compliance guidelines~~ and ~~the relevant compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare~~ ---- **health care** providers; ~~state and foreign laws that~~ require ~~drug~~ manufacturers to ~~report~~

~~information related~~ **adopt certain compliance standards; require disclosure** to ~~payments to physicians and other~~ -- **the** ~~healthcare providers or~~ **government and public of financial interactions; require disclosure of** marketing expenditures ~~; state~~ **or pricing information, regulate drug pricing** and ~~local laws~~ **/ or** ~~requiring~~ **require** the registration of pharmaceutical sales representatives **;** ; and state and foreign laws governing the collection, export, privacy, use, protection and security of biological materials and 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 ~~. Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare and privacy and data protection laws and regulations may involve substantial costs and may require us to undertake or implement additional policies or measures. We may face claims and proceedings by private parties, and claims, investigations and other proceedings by governmental authorities, relating to allegations that our business practices do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations, and it is possible that courts or governmental authorities may conclude that we have not complied with them, or that we may find it necessary or appropriate to settle any such claims or other proceedings. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, including, without limitation, damages, fines, disgorgement, imprisonment, exclusion from participation in government healthcare programs, such as Medicare and Medicaid, integrity oversight and reporting obligations, and the curtailment or restructuring of our operations, which could have a material adverse effect on our business. If any of the physicians or other providers or entities with whom we expect to do business, including our collaborators, is found not to be in compliance with applicable laws, it may be subject to criminal, civil or administrative sanctions, including exclusions from participation in government healthcare programs, which could also materially affect our business. Further, 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~~ . If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business. Our research and development activities involve the controlled use of potentially harmful biological materials as well as hazardous materials, chemicals, and various radioactive compounds typically employed in molecular and cellular biology. For example, we routinely use cells in culture and we employ small amounts of radioisotopes. We cannot completely eliminate the risk of accidental contamination or injury from the use, storage, handling, or disposal of these materials through our maintenance of up- to- date licensing and training programs. In the event of contamination or injury, we could be held liable for damages that result, and any liability could exceed our resources. We currently carry insurance covering certain claims arising from our use of these materials. However, if we are unable to maintain our insurance coverage at a reasonable cost and with adequate coverage, our insurance may not cover any liability that may arise. We are subject to Canadian federal, provincial, and local laws and regulations and may be subject to U. S. and / or foreign, laws and regulations governing the use, storage, handling, and disposal of these materials and specified waste products. Complying with regulations regarding the use of these materials could be costly, and if we fail to comply with these regulations, it could have a material adverse effect on our operations and profitability. We or the third parties upon whom we depend may be adversely affected by earthquakes or other natural disasters and our business continuity and disaster recovery plans may not adequately protect us from serious disaster. Our headquarters are located in Burnaby, British Columbia, Canada. We are vulnerable to natural disasters such as earthquakes that could disrupt our operations. If a natural disaster, power outage, fire or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as the manufacturing facilities of our CMOs, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. Although we carry insurance for earthquakes and other natural disasters, we may not carry sufficient business interruption insurance to compensate us for all losses that may occur. The disaster recovery and business continuity plans we have in place may not be adequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of a natural disaster or earthquake, which could have a material adverse effect on our business. In addition, we may lose samples or other valuable data. The occurrence of any of the foregoing could have a material adverse effect on our business. Risks Related to the Discovery, Development and Commercialization of Our Product Candidates We currently have no products approved for commercial sale and are investing significant efforts and financial resources in the development of our ~~lead~~ **clinical- stage** product candidate, XEN1101 for the treatment of epilepsy **, MDD and potentially other neurological disorders** . Our future business success depends on the continued development and ultimate regulatory approval of XEN1101. We will need to successfully enroll and complete our XEN1101 Phase 3 ~~program~~ **epilepsy clinical trials and any other future Phase 3 clinical trials** . The future regulatory and commercial success of XEN1101 is subject to a number of risks, including: • successful patient enrollment in clinical trials and ultimate completion of clinical trials; • successful efficacy data from our clinical programs that support acceptable risk- benefit profiles of XEN1101 in the intended patient populations; • receipt and maintenance of marketing approvals from applicable regulatory authorities; • completing any post- marketing studies required by applicable regulatory authorities; • obtaining and maintaining patent and trade secret protection and regulatory exclusivity for XEN1101; • making arrangements with third- party manufacturers for both clinical and commercial supplies of XEN1101; • establishing sales, marketing and distribution capabilities and commercial launch of XEN1101, if and when approved, whether alone or in collaboration with others; • successful commercial launch of XEN1101, if and when approved; • acceptance of XEN1101, if and when approved, by patients, the medical community and third- party ~~payors~~ **payers** ; • obtaining and maintaining acceptable pricing, third- party insurance coverage and adequate reimbursement; • maintaining a continued acceptable safety profile of XEN1101 following approval; • effectively competing with other therapies; • enforcing and defending intellectual property rights and claims; and • raising sufficient funds to support ~~the~~ regulatory approval and commercialization activities. Many of these risks are beyond our control, including the risks related to clinical development, the

regulatory submission process, potential threats to our intellectual property rights and the manufacturing, marketing and sales efforts of any future collaborator. If we or any collaborator are unable to develop, receive regulatory approval for, or successfully commercialize XEN1101 for our initial or potential additional indications, or if we experience delays as a result of any of these risks or otherwise, our business could be materially harmed. In addition, of the large number of drugs in development in the pharmaceutical industry, only a small percentage result in the submission of an NDA to the FDA and even fewer are approved for commercialization. Furthermore, even if we do receive regulatory approval for XEN1101 for any indication, any such approval may be subject to limitations on the indications or uses or patient populations for which we may market XEN1101. Accordingly, even if we are able to obtain the requisite financing to continue to fund our development programs, we cannot ensure that we will successfully develop or commercialize XEN1101 for any indication. Our approach to drug discovery is unproven, and we do not know whether we will be able to develop any products of commercial value. Our approach to drug discovery may not reproducibly or cost- effectively result in the discovery of product candidates and development of commercially viable products that safely and effectively treat human disease. Our drug discovery efforts may initially show promise in identifying additional ~~potential~~ product candidates yet fail to yield viable product candidates for clinical development or commercialization. Such failure may occur for many reasons, including that any product candidate may, on further study, be shown to have serious or unexpected side effects or other characteristics that indicate it is unlikely to be safe or otherwise does not meet applicable regulatory criteria and / or not be capable of being produced in commercial quantities at an acceptable cost, or at all. If our discovery activities fail to identify novel targets for drug discovery, or such targets prove to be unsuitable for treating human disease, or if we are unable to develop product candidates with specificity and selectivity for such targets, we will fail to develop viable products. If we fail to develop and commercialize viable products, we will not achieve commercial success. Results of pre- clinical studies and / or earlier clinical trials may not be predictive of the results of later- stage clinical trials and the results of our clinical trials may not satisfy regulatory requirements and we may experience delays or unexpected difficulties in obtaining regulatory approval. The results of pre- clinical studies, either generated by us ~~, such as for XEN901 (licensed to Neurocrine Biosciences and is now known as NBI- 921352)~~ , by our CROs or by other third parties from which we have in- licensed or acquired a product candidate, may not be predictive of results in clinical testing. Moreover, pre- clinical results can often be difficult to compare across different studies for a variety of reasons, including differences in experimental protocols and techniques, personnel, equipment and other factors, which may make the pre- clinical results less reliable and predictive of clinical trial results. In addition, published clinical data or case reports from third parties or early clinical trial data of our product candidates may not be predictive of the results of later- stage clinical trials. Interpretation of results from early, usually smaller, studies that suggest a clinically meaningful response in some patients, requires caution. Results from later stages of clinical trials enrolling more patients may fail to show the desired safety and efficacy results or otherwise fail to be consistent with the results of earlier trials of the same product candidate. Later clinical trial results may not replicate earlier clinical trials for a variety of reasons, including differences in trial design, different trial endpoints (or lack of trial endpoints in exploratory studies), patient population, number of patients, patient selection criteria, trial duration, drug dosage and formulation and lack of statistical power in the earlier studies. These uncertainties are enhanced where the diseases or disorders under study lack established clinical endpoints, validated measures of efficacy, as is often the case with ~~orphan diseases or~~ disorders for which no drugs have been developed previously and where the product candidates target novel mechanisms ~~. For example, to our knowledge, NBI- 921352 is the first selective Nav1. 6 sodium channel inhibitor being developed for the treatment of epilepsy and therefore standard pre- clinical models may not be predictive of clinical efficacy due to its novel molecular mechanism~~ . Further, our product candidates may not be approved even if they achieve their primary endpoint in our Phase 3 clinical trials. The FDA, EMA or foreign regulatory authorities may disagree with our trial design and our interpretation of data from pre- clinical studies and clinical trials or require additional data. In addition, any of these regulatory authorities may change its requirements for the approval of a product candidate even after reviewing and providing comments or advice on a protocol for a pivotal clinical trial that, if successful, would potentially form the basis for an application for approval by the FDA, EMA or another foreign regulatory authority. For example, the FDA may refuse to accept our planned NDA for substantive review or may conclude after review of our data that our application is insufficient to obtain regulatory approval. If the FDA does not approve our planned NDA, it may require that we conduct additional clinical, nonclinical or manufacturing studies before it will reconsider our application. Depending on the extent of these or any other studies required by FDA or another regulatory authority, approval of an NDA or equivalent filing may be significantly delayed or may require us to expend more resources than we have available. Furthermore, applicable regulatory authorities may also approve our product candidates for a narrower indication or population than we request or may grant approval contingent on the performance of costly post- marketing commitments. Interim, initial, " top- line " and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data. From time to time, we may publicly disclose preliminary or top- line data from our pre- clinical studies and clinical trials, which are based on preliminary analyses of then- available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular pre- clinical study or clinical trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the top- line or preliminary results that we report may differ from future results of the same studies or trials, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Top- line data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, top- line data should be viewed with caution until the final data are available. Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which

could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and could have a material adverse effect on the success of our business. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure. If the interim, topline or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, results of operations, prospects or financial condition. Further, disclosure of interim, top- line or preliminary data by us or by our competitors could result in volatility in the price of our common shares. Our and our collaborators' clinical product candidates, which include XEN1101 ~~, XEN496,~~ and NBI- 921352 (being developed by our collaborator Neurocrine Biosciences), along with product candidates we expect to enter clinical development, which include our pre- clinical compounds, are in varying stages of development and will require substantial clinical development, testing and regulatory approval prior to commercialization. Before obtaining regulatory approvals for the commercial sale of our product candidates, we, or our collaborators, must demonstrate through lengthy, complex and expensive pre- clinical testing and clinical trials that each product candidate is both safe and effective for use in each target indication. Failure can occur at any time during the clinical trial process. Clinical trials often fail to demonstrate safety and efficacy of the product candidate studied for the target indication. Most product candidates that commence clinical trials are never approved as products. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials. In addition to the safety and efficacy trials of any product candidate, clinical trial failures may result from a multitude of factors including flaws in trial design, dose selection, statistical analysis plan, placebo effect, patient enrollment criteria, patient compliance and trial execution. Data obtained from trials and studies are susceptible to varying interpretations, and regulators may not interpret our data as favorably as we do, which may delay, limit or prevent regulatory approval. Failure of a clinical trial due to any of these reasons could materially harm our business and the market price of our common shares. In the case of some of our and our collaborators' product candidates, we and our collaborators are seeking to develop treatments for certain diseases or disorders for which there is relatively limited clinical experience, and clinical trials may use novel endpoints and measurement methodologies or subjective patient feedback, which adds a layer of complexity to these clinical trials and may delay regulatory approval. Negative or inconclusive results from our, or our collaborators', clinical trials could lead to a decision or requirement to conduct additional pre- clinical testing or clinical trials or result in a decision to terminate the continued development of a product candidate. For example, in October 2021, we released topline data from our **Phase 2b** X- TOLE clinical trial of XEN1101 in adult patients with focal epilepsy. ~~Even though the~~ **In addition, in November 2023, we released** topline data from our **Phase 2** X- ~~TOLE~~ **NOVA** clinical trial ~~were positive,~~ **of XEN1101 in patients with MDD.** ~~there~~ **There** can be no assurance that our ongoing XEN1101 Phase 3 ~~program~~ **epilepsy clinical trials or any other future Phase 3 clinical trials** will demonstrate adequate efficacy and safety results and that we will be able to obtain regulatory approval of XEN1101. Any of the foregoing outcomes would materially and adversely impact our business, product candidate pipeline and future prospects. If our, or our collaborators', product candidates are not shown to be both safe and effective in clinical trials, such product candidates will be unable to obtain regulatory approval or be successfully commercialized. In addition, our, or our collaborators', failure to demonstrate positive results in clinical trials in any indication for which we, or our collaborators, are developing clinical product candidates could adversely affect development efforts in other indications. In such case, we would need to develop other compounds and conduct associated pre- clinical testing and clinical trials, as well as potentially seek additional financing, all of which would have a material adverse effect on our business, growth prospects, operating results, financial condition and results of operations. We, or our collaborators, may not be able to identify, recruit and enroll a sufficient number of patients, or those with required or desired characteristics to achieve diversity in a study, to complete clinical trials in a timely manner, or at all. Patient enrollment for clinical trials ~~for ultra- orphan, orphan and niche indications and for more prevalent conditions~~ is affected by factors including: • severity of the disease or disorder under investigation; • design of the study protocol; • size of the patient population and geographic dispersion; • identification of patients; • eligibility criteria for the study in question; • perceived risks and benefits of the product candidate under study; • our ability to recruit clinical trial investigators with the appropriate competencies **, staff** and experience; • proximity and availability of clinical trial sites for prospective patients; • availability of competing therapies and clinical trials; • efforts to facilitate timely enrollment in clinical trials; and • patient referral practices of physicians. **Our** ~~The limited patient populations in ultra- orphan, orphan~~ and ~~niche indications, such as KCNQ2- DEE, SCN8A- DEE and other early infantile epileptic encephalopathies, present significant recruitment challenges for clinical trials and a full understanding of the size of these populations is still relatively unknown. Many of these patients may not be suitable or available to participate in our, or~~ our collaborators **'** ~~'~~, ~~clinical trials. This means that we, or our collaborators, will generally have to run multi- site and potentially multi- national trials, which can be expensive and require close coordination and supervision. Our and our collaborator' s~~ clinical trials will compete with other clinical trials for product candidates that are in the same therapeutic areas as our product candidates, and this competition will reduce the number and types of patients available to us, because some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors. Since the number of qualified clinical investigators is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials at such clinical trial sites. Our and our ~~collaborator~~ **collaborators '** ~~' s~~ inability to enroll a sufficient number of patients for our clinical trials would result in significant delays or might require us to abandon one or more clinical trials altogether. Delays in patient enrollment may result in increased costs, affect the timing or outcome of the planned clinical trials, affect product candidate development and approval process and jeopardize our ability to seek and obtain the regulatory approval required to commence product sales and generate revenue, any of which could cause the value of our company to decline and limit our ability to obtain

additional financing if needed. Our success also depends on the collective performance, contributions, and expertise of the personnel who manage our clinical trial sites. There is significant competition for qualified personnel, particularly those with higher educational degrees, in the biopharmaceutical and related services industries. Increased personnel turnover and labor shortages facing the biopharmaceutical services industry could have a negative impact on the third parties we rely on to execute our clinical trials. While we seek to choose trial sites with adequate staffing support, we cannot be certain that personnel turnover or the broader labor market dynamics in this industry will not negatively impact our trial sites. If our sites are negatively impacted by these factors, our ability to enroll our clinical trials in a timely fashion may be hindered and might negatively affect our business, development timelines, and financial condition. To obtain the requisite regulatory approvals to commercialize any of our product candidates, we, or our collaborators, must demonstrate through extensive pre- clinical studies and clinical trials that our, or our collaborators', product candidates are safe and effective in humans. We, or our collaborators, may experience delays in completing our, or our collaborators', clinical trials or pre- clinical studies, and initiating or completing additional clinical trials or pre- clinical studies, including as a result of regulators not allowing or delay in allowing clinical trials to proceed under an IND, or not approving or delaying approval for any clinical trial grant or similar approval we need to initiate a clinical trial. We, or our collaborators, may also experience numerous unforeseen events during our clinical trials that could delay or prevent our, or our collaborators', ability to **complete development for a product candidate, or** receive marketing approval or commercialize the product candidates we, or our collaborators, develop, including: • delay or failure in obtaining the necessary approvals from regulators or institutional review boards, or IRBs, in order to commence a clinical trial at a prospective trial site, or their suspension or termination of a clinical trial once commenced; • inability to reach agreement with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites, or the breach of such agreements; • we may experience challenges or delays in recruiting principal investigators or study sites to lead our clinical trials; • side effects or adverse events in study participants presenting an unacceptable safety risk; • failure of third- party contractors, such as CROs, or investigators to comply with regulatory requirements, including good clinical practices, or GCPs; • difficulty in having patients complete a trial, adhere to the trial protocol, or return for post- treatment follow- up; • the number of subjects or patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be insufficient or slower than we anticipate, and the number of clinical trials being conducted at any given time may be high and result in fewer available patients for any given clinical trial, or patients may drop out of these clinical trials at a higher rate than we anticipate; • clinical sites deviating from trial protocol or dropping out of a trial; • we may have to amend clinical trial protocols submitted to regulatory authorities or conduct additional studies to reflect changes in regulatory requirements or guidance, which it may be required to resubmit to an IRB and regulatory authorities for re- examination; • challenges or delays with accessing certain species of animals to complete our pre- clinical studies; • problems with investigational medicinal product storage, stability and distribution; **•** our inability to manufacture, or obtain from third parties, adequate supply of drug substance or drug product sufficient to complete our pre- clinical studies and clinical trials, including supply chain issues resulting from any events affecting raw material supply or manufacturing capabilities abroad; • a requirement to undertake and complete additional pre-clinical studies to generate data required to initiate clinical development or to support the continued clinical development of a product candidate or submission of an NDA or equivalent; • unforeseen disruptions, caused by man- made or natural disasters, public health pandemics or epidemics, civil unrest or military conflict, or other business interruptions ~~, including, for example, the COVID- 19 pandemic~~ ; and • governmental or regulatory delays and changes in regulatory requirements, policy and guidelines. These risks and uncertainties could impact any of our, or our collaborators', clinical programs and any of the clinical, regulatory or operational events described above could change our, or our collaborators', planned clinical and regulatory activities. ~~For example, we previously experienced a significant reduction in the rate of new patient enrollment in our X- TOLE trial due to the COVID- 19 pandemic. While we were able to complete recruitment for this trial, we cannot be certain that the ongoing COVID- 19 pandemic or related variants will not negatively impact other trials in the future. In addition, we have experienced an impact on the initiation of clinical sites and on enrollment of patients in our EPIK clinical trial due to the ongoing COVID- 19 pandemic. Further challenges~~ **Challenges** in enrolling and retaining patients in our clinical trials, including in our XEN1101 Phase 3 ~~program~~ **epilepsy clinical trials** , whether as a result of ~~the COVID- 19 pandemic~~ **pandemics** , geopolitical events, or for any other reasons, may further delay the trials or cause them to be discontinued. The results of any Phase 3 or other pivotal clinical trials ~~, including without limitation our EPIK trial,~~ may not be adequate to support marketing approval. These clinical trials are lengthy and ~~, with respect to non- orphan indications,~~ usually involve many hundreds to thousands of patients. Clinical trials can also be lengthy due to the challenge of identifying patients ~~, especially in orphan indications such as KCNQ2- DEE~~ . Even if patients are successfully identified, they may fail screening criteria **,** including baseline seizure burden **for epilepsy clinical trials,** and, as a result, not be enrolled in the trial. Any challenges associated with identifying, screening and / or enrolling patients in our trials may extend the time needed to complete our ~~EPIK trial or other~~ clinical trials or require additional sites to be initiated in order to achieve target enrollment numbers and to complete our clinical trials, which may increase the cost of our operations and / or delay the timing of our regulatory approval. In addition, if the FDA, EMA or another foreign regulator disagrees with our, or our collaborators', choice of the key testing criterion, or primary endpoint, or if the results for the primary endpoint are not robust or significant relative to the control group of patients not receiving the experimental therapy, or our statistical analysis is inconclusive, such regulator may refuse to approve our product candidate in the region in which it has jurisdiction. The FDA, EMA or other foreign regulators also may require additional clinical trials as a condition for approving any of these product candidates. We, or our collaborators, could also encounter delays if a clinical trial is suspended or terminated by us, by our collaborators, by the IRBs of the institutions in which such trial is being conducted, by any Data Safety Monitoring Board for such trial, or by the FDA, EMA or other foreign regulatory authorities. Such authorities may impose such a suspension or termination due to a number of factors, including failure to

conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA, EMA or other foreign regulatory authorities resulting in the imposition of a clinical hold, product candidate manufacturing problems, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. In addition, delays can occur due to safety concerns arising from trials or other clinical data regarding another company' s product candidate in the same compound class as one of ours. Additionally, changes in applicable regulatory requirements and guidance may occur and we may need to amend clinical trial protocols to reflect these changes or to include additional objectives that could yield important scientific information critical to our overall development strategy. The protocol amendment process often requires review and approval by several review bodies, including regulatory agencies and scientific, regulatory and ethics boards and IRBs which may affect timely completion of a clinical trial. Further, these protocol amendments may not be accepted by the review bodies in the form submitted, or at all, which may impact costs, timing or successful completion of a clinical trial. ~~Since March 2020, the FDA, EMA and other foreign regulatory authorities have issued various COVID- 19 related guidance documents for sponsors and manufacturers. Recently, President Biden announced that the administration intends to end the COVID- 19 national and public health emergencies on May 11, 2023. The full impact of the termination of the public health emergencies on FDA and other regulatory policies and operations is unclear.~~ If we, or our collaborators, experience delays in the completion of, or termination of, any clinical trial of one of our product candidates, the commercial prospects of the product candidate may be harmed, the period during which we may have the exclusive right to commercialize our products under patent protection could be shortened, and our, or our collaborators', ability to commence product sales and generate product revenue from the product will be delayed. In addition, any delays in completing our clinical trials will increase our costs and slow down our product candidate development and approval process **and may ultimately lead to the termination of a clinical trial and development of a product candidate** . Any of these occurrences may harm our business, financial condition and prospects significantly. In addition, many of the factors that cause or lead to a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our, or our collaborators', product candidates ~~. XEN496 targets an ultra- orphan indication of KCNQ2- DEE and the FDA has indicated that a single, small pivotal trial may be sufficient to demonstrate effectiveness and safety in KCNQ2- DEE provided that no new or unexpected safety issues arise during drug development. However, other regulatory authorities may require additional data. Further, even though we believe the safety and efficacy profile of ezogabine, the active ingredient in XEN496, in pediatric patients with KCNQ2- DEE generated to date by others appears promising based on published clinical case reports, we do not yet know if our pediatric- specific formulation of XEN496 will have the same or similar safety, pharmacokinetic and / or efficacy profile in pediatric patients with KCNQ2- DEE as the original formulation of ezogabine. If we are unable to replicate the published clinical case reports, due to the new formulation or any other factors, the clinical development of XEN496 may not be successful and the FDA, EMA or other regulatory authorities may require additional data in more patients or we may not be able to generate sufficient data for approval in this patient population~~ . Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following regulatory approval, if obtained. Undesirable side effects caused by any of our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA, EMA or comparable foreign regulatory authorities. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. For example, **while adverse events** in **our X- TOLE and X- NOVA** clinical trials ~~of XEN1101 to date, adverse events~~ were generally mild or moderate in severity ~~. However~~ , there can be no guarantee that we ~~would~~ **will** observe a similar tolerability profile of XEN1101 in our ongoing ~~or planned~~ Phase 3 **epilepsy or other** clinical trials or in other future clinical trials. Many compounds that initially showed promise in clinical or earlier- stage testing are later found to cause undesirable or unexpected side effects that prevented further development of the compound. If unacceptable side effects arise in the development of our product candidates, we, the FDA, EMA or comparable foreign regulatory authorities, the IRBs, or independent ethics committees at the institutions in which our trials are conducted, could suspend, limit or terminate our clinical trials, or the independent safety monitoring committee could recommend that we suspend, limit or terminate our trials, or the FDA, EMA or comparable foreign regulatory authorities could order us to cease clinical trials or deny approval of our product candidates for any or all targeted indications. Treatment- emergent side effects that are deemed to be drug- related could delay recruitment of clinical trial subjects or ~~may~~ cause subjects that enroll in our clinical trials to discontinue participation in our clinical trials. In addition, these side effects may not be appropriately recognized or managed by the treating medical staff. We may need to train medical personnel using our product candidates to understand the side effect profiles for our clinical trials and upon any commercialization of any of our product candidates. Inadequate training in recognizing or managing the potential side effects of our product candidates could result in harm to patients that are administered our product candidates. Any of these occurrences may adversely affect our business, financial condition and prospects significantly. Moreover, clinical trials of our product candidates are conducted in carefully defined sets of patients who have agreed to enter into clinical trials. Consequently, it is possible that our clinical trials may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any, or alternatively fail to identify undesirable side effects. Changes in methods of product candidate manufacturing or formulation may result in additional costs or delay. As product candidates are developed through pre- clinical to late- stage clinical trials towards approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods and formulations, are altered along the way in an effort to optimize products, processes and results, to extend patent protection and / or to target different populations. For example, ~~XEN496 is a pediatric- specific formulation of ezogabine and~~ we have ~~also~~ developed a pediatric formulation for NBI- 921352 that was included in the license to Neurocrine Biosciences. Any of these changes could cause our product candidates to perform

differently and not provide the same drug exposure profile in children and / or cause side effects different to those observed with the same formulation in adults or with other formulations. Unexpected changes in the performance of a new formulation may affect the results of planned clinical trials or other future clinical trials conducted with the altered materials. This could delay completion of clinical trials, require the conduct of additional bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs and / or delay or jeopardize approval of our product candidates and / or jeopardize our, or our collaborators', ability to commence product sales and generate revenue. The regulatory approval process is expensive and the time required to obtain approval from the FDA, EMA or other foreign regulatory authorities in other jurisdictions to sell any product is uncertain and may take years. Whether regulatory approval will be granted is unpredictable and depends upon numerous factors, including the substantial discretion of the regulatory authorities. Approval policies, regulations, or the type and amount of pre- clinical and clinical data necessary to gain approval may change during the course of a product candidate' s clinical development and may vary among jurisdictions. Moreover, pre- clinical and clinical data are often susceptible to varying interpretations and analyses, and even if the pre- clinical studies show promising results and clinical trials are successfully completed, we cannot guarantee that the FDA, EMA or other foreign regulatory authorities in other jurisdictions will interpret the results as we do, and more trials, manufacturing- related studies or non- clinical studies could be required before we submit our product candidates for approval. Many companies that have believed their product candidates performed satisfactorily in pre- clinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products. To the extent that the results of our studies and trials are not satisfactory to the FDA, EMA or other foreign regulatory authorities in other jurisdictions for support of a marketing application, approval of our product candidates may be significantly delayed, or we may be required to expend significant additional resources, which may not be available to us, to conduct additional trials in support of potential approval of our product candidates. It is also possible that none of our existing product candidates or any of our future product candidates will ever obtain regulatory approval, even if we expend substantial time and resources seeking such approval. Our product candidates could fail to receive regulatory approval for many reasons, including the following: • the FDA, EMA or other foreign regulatory authorities may disagree with the design or implementation of our, or our collaborators', clinical trials; • we, or our collaborators, may be unable to demonstrate to the satisfaction of the FDA, EMA or foreign other regulatory authorities that a product candidate is safe and effective for its proposed indication; • the results of clinical trials may not meet the level of statistical significance required by the FDA, EMA or other foreign regulatory authorities for approval; • we, or our collaborators, may be unable to demonstrate that a product candidate' s clinical and other benefits outweigh its safety risks; • the FDA, EMA or other foreign regulatory authorities may disagree with our, or our collaborators', interpretation of data from pre- clinical studies or clinical trials; • the data collected from clinical trials of our product candidates may not be sufficient to support the submission of **an** ~~a New Drug Application, or~~ NDA, or other submission or to obtain regulatory approval in the U. S. or elsewhere; • the FDA, EMA or other foreign regulatory authorities may fail to approve the manufacturing processes, controls or facilities of third- party manufacturers with which we, or our collaborators, contract for clinical and commercial supplies; • the pre- approval inspections of Xenon, manufacturing, clinical sites, pre- clinical or clinical service providers, conducted by regulatory authorities may identify errors or omissions that may result in the product candidate not being approved; and • the approval policies or regulations of the FDA, EMA or other foreign regulatory authorities may significantly change in a manner rendering our, or our collaborators', clinical data insufficient for approval. Even if we, or our collaborators, obtain approval for a particular product, regulatory authorities may grant approval contingent on the performance of costly post- approval commitments including clinical trials, or may approve a product with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product. In addition, the FDA, EMA or other foreign regulatory authorities' policies with respect to clinical trials may change and additional government regulations may be enacted. For instance, the regulatory landscape related to clinical trials in the EU recently evolved. The EU Clinical Trials Regulation, or CTR, which was adopted in April 2014 and repealed the EU Clinical Trials Directive, became applicable on January 31, 2022. The implementation of the CTR also includes the implementation of the Clinical Trials Information System, or CTIS, a new clinical trial portal and database that will be maintained by the European Medicines Agency, or EMA, in collaboration with the European Commission and the EU Member States. The objectives of the CTR include consistent rules for conducting trials throughout the EU, consistent data standards and adverse events listing, and consistent information on the authorization status. Information on the conduct and results of each clinical trial carried out in the EU will be made publicly available. The CTR authorizes EU Member States to regulate certain aspects of clinical trials at the national level. To the extent an EU Member State where we plan to conduct any of our clinical trials is slow to adopt CTIS or implements other regulatory changes at the national level, **or technical issues are encountered with the CTIS system and / or process,** our clinical trial may be delayed in such EU Member State, and our costs may be increased. The main legislation that applies to clinical trials in the **United Kingdom, or** UK **,** is the UK Medicines for Human Use (Clinical Trials) Regulations 2004, which transposes the EU Clinical Trials Directive into domestic law. The UK has implemented the Integrated Research Application System, which allows a single application to be reviewed by both the Medicines and Healthcare products ~~–~~Regulatory Agency and a research ethics committee at the same time. Requirements and obligations that relate to the conduct of clinical trials in the UK remain largely aligned with the EU position. Complying with changes in regulatory requirements in different jurisdictions can result in additional costs, delay our clinical development plans, or expose us to greater liability if we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies governing clinical trials, our development plans, including **our** XEN1101 Phase 3 ~~development program~~ **epilepsy clinical trials** , may be impacted. Additionally, because there may be approved treatments for some of the diseases or disorders for which we may seek approval, in order to receive regulatory approval, we may need to demonstrate in clinical trials that the product candidates we develop to treat those diseases or disorders are not only safe and effective, but may need to be compared to existing products, which may make it more difficult for our product candidates to receive regulatory approval or adequate reimbursement. Even if we obtain and maintain approval

for our product candidates from one jurisdiction, we may never obtain approval for our product candidates in other jurisdictions, which would limit our market opportunities and adversely affect our business. Sales of our approved products, if any, will be subject to the regulatory requirements governing marketing approval in the countries in which we obtain regulatory approval, and we plan to seek, ourselves or with collaborators, regulatory approval to commercialize our product candidates in North America, the EU and in additional foreign countries. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries and regulatory approval in one country does not ensure approval in any other country, while a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory approval process in others. For example, approval in the U. S. by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one foreign regulatory authority does not ensure approval by the FDA, EMA or regulatory authorities in other countries. Approval procedures vary among jurisdictions and can be lengthy and expensive, and involve requirements and administrative review periods different from, and potentially greater than, those in the U. S., including additional pre- clinical studies or clinical trials. Even if our product candidates are approved, regulatory approval for any product may be withdrawn by the regulatory authorities in a particular jurisdiction. We do not have experience in obtaining regulatory approval in international markets. If we, or our collaborators, fail to comply with regulatory requirements or to obtain and maintain required approvals, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed. **Although** ~~If we fail to obtain or maintain~~ orphan drug designation **has been granted in the United States and Europe to NBI- 921352** ~~or~~ **for** ~~other~~ ~~-~~ **the treatment** ~~regulatory exclusivity for some~~ of ~~our product candidates~~ **SCN8A- DEE** , **we may not** ~~our competitive position would~~ be **able** ~~harmed. Although we have pending provisional and non- provisional patent applications related~~ to ~~XEN496~~ **realize any value from such designations. NBI- 921352** , **being developed** ~~this product candidate is not currently covered~~ by **our collaborator Neurocrine Biosciences, has received** ~~any issued patents and we may have to rely solely on~~ orphan drug designation ~~to gain market exclusivity for this~~ **from the FDA and orphan medicinal** product ~~candidate~~ **designation was granted by the European Commission for the treatment of SCN8A- DEE** . Currently, ~~this~~ **orphan drug** designation provides market exclusivity in the U. S. and the EU for seven years and ten years, respectively, if a product is the first such product approved for such orphan indication. In the EU, for orphan medicines, a valid and completed Pediatric Investigation Plan, or PIP, could qualify the sponsor for a two- year marketing exclusivity extension to the ten- year marketing exclusivity which is granted at the time of review of the orphan medicinal designation. The orphan drug market exclusivity does not, however, pertain to indications other than those for which the drug was specifically designated in the approval, nor does it prevent other types of drugs from receiving orphan designations or approvals in these same indications. Further, even after an orphan drug is approved, the FDA can subsequently approve a drug with similar chemical structure for the same condition if the FDA concludes that the new drug is clinically superior to the orphan product or a market shortage occurs. **Orphan drug designation does not provide the drug any advantage in the regulatory review or approval process other than potential fee reductions, nor does such designation increase the likelihood that the drug will receive marketing approval.** In Catalyst Pharms., Inc. v. Becerra, 14 F. 4th 1299 (11th Cir. 2021), the court disagreed with the FDA' s longstanding position that the orphan drug exclusivity only applies to the approved use or indication within an eligible disease. This decision created uncertainty in the application of the orphan drug exclusivity in the U. S. ~~.~~ On January 24, 2023, the FDA published a notice in the Federal Register to clarify that while the FDA ~~complies~~ **complied** with the court' s order in Catalyst, the FDA intends to continue to apply its longstanding interpretation of the regulations to matters outside of the scope of the Catalyst order – that is, the FDA will continue tying the scope of orphan- drug exclusivity to the uses or indications for which a drug is approved, which permits other sponsors to obtain approval of a drug for new uses or indications within the same orphan designated disease or condition that have not yet been approved. It is unclear how future litigation, legislation, agency decisions and administrative actions will impact the scope of the orphan drug exclusivity. In the EU, orphan exclusivity may be reduced to six years if the drug no longer satisfies the original designation criteria or can be lost altogether if the marketing authorization holder consents to a second orphan drug application or cannot supply enough drug, or when a second applicant demonstrates its drug is " clinically superior " to the original orphan drug. **Although** ~~We have received orphan drug designation from~~ the FDA **has** ~~and orphan medicinal product designation was~~ granted ~~by the European Commission to XEN496 as a treatment of KCNQ2- DEE and Neurocrine Biosciences received orphan drug designation from the FDA for NBI- 921352 as a treatment of SCN8A- DEE. If we seek orphan drug designations for other indications or in other jurisdictions, we may fail to receive such orphan drug designations and, even if we succeed, such orphan drug designations may fail to result in or maintain orphan drug exclusivity upon approval, which would harm our competitive position. Further, not all jurisdictions, such as Canada, have orphan drug designations. Neither orphan drug designation, nor~~ rare pediatric disease, or RPD, ~~designation gives the drug any advantage in the regulatory review or approval process other than potential fee reductions, and in the case of RPD, priority review vouchers. Although the FDA has granted RPD~~ designation to NBI- 921352 for the treatment of SCN8A- DEE, we may not be able to realize any value from such designation. NBI- 921352, being developed by our collaborator Neurocrine Biosciences, has received RPD designation for the treatment of SCN8A- DEE. The FDA defines a " rare pediatric disease " as a disease that affects fewer than 200, 000 individuals in the U. S. primarily under the age of 18 years old. Under the FDA' s RPD priority review voucher program, upon the approval of an NDA or a biologics license application, BLA, for the treatment of an RPD, the sponsor of such application would be eligible for a priority review voucher that can be used to obtain priority review for a subsequent NDA or BLA. There is no assurance Neurocrine Biosciences will receive a RPD priority review voucher or that use of the priority review voucher will result in a faster review or approval for a subsequent marketing application. It is possible that even if Neurocrine Biosciences obtains approval for NBI- 921352 in SCN8A- DEE and qualifies for such a priority review voucher, the program may no longer be in effect at the time of approval of this product candidate. Also, although priority review vouchers may be freely sold or transferred to third parties, there is no guarantee that we will be able to realize any value if we or any of our collaborators were to sell a priority review voucher to a third- party. In addition, Congress extended FDA

authorization to designate RPDs through September 30, 2024 and award RPD priority review vouchers through September 30, 2026. RPD designation does not ~~lead to faster development or~~ **provide the drug any advantage in the** regulatory review ~~of~~ **or approval process** ~~the~~ **other** ~~product~~ **than potential fee reductions** , **and priority review vouchers,** ~~or~~ **nor does such designation** increase the likelihood that ~~it~~ **the drug** will receive marketing approval ~~. Even though XEN496 has Fast Track designation from FDA for the treatment of KCNQ2- DEE, it may not lead to a faster development or regulatory review or approval process, and will not increase the likelihood that XEN496 will receive marketing approval. If a drug is intended for the treatment of a serious or life- threatening condition or disease, and non- clinical or clinical data demonstrate the potential to address an unmet medical need, the product may qualify for FDA Fast Track or Breakthrough Therapy designations and / or PRIority Medicines, or PRIME, designation from the EMA, for which sponsors must apply. The FDA and the EMA have broad discretion whether or not to grant those designations. Although we have received Fast Track designation for the investigation of XEN496 for the treatment of KCNQ2- DEE, we may not experience a faster development process, review or approval compared to conventional FDA procedures. In addition, the FDA may withdraw Fast Track or Breakthrough Therapy designation and the EMA may withdraw PRIME designation if the relevant agency believes that the designation is no longer supported by data from the applicable clinical development program~~ . If product liability lawsuits are brought against us, we may incur substantial liabilities in excess of our limited product liability insurance coverage and may be required to limit commercialization of our current and any future products. We face an inherent risk of product liability as a result of the clinical testing of our product candidates, and we will face an even greater risk if we commercialize any product candidates. For example, we may be sued if any of our product candidates, including any that are developed in combination with other therapies, allegedly causes injury or is found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability and a breach of warranties. Claims could also be asserted under state or provincial consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Even successful defense would require significant financial and management resources. There is also risk that third parties we have agreed to indemnify could incur liability. Regardless of the merits or eventual outcome, liability claims may result in: • decreased demand for our product candidates or any resulting products; • injury to our reputation; • withdrawal of clinical trial participants; • costs to defend the related litigation; • a diversion of management' s time and our resources; • substantial monetary awards to trial participants or patients; • product recalls, withdrawals or labeling, marketing or promotional restrictions; • loss of revenue; • the inability to commercialize our product candidates; and • a decline in the market price of our common shares. We currently carry product liability insurance with amounts of coverage that we believe are appropriate relative to our current clinical programs; however, 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. If and when we obtain marketing approval for product candidates, we intend to expand our insurance coverage to include the sale of commercial products; however, we may then be unable to obtain product liability insurance on commercially reasonable terms or in adequate amounts. On occasion, large judgments have been awarded in class action lawsuits based on drugs or medical treatments that had unanticipated adverse effects. A successful product liability claim or series of claims brought against us could cause the market price of our common shares to decline and, if judgments exceed our insurance coverage, could adversely affect our future results of operations and business. Patients with certain of the diseases, or disorders, targeted by our product candidates are often already in severe and advanced stages of disease and have both known and unknown significant pre- existing and potentially life- threatening conditions. During the course of treatment, patients have in the past and may in the future suffer adverse events, including death, for reasons that may be related to our product candidates. Such events could subject us to costly litigation, require us to pay substantial amounts of money to injured patients, delay, negatively impact or end our opportunity to receive or maintain regulatory approval to market those product candidates, or require us to suspend or abandon our commercialization efforts. Even in a circumstance in which we do not believe that an adverse event is related to our products, the investigation into the circumstance may be time- consuming or inconclusive. These investigations may interrupt our sales efforts, delay our regulatory approval process in other countries, or impact and limit the type of regulatory approvals our product candidates receive or maintain. As a result of these factors, a product liability claim, even if successfully defended, could have a material adverse effect on our business, financial condition or results of operations. We do not have a sales or marketing infrastructure and, as a company, have no sales, marketing or distribution experience. Our strategy involves building our own commercial infrastructure to selectively commercialize future products in certain commercial markets which will be expensive and time consuming. For certain products, including ~~XEN496 and~~ XEN1101, and / or specific commercial markets, we evaluate commercial partners from time to time. In some cases, we may seek to retain the right to participate in the future development and commercialization of such products if we believe such involvement would advance our business. We cannot be certain that we will be successful in consummating any such commercial partnerships or, if consummated, whether such partnerships will be successful. To develop internal sales, distribution and marketing capabilities in the U. S., we will have to invest significant amounts of financial and management resources, some of which will need to be committed prior to any confirmation that any of our product candidates will be approved. We have no prior experience as a company in the marketing, sale and distribution of biopharmaceutical products and there are significant risks involved in building and managing a commercial organization. For any future products for which we decide to perform sales, marketing and distribution functions ourselves, we could face a number of additional risks, including: • the maintenance of existing or the establishment of new supply arrangements with third- party logistics providers and secondary packagers; • the maintenance of existing or the establishment of new scaled production arrangements with third- party manufacturers to obtain finished products that are appropriately packaged for sale; • a continued acceptable safety profile following any marketing approval; • our ~~inability~~ -- **ability** to recruit and retain adequate numbers of qualified sales and marketing personnel or develop alternative sales channels;

• the ~~inability~~ -- **ability** of our products to secure acceptance from physicians, healthcare providers, patients, third- party payers and the medical community including identifying an adequate number of physicians and patients ~~, especially for ultra- orphan, orphan or niche indications~~ ; • the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; • unforeseen costs and expenses associated with creating and maintaining an independent sales and marketing organization; and • our ability to compete with other therapies. Where and when appropriate, we may elect to utilize contract sales forces, distribution partners or collaborators that have ~~s ales~~ **sales** , marketing and distribution capabilities to assist in the commercialization of or to independently commercialize our product candidates. If we enter into arrangements with third parties to perform sales, marketing and distribution services for a product, the resulting revenue or the profitability from this revenue to us is likely to be lower than if we had sold, marketed and distributed that product ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell, market, and distribute our product candidates or may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties, and any of these third parties may fail to devote the necessary resources and attention to sell, market, and distribute our current or any future products effectively. Even if we receive regulatory approval to commercialize any of our product candidates, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense and delays. Any of our product candidates for which we, or any existing or future collaborators, obtain regulatory approval, as well as the manufacturing processes, post- approval studies, labeling, advertising and promotional activities for such product, among other things, will be subject to ongoing requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post- marketing information and reports, registration and listing requirements, requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. We and our contract manufacturers will also be subject to user fees and periodic inspection by the FDA and other regulatory authorities to monitor compliance with these requirements and the terms of any product approval we may obtain. In addition, our product candidates may receive schedule classifications under the Controlled Substances Act of 1970 (or scheduling classifications under similar legislation outside of the U. S.) which will result in additional complexity and may result in delays and restrictions with respect to manufacturing, supply chain, licensing, import / export and distribution. Even if a product is approved, the FDA or another applicable regulatory authority, as the case may be, may limit the indications for which the product may be marketed, require extensive precautions and warnings on the product labeling or require expensive and time- consuming post- approval commitments including clinical trials or onerous risk management activities, including Risk Evaluation and Mitigation Strategies, or REMS, in the U. S. as conditions of approval to help ensure that the benefits of the drug outweigh the potential risks. REMS can include medication guides, communication plans for ~~health~~ **healthcare** ~~care~~ professionals, and elements to assure safe use, or ETASU. ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries. The requirement for a REMS can materially affect the potential market and profitability of the drug. For any approved product, we, or our collaborators, will need to ensure continued compliance with extensive regulations and requirements regarding the manufacturing processes, labeling, packaging, serialization, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for the product. These requirements include submissions of safety and other post- approval information and reports, as well as continued compliance with current good manufacturing practices, or cGMP, good distribution practices, or GDP, and current good clinical practices, or cGCP, for any clinical trials that we, or our collaborators, are required to conduct post- approval. Post- approval discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or other problems with our product or with third- party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, amongst other things, restrictions on the labeling or marketing, withdrawals, consent decrees, clinical holds, post- approval requirements or restrictions, recalls, fines, warning letters, injunctions, penalties, exclusions from federal ~~health~~ **healthcare** ~~care~~ programs, seizures and / or detentions, among other consequences and adverse actions. Occurrence of any of the foregoing could have a material and adverse effect on our business and results of operations. In addition, prescription drugs may be promoted only for the approved indications in accordance with the approved label. The FDA, EMA and other agencies actively enforce the laws and regulations prohibiting the promotion of off- label uses, and a company that is found to have improperly promoted off- label use may be subject to significant liability. However, physicians may, in their independent medical judgment, prescribe legally available products for off- label uses. The FDA does not regulate the behavior of physicians in their choice of treatments but the FDA, EMA and other foreign regulators do restrict ~~manufacturer~~ **manufacturers '** ~~'~~ s communications on the subject of off- label use of their products. To the extent we develop and commercialize product candidates that contain or are considered controlled substances, any failure by us or our CROs, CMOs and other contractors to comply with controlled substance laws and regulations, may adversely affect the results of our business operations and our financial condition. ~~XEN496 contains ezogabine, a Schedule V controlled substance, and is subject to controlled substance laws and regulations in the U. S. We have received letters of no objection which confirm XEN496 is not considered a controlled substance in Canada, Australia and the European countries where XEN496 will be imported for the EPIK trial.~~ We may in the future develop ~~other~~ product candidates that are considered controlled substances in multiple jurisdictions, such as the U. S., Canada, and the EU, which will expose us to additional controlled substance regulatory requirements in each applicable jurisdiction where we engage in regulated activities, including storage, manufacture, research, clinical trials, import, and export, among other activities. For example, obtaining and maintaining the necessary registrations may result in delay of the importation, manufacturing or distribution of our controlled substance product candidates and may extend our anticipated timelines for ~~our EPIK trial or other~~ clinical trials we run. Controlled substances or scheduled substances are regulated by the DEA under the CSA. The DEA regulates compounds as Schedule I, II, III, IV or V substances. Pharmaceutical products

approved for use in the U. S. may be listed as Schedule II, III, IV or V, with Schedule II substances considered to present the highest potential for abuse or dependence and Schedule V substances the lowest relative risk of abuse among such substances. Scheduling determinations by the DEA are dependent on FDA approval of a substance or a specific formulation of a substance. This scheduling determination will be dependent on FDA approval and the FDA' s recommendation as to the appropriate schedule, which may introduce a delay into the approval and any potential rescheduling process. There can be no assurance that the DEA will make a favorable scheduling decision. Substances that are Schedule II, III, IV or V controlled substances at the federal level may also require scheduling determinations under state laws and regulations, as well as similar foreign controlled substances regulations, if applicable. If approved by the FDA, a number of post- approval activities involving controlled substances will be subject to regulation by the DEA, including DEA regulations relating to registration and inspection of facilities, manufacturing, storage, distribution and physician prescription procedures, among others. Furthermore, failure of our contractors, such as our CROs and CMOs, to maintain compliance with the CSA during development and / or commercialization, as applicable, can result in a material adverse effect on our business, financial condition and results of operations. Individual U. S. states and countries outside of the U. S. have also established controlled substance laws and regulations. Those laws and regulations, including state - controlled substances laws that often but not necessarily mirror federal law, may separately schedule our product candidates. Complying with different controlled substances requirements across different jurisdictions can increase the cost of our operations and expose us to additional liabilities. Even if we obtain marketing approval for our product candidates, the presence of a controlled substance in the product candidate may lead to adverse publicity or public perception regarding our current or future product candidates. ~~Our product candidate XEN496 contains a Schedule V controlled substance.~~ If ~~XEN496 or~~ **our** ~~our other~~ product candidates that are subject to controlled substances regulation are approved for commercial sale, adverse publicity or public perception of controlled substances in general or other controlled substances could negatively impact market acceptance or consumer perception of our product candidates. We may face limited adoption if clinicians or patients are unwilling to try a novel treatment that contains a controlled substance. Any adverse publicity associated with illness or other adverse effects resulting from patients' use or misuse of our or similar therapies distributed by other companies could have a material adverse impact on our business, prospects, financial condition and results of operations. Future adverse events and research in controlled substances that are present in the product candidates could also result in greater governmental regulation, stricter labeling requirements and potential regulatory delays in the testing or approvals of our product candidates. Any increased scrutiny could delay or increase the costs of obtaining regulatory approval for our product candidates ~~. If the market opportunities for our product candidates are smaller than we believe they are, our revenue may be adversely affected, and our business may suffer. Because the target patient populations for some of our product candidates are small, we must be able to successfully identify patients and acquire a significant market share to achieve profitability and growth. Some of our product candidates focus on treatments for rare and ultra- rare disorders. Given the small number of patients who have some of the disorders that we are targeting, our profitability and growth depend on successfully identifying patients with these rare and ultra- rare disorders. Currently, most reported estimates of the prevalence of these disorders are based on studies of small subsets of the population in specific geographic areas, which are then extrapolated to estimate the prevalence of the disorders in the U. S. or elsewhere. Our projections of both the number of people who have these disorders, as well as the subset of people with these disorders who have the potential to benefit from treatment with our product candidates, are based on our internal estimates. These estimates have been derived from a variety of sources, including scientific literature, surveys of clinics, patient foundations, and market research, and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these disorders, and, as a result, the number of patients with these disorders may turn out to be lower than expected. Our effort to identify patients with diseases or disorders we seek to treat is in early stages, and we cannot accurately predict the number of patients for whom treatment might be possible. Additionally, the potentially addressable patient population for some of our product candidates may be limited or may not be amenable to treatment with our product candidates, and new patients may become increasingly difficult to identify or gain access to, which would adversely affect our results of operations and our business. Finally, even if we obtain significant market share for our product candidates focused on treatments for rare and ultra- rare disorders, because the potential target populations are very small, we may never achieve profitability despite obtaining such significant market share~~ . Any product candidates we develop may become subject to unfavorable third- party coverage and reimbursement practices, as well as pricing regulations. Our, or our collaborators', ability to commercialize any products successfully will depend, in part, on the extent to which coverage and reimbursement for these products and related treatments will be available from government healthcare programs, **such as Medicare and Medicaid, and** private ~~health insurers, managed care plans, and other organizations. Government authorities and~~ third- party payers, such as private health insurers **, managed care plans,** and **other** ~~health maintenance~~ organizations ~~,~~ **. Government authorities and private third- party payers** decide which ~~medications~~ **drugs** they will pay for and establish reimbursement levels. A primary trend in the U. S. healthcare industry is cost containment. Government authorities and third- party payers have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications ~~. Increasingly, third- party payers are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products~~ . We cannot be sure that coverage and reimbursement will be available for any product that we, or our collaborators, commercialize and, if reimbursement is available, the level of reimbursement. In addition, coverage and reimbursement may impact the demand for, or the price of, any product candidate for which we or a collaborator obtains marketing approval. If coverage and reimbursement are not available or reimbursement is available only to limited levels, we, or our collaborators, may not be able to successfully commercialize any product candidate for which marketing approval is obtained. There is significant uncertainty related to third- party ~~payor~~ **payer** coverage and reimbursement of newly approved products. ~~In~~ **Within** the U. S., **coverage and** ~~for example, principal decisions about~~ reimbursement **varies from** ~~for new products are typically made by the Centers for Medicare & Medicaid Services, or CMS, an~~

~~agency within the U. S. Department of Health and Human Services, or HHS. CMS decides whether and to what extent a new product will be covered and reimbursed under Medicare, and private third- party payors often follow CMS' s decisions regarding coverage and reimbursement to a substantial degree. However,~~ one third ~~-~~ party ~~payor~~ **payer to another. One third-party payer** ' s determination to provide coverage for a product candidate does not assure that other ~~payors~~ **payers** will also provide coverage for the product candidate. As a result, the coverage determination process is often time- consuming and costly. Factors ~~payors~~ **payers** consider in determining reimbursement are based on whether the product is: (i) a covered benefit under its health plan; (ii) safe, effective and medically necessary; (iii) appropriate for the specific patient; (iv) cost- effective; and (v) neither experimental nor investigational. ~~This process will~~ **We may be** ~~require~~ **required** ~~us~~ to provide scientific and clinical support for the use of our products to each third- party ~~payor~~ **payer** separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. As federal and state governments implement additional ~~health~~ **healthcare** ~~care~~ cost containment measures, including measures to lower prescription drug pricing, we cannot be sure that our products, if approved, will be covered by private or public ~~payors~~ **payers**, and if covered, whether the reimbursement will be adequate or competitive with other marketed products. Actions by federal and state governments and health plans may put additional downward pressure on pharmaceutical pricing and ~~health~~ **healthcare** ~~care~~ costs, which could negatively impact coverage and reimbursement for our products if approved, our revenue, and our ability to compete with other marketed products and to recoup the costs of our research and development. Additionally, net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private ~~payors~~ **payers** and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the U. S. ~~. Increasingly, third- party payors~~ **In order to obtain and maintain acceptable reimbursement levels and access for patients at copay levels that** are ~~requiring that drug companies provide them with predetermined~~ **reasonable and customary, we may have to offer** discounts **or rebates** from list prices ~~and are challenging the prices charged for -~~ **or** ~~medical products~~ **to implement other unfavorable pricing modifications**. We cannot be sure that reimbursement will be available for any product candidate that we commercialize and, if reimbursement is available, the level of reimbursement. Outside the U. S., the commercialization of therapeutics is generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost containment initiatives in Europe, Canada and other countries has and will continue to put pressure on the pricing and usage of therapeutics such as our product candidates. In many countries, particularly the countries of ~~the European Union, or~~ the EU, medical product prices are subject to varying price control mechanisms as part of national health systems. In these countries, pricing negotiations with governmental authorities can take considerable time after a product receives marketing approval. To obtain reimbursement 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 product candidate to other available therapies. In general, product prices under such systems are substantially lower than in the U. S. Other countries allow companies to fix their own prices for products but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we, or our collaborators, are able to charge for our product candidates. Accordingly, in markets outside the U. S., the reimbursement for our products may be reduced compared with the U. S. and may be insufficient to generate commercially reasonable revenue and profits. Some of our ~~and~~ **or** our collaborators ~~'~~ **'** target patient populations **may be** in orphan ~~and~~ **or** niche indications, such as ~~KCNQ2- DEE and~~ SCN8A- DEE. In order for therapies that are designed to treat smaller patient populations to be commercially viable, the pricing, coverage and reimbursement for such therapies needs to be higher, on a relative basis, to account for the lack of volume. Accordingly, we ~~will~~ **or our collaborators may** need to implement pricing, coverage and reimbursement strategies for any approved product that accounts for the smaller potential market size. If we **or our collaborators** are unable to establish or sustain coverage and adequate reimbursement for our **or our collaborators'** current and any future products from third- party payers or the government, the adoption of those products and sales revenue will be adversely affected, which, in turn, could adversely affect the ability to market or sell those products. **Healthcare** ~~Recently enacted~~ and ~~future legislation~~ **other reforms** may increase the difficulty and cost for us to commercialize any products that we, or our collaborators, develop and affect the prices we may obtain. The U. S. and some foreign jurisdictions are considering or have enacted a number of legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to sell any of our products profitably, once such products are approved for sale. Among policy makers and payers in the U. S. and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and / or expanding access. In the U. S., the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. For example, in 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, collectively, the PPACA, was enacted and includes measures that have significantly changed the way healthcare is financed by both governmental and private insurers. ~~Since its enactment~~ **Beyond the ACA**, there **are ongoing and widespread health care reform efforts, a number of which** have **focused** ~~been legislative and judicial challenges to the PPACA. In June 2021, the U. S. Supreme Court held that Texas and other challengers had no legal standing to challenge the PPACA, dismissing the case without specifically ruling~~ on ~~the constitutionality of the PPACA. Accordingly, the PPACA remains in effect in its current form. It is unclear how future litigation, and healthcare measures promulgated by the Biden administration will impact the implementation of the PPACA, our business, financial condition and results of operations. Complying with any new legislation or changes in healthcare~~ regulation **of prices** ~~could be time- intensive and expensive, resulting in a material adverse effect on our -~~ **or** ~~business~~ **payment for drug products**. ~~In addition,~~ **Drug pricing and payment reform was a focus of** ~~there~~ ~~--~~ **the Trump Administration and** has been **a focus of** ~~heightened governmental scrutiny over the manner in which manufacturers set prices for their --~~ **the Biden Administration** ~~marketed products, which has resulted in several presidential executive orders, Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the~~

~~relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for pharmaceutical products~~ . For example, **federal legislation enacted in** ~~under the American Rescue Plan Act of~~ 2021 **eliminates a** ~~, effective January 1, 2024, the~~ statutory cap on Medicaid ~~Drug~~ **drug** ~~Rebate~~ **rebate** ~~Program~~ **program** rebates ~~that manufacturers pay to state Medicaid programs will be eliminated. Elimination of this cap may require pharmaceutical manufacturers to pay more in rebates than they receive on the sale of products, which could have a material impact on our business. In July 2021, the Biden administration released an executive~~ **effective** ~~order~~ **January 1** , ~~" Promoting Competition in the American Economy, " with multiple provisions aimed at increasing competition for prescription drugs. In August 2022~~ **2024 . As another example** , ~~Congress passed~~ the Inflation Reduction Act **(IRA)** of 2022 **contains various** ~~, which includes prescription~~ drug **price negotiation, inflationary rebate, and pricing** provisions **with varying implementation dates. The IRA allows** ~~that have significant implications for the pharmaceutical industry and Medicare beneficiaries, including allowing~~ the federal government to negotiate a maximum fair price for certain high- priced single **-** source Medicare drugs, ~~imposing~~ **impose** penalties and excise tax for manufacturers that fail to comply with the drug price negotiation requirements, ~~requiring~~ **require** inflation rebates for all Medicare Part B and Part D drugs ~~,~~ **(** with limited exceptions ~~,~~ **)** if their drug prices increase faster than inflation, and ~~redesigning~~ **redesigns** Medicare Part D to reduce out- of- pocket prescription drug costs for beneficiaries, among other changes. The impact of ~~these~~ -- **the** ~~regulations~~ **IRA on our business** and ~~any future healthcare measures and agency rules implemented by~~ **the broader pharmaceutical industry remains uncertain as implementation is ongoing. As another example, in 2022, subsequent to the enactment of the IRA,** the Biden administration **released an executive order directing the HHS to report** on **how** ~~us and~~ the ~~pharmaceutical industry~~ **Center for Medicare and Medicaid Innovation (" CMMI ") could be leveraged to test new models for lowering drug costs for Medicare and Medicaid beneficiaries. The report** ~~as~~ **was** ~~a whole~~ **issued in 2023 and proposed various models that CMMI** is currently ~~unknown~~ **developing which seek to lower the cost of drugs, promote accessibility and improve quality of care** . ~~At~~ **These changes or** ~~the~~ **other changes could affect the market conditions for our products. We expect continued scrutiny on drug pricing and government price reporting from Congress, agencies, and other bodies. Further, a number of** ~~state~~ **states** ~~level, legislatures~~ have ~~increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Further, a number of states are considering or have recently~~ enacted state drug price transparency and reporting laws that could substantially increase our compliance burdens and expose us to greater liability under such state laws ~~once~~ **if and when** we ~~begin commercialization~~ **have marketed products** . These and other health reform measures that are implemented may have a material adverse effect on our operations. We are unable to predict the future course of federal or state healthcare legislation in the U. S. **Any** ~~directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. These and any~~ further changes in the law or regulatory framework could reduce our ability to generate revenue in the future or increase our costs, either of which could have a material and adverse effect on our business, financial condition and results of operations. The continuing efforts of the government ~~, insurance companies, managed care organizations,~~ and other **third- party** ~~payors~~ **payers** ~~of healthcare services and medical products~~ to contain or reduce costs of healthcare and / or impose price controls may adversely affect the demand for our product candidates, if approved, and our ability to achieve or maintain profitability. In the EU, similar political, economic and regulatory developments may affect our, or our collaborators', ability to profitably commercialize our current or any future products. In addition to continuing pressure on prices and cost containment measures, legislative developments at the EU or member state level may result in significant additional requirements or obstacles that may increase our operating costs. In international markets, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. Our future products, if any, might not be considered medically reasonable and necessary for a specific indication or cost- effective by third-party payers. An adequate level of reimbursement might not be available for such products and third- party payers' reimbursement policies might adversely affect our, or our collaborators', ability to sell any future products profitably. Legislative and regulatory proposals have been made to expand post- approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by the U. S. Congress of the FDA' s approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-approval testing and other requirements. **In addition, other broader legislative changes have been adopted that could have an adverse effect upon, and could prevent, our products' commercial success. For example, the Budget Control Act of 2011, as amended, resulted in the imposition of reductions in Medicare (but not Medicaid) payments to providers in 2013 and remains in effect through 2032 unless additional Congressional action is taken. Any significant spending reductions affecting Medicare, Medicaid or other publicly funded or subsidized health programs that may be implemented and / or any significant taxes or fees that may be imposed on us could have an adverse impact on our results of operations.** We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the U. S. or in other jurisdictions. If we, or our collaborators, are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we, or our collaborators, are not able to maintain regulatory compliance, our product candidates may lose any marketing approval that may have been obtained and we may not achieve or sustain profitability, which would adversely affect our business. Risks Related to Our Dependence on Third Parties We have no control over the resources, time and effort that our collaborators may devote to our programs and limited access to information regarding or resulting from such programs. We are dependent on our collaborators, including Neurocrine Biosciences, to fund and conduct the research and any clinical development of product candidates under our agreements with each of them, and for

the successful regulatory approval, marketing and commercialization of one or more of such products or product candidates. Such success will be subject to significant uncertainty. Our ability to recognize revenue from successful collaborations may be impaired by multiple factors including: • a collaborator may shift its priorities and resources away from our programs due to a change in business strategies, or a merger, acquisition, sale or downsizing of its company or business unit; • a collaborator may cease development in therapeutic areas which are the subject of our strategic alliances; • a collaborator may change the success criteria for a particular program or product candidate thereby delaying or ceasing development of such program or candidate; • a significant delay in initiation of certain development activities by a collaborator will also delay payment of milestones tied to such activities, thereby impacting our ability to fund our own activities; • a collaborator could develop a product that competes, either directly or indirectly, with our current or future products, if any; • a collaborator with commercialization obligations may not commit sufficient financial or human resources to the marketing, distribution or sale of a product; • a collaborator with manufacturing responsibilities may encounter regulatory, resource or quality issues and be unable to meet demand requirements; • a collaborator may exercise its rights under the agreement to terminate our collaboration; • a dispute may arise between us and a collaborator concerning the research or development of a product candidate, commercialization of a product or payment of royalties or milestone payments, any of which could result in a delay in milestones, royalty payments or termination of a program and possibly resulting in costly litigation or arbitration which may divert management attention and resources; • a collaborator may not adequately protect the intellectual property rights associated with a product or product candidate; • a collaborator may use our proprietary information or intellectual property in such a way as to invite litigation from a third- party; and • disruptions caused by man- made or natural disasters or public health pandemics or epidemics or other business interruptions ~~, including, for example, the COVID- 19 pandemic~~ . If our collaborators do not perform in the manner we expect or fulfill their responsibilities in a timely manner, or at all, the clinical development, regulatory approval and commercialization efforts could be delayed, terminated or be commercially unsuccessful. Conflicts between us and our collaborators may arise. In the event of termination of one or more of our collaboration agreements, it may become necessary for us to assume the responsibility of any terminated product or product candidates at our own expense or seek new collaborators. In that event, we could be required to limit the size and scope of one or more of our independent programs or increase our expenditures and seek additional funding which may not be available on acceptable terms or at all, and our business could be materially and adversely affected ~~. We depend on our collaborative relationship with Neurocrine Biosciences to further develop and commercialize NBI- 921352, and if our relationship is not successful or is terminated, we may not be able to effectively develop and / or commercialize NBI- 921352. We depend on Neurocrine Biosciences to develop and commercialize NBI- 921352. Under the agreement and subject to input from the joint steering committee, Neurocrine Biosciences controls all decision- making with respect to the clinical development and commercialization for NBI- 921352. As a result of our collaboration with Neurocrine Biosciences, the eventual success or commercial viability of NBI- 921352 is largely beyond our control. The financial returns to us, if any, depend in large part on the achievement of development and commercialization milestones, plus a share of any revenue from sales. Therefore, our success, and any associated financial returns to us and our investors, will depend in part on Neurocrine Biosciences' performance under the agreement. We are subject to a number of additional specific risks associated with our dependence on our collaborative relationship with Neurocrine Biosciences, including: • adverse decisions by Neurocrine Biosciences regarding the development and commercialization of NBI- 921352; • Neurocrine Biosciences' failure to collect all data required by FDA or any other regulatory authority to address any deficiencies or compliance issues raised by FDA or any other regulatory authority, or comply with all regulatory requirements in order to advance clinical development of NBI- 921352 to approval; • possible disagreements as to the timing, nature and extent of development plans, including clinical trials or regulatory strategy; • loss of significant rights if we fail to meet our obligations under the agreement; • changes in key management personnel at Neurocrine Biosciences, including in members of the joint steering committee; and • possible disagreements with Neurocrine Biosciences regarding the agreement, for example, with regard to ownership of intellectual property rights. Although we have previously announced that Neurocrine Biosciences is conducting a Phase 2 clinical trial evaluating NBI- 921352 in adult patients with focal onset seizures and a Phase 2 clinical trial evaluating NBI- 921352 in pediatric patients (aged between 2 and 21 years) with SCN8A- DEE, we cannot be certain that Neurocrine Biosciences will continue to pursue these indications and we may not qualify for additional payments under our collaboration agreement. If either we or Neurocrine Biosciences fail to perform our respective obligations, any clinical trial, regulatory approval or development progress could be significantly delayed or halted, could result in costly or time- consuming litigation or arbitration and could have a negative impact on our business. Decisions by Neurocrine Biosciences to emphasize other drug candidates currently in its portfolio ahead of our product candidates, or to add competitive agents to its portfolio could result in a decision to terminate the agreement, in which event, among other things, we may be responsible for paying any remaining costs of all ongoing or future clinical trials, including expending additional time and resources needed to address any prior deficiencies or regulatory noncompliance issues that we may inherit from Neurocrine Biosciences upon any such termination. Any of the above discussed scenarios could adversely affect the timing and extent of the development and commercialization activities related to NBI- 921352, which could negatively impact our business~~ . We may not be successful in establishing new collaborations or maintaining our existing alliances, which could adversely affect our ability to develop product candidates and commercialize products. In the ordinary course, we engage with other biotechnology and pharmaceutical companies to discuss potential in- licensing, out- licensing, alliances and other strategic transactions. The advancement of our product candidates and development programs and the potential commercialization of our current and future product candidates will require substantial additional cash to fund expenses. Additionally, there are certain jurisdictions where a collaborator may be able to realize the market potential of our product candidates better than us. For these or other reasons, we may decide to collaborate with additional pharmaceutical and biotechnology companies with respect to development and potential commercialization. We face significant competition in seeking appropriate collaborators and the negotiation process is time- consuming and complex. Moreover, we

may not be successful in our efforts to establish other collaborations or other alternative arrangements for any current or future product candidates because our research and development pipeline may be insufficient, our current or future product candidates may be deemed to be at too early of a stage of development for collaboration effort and / or third parties may view our product candidates as lacking the requisite potential to demonstrate safety and efficacy. Even if we are successful in our efforts to establish collaborations, the terms that we agree upon may not be favorable to us and we may not be able to maintain such collaborations if, for example, development or approval of a product candidate is delayed or sales of an approved product are disappointing. If any of our existing collaboration agreements are terminated, or if we determine that entering into other product collaborations is in our best interest but we either fail to enter into, delay in entering into or fail to maintain such collaborations: • the development of certain of our current or future product candidates may be terminated or delayed; • our cash expenditures related to development or commercialization of any such product candidates would increase significantly and we may need to seek additional financing sooner than expected; • we may be required to hire additional employees or otherwise develop expertise, such as clinical, regulatory, sales and marketing expertise, some of which we do not currently have; • we may delay commercialization or reduce the scope of any sales or marketing activities; • we will bear all of the risk related to the development or commercialization of any such product candidates; and • the competitiveness of any product that is commercialized could be reduced. We do not own or operate manufacturing facilities for the production of clinical or commercial quantities of our product candidates, and we lack the resources and the capabilities to do so. As a result, we currently rely on third parties for the manufacture and supply of the active pharmaceutical ingredients, or APIs, in our product candidates and the final drug product formulation for all of our product candidates that are being used in our clinical trials and pre- clinical studies **as well as packaging, labelling and distribution of clinical trial supplies** . Our current strategy is to outsource all manufacturing of our product candidates to third parties. In addition, we rely on our collaborators, either directly or through CMOs, to manufacture product candidates licensed to them or to work with CMOs to produce sufficient quantities of materials required for the manufacture of our product candidates for pre- clinical testing and clinical trials and intend to do so for the commercial manufacture of our products. If we, or our collaborators, are unable to arrange for such third- party manufacturing sources, or fail to do so on commercially reasonable terms, we, or our collaborators, may not be able to successfully produce sufficient supply of a product candidate or we, or our collaborators, may be delayed in doing so. Such failure or substantial delay could delay our clinical trials and materially harm our business. The manufacture of biopharmaceutical products is complex and requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. The process of manufacturing our product candidates is susceptible to product loss due to contamination, equipment failure or improper installation or operation of equipment, vendor or operator error, contamination and inconsistency in yields, variability in product characteristics and difficulties in scaling the production process. Even minor deviations from normal manufacturing processes could result in reduced production yields, product defects and other supply disruptions. If microbial, viral or other contaminations are discovered in our product candidates or in the third- party manufacturing facilities in which our product candidates are made, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination. Any adverse developments affecting manufacturing operations for our product candidates, if any are approved, may result in shipment delays, inventory shortages, lot failures, product withdrawals or recalls, or other interruptions in the supply of our products. We may also have to take inventory write- offs and incur other charges and expenses for products that fail to meet specifications, undertake costly remediation efforts or seek more costly manufacturing alternatives. Reliance on third- party manufacturers entails risks to which we would not be subject if we manufactured product candidates ourselves, including reliance on these third parties for regulatory compliance and quality control and assurance, volume production, the possibility of breach of the manufacturing agreement by the third- party because of factors beyond our control (including a failure to synthesize and manufacture our product candidates in accordance with our product specifications) **, the impact of industry consolidation, including business combinations involving such third parties,** and the possibility of termination or nonrenewal of the agreement by the third- party at a time that is costly or damaging to us. Although we believe that there are several potential alternative manufacturers who could manufacture our product candidates, we may incur added costs and delays in identifying and qualifying any such replacement. In addition, we typically order raw materials, ~~API~~ **APIs** and drug product and services on a purchase order basis and do not enter into long- term dedicated capacity or minimum supply arrangements with any commercial manufacturer. There is no assurance that we will be able to timely secure needed supply arrangements on satisfactory terms, or at all. Our failure to secure these arrangements as needed could have a material adverse effect on our ability to complete the development of our product candidates or, to commercialize them, if approved. We may be unable to conclude agreements for commercial supply with third- party manufacturers or may be unable to do so on acceptable terms. There may be difficulties in scaling up to commercial quantities and formulation of our product candidates, and the costs of manufacturing could be prohibitive. Further, the FDA, EMA and other foreign regulatory authorities require that our product candidates be manufactured according to cGMP and similar foreign standards. Pharmaceutical manufacturers and their subcontractors are required to register their facilities and / or products manufactured at the time of submission of the marketing application and then annually thereafter with the FDA, EMA and other foreign regulatory agencies. They are also subject to pre- approval inspections and periodic unannounced inspections by the FDA, EMA and other foreign regulatory agencies. Any subsequent discovery of problems with a product, or a manufacturing or laboratory facility used by us or our collaborators, may result in restrictions on the product or on the manufacturing or laboratory facility, including product recall, suspension of manufacturing, importation bans, product seizure or a voluntary withdrawal of the drug from the market. Any failure by our, or our collaborators', third- party manufacturers to comply with cGMP or any failure to deliver sufficient quantities of product candidates in a timely manner, could lead to a delay in, or failure to obtain, regulatory approval of any of our product candidates. In addition to third- party manufacturers, we rely on other third parties to store, monitor, label **, package** and transport bulk drug substance and drug product. If we are unable to arrange for such third-

party sources, or fail to do so on commercially reasonable terms, we may not be able to successfully supply sufficient product candidate or we may be delayed in doing so. Such failure or substantial delay could materially harm our business. If any third-party manufacturer of our product candidates is unable to increase the scale of its production of our product candidates, and / or increase the product yield of its manufacturing, then our costs to manufacture the product may increase and commercialization may be delayed. In order to produce sufficient quantities to meet the demand for clinical trials and, if approved, subsequent commercialization of our product candidates, our third- party manufacturers will be required to increase their production and optimize their manufacturing processes while maintaining the quality of the product. The transition to larger scale production could prove difficult. In addition, if our third- party manufacturers are not able to optimize their manufacturing processes to increase the product yield for our product candidates, or if they are unable to produce increased amounts of our product candidates while maintaining the quality of the product, then we may not be able to meet the requirements for registration and validation and the demands of clinical trials or market demands, which could delay regulatory approvals and decrease our ability to generate profits and have a material adverse impact on our business and results of operation. We rely on entities outside of our control, which may include academic institutions, CROs, hospitals, clinics and other third- party collaborators, to monitor, support, conduct and / or oversee pre- clinical and clinical studies of our current and future product candidates. As a result, we have less control over the timing and cost of these studies and the ability to recruit trial subjects than if we conducted these trials with our own personnel. For example, an investigator- sponsored Phase 2 proof- of- concept clinical trial examining XEN1101 in MDD and anhedonia is being conducted in partnership with academic collaborators at the Icahn School of Medicine at Mount Sinai. If we are unable to maintain or enter into agreements with these third parties on acceptable terms, or if any such engagement is terminated prematurely, we may be unable to enroll patients on a timely basis or otherwise conduct our trials in the manner we anticipate. In addition, there is no guarantee that these third parties will devote adequate time and resources to our studies or perform as required by our contract or in accordance with regulatory requirements, including maintenance of clinical trial information regarding our product candidates. If these third parties fail to meet expected deadlines, fail to transfer to us any regulatory information in a timely manner, fail to adhere to protocols or fail to act in accordance with regulatory requirements or our agreements with them, or if they otherwise perform in a substandard manner or in a way that compromises the quality or accuracy of their activities or the data they obtain, then clinical trials of our future product candidates may be extended or delayed with additional costs incurred, or our data may be rejected by the FDA, EMA or other foreign regulatory agencies. Ultimately, we are responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards, and our reliance on third parties does not relieve us of our regulatory responsibilities. We, our CROs and CMOs are required to comply with current good laboratory practices, or cGLP, cGCP and cGMP regulations and guidelines enforced by the FDA, the competent authorities of the member states of the European Economic Area and comparable foreign regulatory authorities for products in clinical development. Regulatory authorities enforce these regulations through periodic inspections of clinical trial sponsors, principal investigators, clinical trial sites, manufacturing facilities, nonclinical testing facilities and other contractors. If we or any of our CROs or CMOs fail to comply with these applicable regulations, the clinical data generated in our non- clinical studies and clinical trials may be deemed unreliable and our submission of marketing applications may be delayed or the FDA, EMA or another foreign regulatory authority may require us to perform additional clinical trials before approving our marketing applications. Upon inspection, the FDA, EMA or another foreign regulatory authority could determine that any of our clinical trials fail or have failed to comply with applicable cGCP regulations. In addition, our clinical trials must be conducted with product produced under the cGMP regulations enforced by the FDA, EMA and other foreign regulatory authorities, and our clinical trials may require a large number of test subjects. Our failure to comply with cGLP, cGCP and cGMP regulations may require us to repeat clinical trials or manufacture additional batches of drug **,** which would delay the regulatory approval process and increase our costs. Moreover, our business may be implicated if any of our CROs or CMOs violates federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws, or if this is asserted or reported to have occurred. If any of our clinical trial sites terminates for any reason, we may experience the loss of follow- up information on patients enrolled in our ongoing clinical trials unless we are able to transfer the care of those patients to another qualified clinical trial site. Further, if our relationship with any of our CROs or CMOs is terminated, we may be unable to enter into arrangements with alternative CROs or CMOs on commercially reasonable terms, or at all. Switching or adding CROs, CMOs or other suppliers can involve substantial cost and require extensive management time and focus. In addition, there is a natural transition period when a new CRO, CMO or supplier commences work. As a result, delays may occur, which can materially impact our ability to meet our desired clinical development timelines. If we are required to seek alternative supply arrangements, the resulting delays and potential inability to find a suitable replacement could materially and adversely impact our business. Risks Related to Intellectual Property **We could be unsuccessful in obtaining or maintaining adequate patent protection for one or more of our product candidates or future products.** Our commercial success will depend, in ~~large~~ part, on our ability to obtain and maintain patent, trademark and trade secret protection of our product candidates **and future products** , their respective components, formulations, methods used to manufacture them and methods of treatment, as well as successfully defending ~~these patents~~ against third- party challenges. We evaluate our global patent portfolio in the ordinary course of business to enhance patent protection in areas of our strategic focus and in key markets for our ~~potential~~ **product candidates and future** products and may abandon existing patents or patent applications related to terminated development programs, areas, or markets of low strategic importance. Patents might not ~~be issued~~ **issue** ~~or granted~~ with respect to our patent applications that are currently pending, and issued ~~or granted~~ patents might later be found to be invalid or unenforceable, be interpreted in a manner that does not adequately protect our ~~current~~ product **candidates** or any future products, or fail to otherwise provide us with any competitive advantage. The patent position of biotechnology and pharmaceutical companies is generally **highly** uncertain because it involves complex legal and factual considerations **that may be impacted by changes in the law** . ~~The~~ **In addition,**

the standards applied by the U. S. Patent and Trademark Office, or USPTO, and foreign patent offices in ~~granting~~ **issuing** patents are not always applied uniformly or predictably ~~. For example~~ , **and also may be** ~~there is no uniform worldwide policy regarding patentable~~ subject **to changing law** ~~matter or the scope of claims allowable in biotechnology and pharmaceutical patents~~ . Consequently, patents may not issue from our pending patent applications, or we may end up with patent claims of different scope in different jurisdictions. As such, we do not know the degree of future protection that we will have on our **future products and** proprietary ~~products and~~ technology, if any, and a failure to obtain adequate intellectual property protection with respect to our product candidates and **future products, as well as other** proprietary technology could have a material adverse impact on our business and ability to achieve profitability. Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and / or **patent** applications will be due to be paid to the USPTO and various governmental patent ~~agencies~~ **offices** outside of the U. S. in several stages over the lifetime of the patents and / or applications. The USPTO and **foreign** ~~various non- US~~ governmental patent ~~agencies~~ **offices** require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application and maintenance process. We employ reputable law firms and other professionals to help us comply with respect to the patents and patent applications that we own **or co- own** , and we rely upon ~~our licensors or our other~~ collaborators to effect compliance with respect to the patents and patent applications that we **out-** license ~~. In some cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. However, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, our competitors might be able to enter the market and this circumstance would have a material adverse effect on our business~~ . Our intellectual property rights will not necessarily provide us with competitive advantages. The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business, or may not permit us to maintain our competitive advantage. The following examples are **by way of** ~~illustrative~~ **illustration only** : • others may be able to make compounds that are similar to our product candidates **or future products** but that are not covered by the claims of the patents that we ~~, or our collaborators,~~ own **, co- own** or ~~have exclusively~~ **may in-** ~~licensed~~ **license** ; • others may independently develop similar or alternative technologies without infringing our intellectual property rights; • ~~issued~~ patents that we own **, co- own** or ~~have exclusively~~ **may in-** ~~licensed~~ **license** may not provide us with any competitive advantages, or may be held invalid or unenforceable, as a result of legal challenges by our competitors; • we may obtain patents for certain compounds many years before we obtain marketing approval for products containing such compounds, and because patents have a limited life, ~~which~~ **the term (s)** may begin to run out prior to the commercial sale of the related product, the commercial value of our patents may be limited **; • we might not have been the first to make or file upon the inventions covered by the patents or pending patent applications; • it is possible that our pending patent applications will not issue as patents; • we cannot predict the scope of protection of any patent issuing from our patent applications, including whether the patent applications that we own will result in patents with claims directed to our product candidates or future products or uses thereof in the United States or in foreign countries** ; • our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets; • we may fail to develop additional proprietary technologies that are patentable **and / or may fail to adequately protect such technologies** ; • the laws of certain foreign countries may not protect our intellectual property rights to the same extent as the laws of the U. S., or we may fail to apply for or obtain adequate intellectual property protection in all the jurisdictions in which we operate; and • the patents of others may have an adverse effect on our business, for example by preventing us from **commercializing** ~~marketing one or~~ **our future** ~~more of our product~~ **products** ~~candidates for one or more indications~~ . Any of the aforementioned threats to our competitive advantage could have a material adverse effect on our business. Filing, prosecuting, enforcing and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the U. S. can be less extensive than those in the U. S. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as **the** ~~federal and state~~ laws in the U. S. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the U. S., or from offering to sell, selling, using, making or importing products made using our inventions in and into the U. S. or other jurisdictions. Competitors may use our ~~technologies~~ **inventions** in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the U. S. These products may compete with our ~~current or~~ future products ~~, if any~~ , and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. Many companies have encountered significant problems in protecting **, enforcing** and defending intellectual property rights in **certain** foreign ~~jurisdictions~~ **countries** . The legal systems of ~~certain~~ **some** countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property ~~protection~~ **rights** , particularly those relating to biotechnology and pharmaceutical products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign ~~jurisdictions~~ **countries** could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing **as patents** and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from ~~the~~ **our** intellectual property ~~that we develop~~ **. We may be involved in lawsuits to enforce** ~~or~~ **our** ~~license. Our~~ patents ~~covering one or more of our~~ **or** ~~products~~ **the patents of** ~~or~~ **our** ~~product candidates~~ **licensors, which could be expensive, time consuming and unsuccessful, and those patents** could be found invalid or unenforceable if challenged.

Any of our intellectual property rights could be challenged or invalidated despite measures we **or our licensors** take to obtain patent and other intellectual property protection with respect to our product candidates and proprietary technology. ~~could be expensive,time consuming and unsuccessful.~~ Competitors may infringe our patents or the patents of our licensors.To ~~counter~~ **stop** infringement or unauthorized use,we may be required to file infringement claims,which can be expensive and time-consuming.In addition,in an infringement proceeding,a court may decide that a patent **in suit** ~~of ours or one of our licensors~~ is not valid or is **not** ~~unenforceable~~ -- **enforceable.In such case third parties may be able to use** ~~or~~ **our technology without paying licensing fees or royalties.Even if the validity of our patents is upheld,a court** may refuse to stop the other party ~~in such infringement proceeding~~ from using the technology at issue on the ~~grounds~~ - **ground** that ~~our patents do~~ **the other party' s activities are** not ~~cover~~ **covered by our patents.In addition,third parties may affirmatively challenge our rights to,or** the ~~technology in question~~ **scope or validity of,our patents** .An adverse result in any litigation or ~~defense~~ **post- grant** proceedings could put **additional** ~~one or more of our~~ patents at risk of being invalidated,held unenforceable or interpreted narrowly,and could put any of our patent applications at risk of not yielding an issued patent. ~~Interference proceedings,derivation proceedings,entitlement proceedings,ex parte reexamination,inter partes review,post- grant review,and opposition proceedings provoked by third parties or brought by the USPTO or any foreign patent authority may be used to challenge inventorship,ownership,claim scope,or validity of our patent applications.An~~ **Any** ~~unfavorable outcome could~~ **efforts to enforce our intellectual property rights are likely to be costly and may divert the efforts of our scientific and management personnel.** For example, if we were to initiate legal proceedings against a third- party to enforce a patent covering one of our product candidates **or future products** , the defendant could **defend or** counterclaim that our patent is invalid and / or unenforceable. In patent litigation in the U. S. and in some ~~other jurisdictions~~ **foreign countries** , defendant **defenses and** counterclaims alleging invalidity and / or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, for example, lack of novelty, obviousness, ~~broken~~ **patent ineligibility, loss of** priority **claims** , lack of written description, ~~insufficient~~ or ~~non-~~ **lack of** enablement. Grounds for an **assertion of** unenforceability ~~assertion~~ could be an allegation that someone connected with prosecution of the patent withheld material information from the USPTO or ~~the~~ **an** applicable foreign counterpart **where such a duty to disclose exists** , or made a misleading statement, during prosecution. ~~A one of our licensors is not valid or~~ **For example,administrative proceedings** ~~is unenforceable or may refuse to stop the other party in~~ such **as** ~~infringement proceeding from using the technology at issue on the grounds that our patents do not cover the technology in question.An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated,held unenforceable or interpreted narrowly,and could put any of our patent applications at risk of not yielding an issued patent.Interference proceedings,~~ derivation proceedings,entitlement proceedings,ex parte reexamination,inter partes review, **postgrant** ~~post- grant~~ review, ~~and~~ **or** opposition proceedings **,** provoked by third parties or ~~brought~~ **initiated** by the USPTO or any foreign patent authority may be used to challenge inventorship,ownership,claim scope,or validity of our ~~patent~~ **patents** ~~applications~~ **or a patent of our licensor** .An unfavorable outcome **in any of these proceedings** could require us to cease using the related technology or to attempt to license rights to it from the prevailing party.Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms,if any license is offered at all.Litigation or ~~interference~~ **administrative** proceedings may fail and,even if successful,may result in substantial costs and distract our management and other employees. ~~We may not~~ **With respect to challenges to the validity of our patents or the patents of our licensors,for example,there might** be ~~able~~ **prior art of which we and the patent examiner were unaware during prosecution.If a defendant were** to ~~prevent~~ **prevail on a legal assertion of invalidity and / or unenforceability,we would lose at least part,and perhaps all,of the patent protection on a product candidate or future product.As another example,a** litigant or the USPTO itself could challenge our patents on this basis even if we believe that we have conducted our patent prosecution in accordance with the duty of candor and in good faith. The outcome following such ~~a challenge~~ **challenges** is unpredictable. ~~With respect to challenges to the validity of our patents, for example, there might be invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and / or unenforceability, we would lose at least part, and perhaps all, of the patent protection on a product candidate.~~ Even if a ~~defendant~~ **challenger** does not prevail ~~on a legal assertion of invalidity and / or unenforceability~~ , our patent claims may be construed in a manner that would limit our ability to enforce such claims against the ~~defendant~~ **challenger** and others. The cost of defending such a challenge, particularly in a foreign ~~jurisdiction~~ **country** , and any resulting loss of patent protection could have a material adverse impact on one or more of our product candidates and our business. ~~Enforcing our intellectual property rights against third parties may also cause such third parties to file other counterclaims against us, which could be costly to defend, particularly in a foreign jurisdiction, and could require us to pay substantial damages, cease the sale of certain products or enter into a license agreement and pay royalties (which may not be possible on commercially reasonable terms, or at all). Any efforts to enforce our intellectual property rights are also likely to be costly and may divert the efforts of our scientific and management personnel.~~ Patent protection and patent prosecution for some of our product candidates **and future products** is dependent on, and the ability to assert patents and defend them against claims of invalidity is maintained by, third parties. There have been and may be times in the future when certain patents that relate to our product candidates or any ~~approved~~ **future** products are controlled by our **collaborators, including** licensees, sublicensees ~~,~~ **or** licensors ~~or other collaborators~~ . Although we may, under such arrangements, have rights to consult with our collaborators on actions taken as well as back- up rights of prosecution and enforcement, we have in the past and may in the future relinquish rights to prosecute and maintain patents and patent applications within our portfolio as well as the ability to assert such patents against infringers. For example, currently the rights relating to the patent portfolio for XEN901 (now known as NBI- 921352), other selective Nav1. 6 inhibitors and dual Nav1. 2 / 1. 6 inhibitors are exclusively licensed to Neurocrine Biosciences **, and Neurocrine Biosciences has the first right to bring and control any action in connection with product infringement** . If any current or future ~~licensee, sublicensee, licensor or other collaborators~~ - **collaborator** with rights to **file,** prosecute, ~~assert~~

enforce and / or defend patents related to our product candidates **or future products** fails to appropriately prosecute and maintain patent protection for patents covering any of our product candidates, or if patents covering any of our product candidates **or future products** are asserted against infringers or defended against claims of invalidity or unenforceability in a manner which adversely affects such coverage, our ability to develop and commercialize any such product ~~candidate~~ **candidates or future products** may be adversely affected and we may not be able to prevent competitors from making, using, importing, offering for sale, and / or selling competing products. We may be involved in lawsuits to....., results of operations and prospects. Claims that our product candidates or the sale, offer for sale, importation, manufacture, or use of our future products infringe the patent or other intellectual property rights of third parties could result in costly litigation ~~or~~ **,** could require substantial time and money to resolve, even if litigation is avoided **, and could prevent or delay us from developing or commercializing our product candidates** . Our commercial success depends **, in part,** upon our ability to develop product candidates and commercialize **our future** products ~~that may be approved in the future~~ , ~~using our proprietary technology~~ without infringing the intellectual property rights **or other proprietary rights** of others ~~. Our product or product candidates or any uses of them may now and in the future infringe third- party patents or other intellectual property rights~~ . Third parties might allege that we, or our collaborators, are infringing **,** ~~their patent rights or that we have misappropriated~~ **misappropriating** ~~their trade secrets~~ , or ~~that we are~~ otherwise violating their intellectual property rights ~~, whether with respect to the manner in which we have conducted our research or to the composition, use or manufacture of the compounds we have developed or are developing with our collaborators~~ . Such third parties might resort to litigation against us or other parties we have agreed to indemnify, which litigation could be based on either existing intellectual property or intellectual property that arises in the future. It is possible that relevant patents or patent applications held by third parties will cover our product candidates at the time of launch and we may also fail to identify ~~,~~ relevant patents or patent applications held by third parties that **might be asserted to** cover our product candidates. For example, U. S. applications filed before November 29, 2000, and certain applications filed after that date that ~~will~~ **were** not ~~be~~ filed outside the U. S. remain confidential until patents issue. Other patent applications in the U. S. and several other jurisdictions are published approximately 18 months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Furthermore, publication of discoveries in the scientific or patent literature often lags behind actual discoveries. Therefore, we cannot be certain that we, or our collaborators, were the first to invent, or the first to file patent applications on our product candidates or for their uses, or that our product candidates will not infringe patents that are currently issued or that will be issued in the future. ~~In the event that a third- party has also filed a patent application covering one of our product candidates or a similar invention, we may have to participate in an adversarial proceeding, known as an interference or derivation proceeding, declared by the USPTO or its foreign counterpart to determine priority of invention.~~ Additionally, pending patent applications and patents which have been published can, subject to certain limitations, be later amended in a manner that could cover our current or future products, if any, or their use. **The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. If we were sued for patent infringement, we would need to demonstrate that our product candidates, our future products, or methods of use either do not infringe the patent claims of the relevant patent or that the patent claims are invalid or unenforceable, and we may not be able to do this. Proving invalidity may be difficult. Even if we are successful in these proceedings, we may incur substantial costs and the time and attention of our management and scientific personnel could be diverted in pursuing these proceedings, which could have a material adverse effect on our business and operations. Furthermore, we may not have sufficient resources to bring these actions to a successful conclusion. We may choose to challenge the enforceability or validity of claims of a third party' s patent by requesting an administrative proceedings, for example, derivation proceedings, entitlement proceedings, ex parte reexamination, inter partes review, postgrant review, or opposition proceedings, before the USPTO or any foreign patent authority. These administrative proceedings are expensive and may consume our time or other resources. The costs of these administrative proceedings could be substantial and may consume our time or other resources. If we fail to obtain a favorable result in the USPTO, EPO or other foreign patent office then we may be exposed to litigation by a third party alleging that the patent may be infringed by our product candidates or future products.** Defending against claims of patent infringement ~~, misappropriation of trade secrets~~ or other violations of intellectual property rights could be costly and time consuming, regardless of the outcome. Thus, even if we were to ultimately prevail, or to settle at an early stage, such **litigation or threatened** litigation could burden us with substantial unanticipated costs. In addition, litigation or threatened litigation could result in significant demands on the time and attention of our management team, distracting them from the pursuit of other company business. Claims that **the selling, using, making, offering to sell, or importing, of** our product candidates or ~~the selling, using, making, offering to sell, or importing, of our~~ future products infringe, misappropriate or otherwise violate third- party intellectual property rights could therefore have a material adverse impact on our business. **Third parties may** ~~Most of our competitors are larger than we are and have substantially greater financial resources. They are, therefore, likely to~~ be able to sustain the costs of complex intellectual property litigation ~~longer~~ **or proceedings more effectively** than we ~~could~~ **can** . In addition, the uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to conduct our clinical trials, continue our internal research programs, in- license needed technology, or enter into strategic collaborations that would help us bring our product candidates to market. ~~In addition, any~~ **Unfavorable outcomes in intellectual property litigation could limit our research and development activities and / or our ability to commercialize certain products. Any** future intellectual property litigation ~~, interference or~~ other administrative proceedings will result in additional expense and distraction of our personnel. **There is inevitable uncertainty in intellectual property litigation, and we could lose, even if the case against us is weak or flawed.** An ~~adverse~~ **unfavorable** outcome in such litigation or proceedings may expose us or any future strategic collaborators to loss of our proprietary position, expose us to significant liabilities, or require us to seek licenses that may not be available on commercially acceptable terms, if at all, each of which could have a material adverse effect on our business. ~~Unfavorable~~

outcomes in **If we are found to infringe a third- party' s** intellectual property litigation **rights, we** could limit **be forced, including by court order, to cease developing, manufacturing** our **or** research and development activities and / or our ability to commercialize **commercializing** certain **the infringing** products **product candidate or future product** . If **Alternatively, we may be required to obtain a license from such third- party in order to use the infringing technology and continue developing, manufacturing or marketing the infringing product candidate or future product. For example, if** third parties successfully assert their intellectual property rights against us, we might be barred from using certain aspects of our technology or barred from developing and commercializing certain **future** products. **Alternatively** Prohibitions against using certain technologies , **we may** or prohibitions against commercializing certain products, could be **required** imposed by a court or by a settlement agreement between us and a plaintiff. In addition, if we are unsuccessful in defending against allegations that we have infringed, misappropriated or otherwise violated patent or other intellectual property rights of others, we may be forced to pay substantial damage awards to the plaintiff . There is inevitable uncertainty in intellectual property litigation , **including up to treble damages** and **attorneys' fees if** we **are found** could lose, even if the case against us is weak or flawed. If litigation leads to an outcome unfavorable to us **have willfully infringed a patent. As another alternative** , we may be required to obtain a license from the intellectual property owner in order to continue our research and development programs or to market any resulting product. It is **also** possible that the necessary license will not be available to us on commercially acceptable terms, or at all. Alternatively, we may be required to modify or redesign our current **product candidates** or future products, if any, in order to avoid infringing or otherwise violating third- party intellectual property rights. This may not be technically or commercially feasible, may render those products less competitive, or may delay or prevent the entry of those products to the market. Any of the foregoing could limit our research and development activities, our ability to commercialize one or more product candidates, or both. **If** In order to avoid or settle potential claims with respect to any patent or other intellectual property rights of third parties, we may choose or be **are** required to seek a license from a third- party and **, we may** be required to pay license fees or royalties or both, which could be substantial. These licenses may not be available on acceptable terms, or at all. Even if we or any future collaborators were able to obtain a license, the rights may be nonexclusive, which could result in our competitors gaining access to the same intellectual property. Ultimately, we could be prevented from commercializing a product, or be forced, by court order or otherwise, to cease some or all aspects of our business operations , if, as a result of actual or threatened **litigation** patent or other intellectual property claims , we are unable to enter into licenses on acceptable terms. Further, we could be found liable for significant monetary damages as a result of claims of intellectual property infringement. In the future, we may receive offers to license and demands to license from third parties claiming that we are infringing their intellectual property or owe license fees and, even if such claims are without merit, we could fail to successfully avoid or settle such claims. If Neurocrine Biosciences or other collaborators license or otherwise acquire rights to intellectual property controlled by a third - party in various circumstances, for example, where a product could not be legally developed or commercialized in a country without the third- party intellectual property right or, where it is decided that it would be useful to acquire such third- party right to develop or commercialize the product, they are eligible under our collaboration agreements to decrease payments payable to us on a product- by - product basis and, in certain cases, on a country- by- country basis. Any of the foregoing events could harm our business significantly. If we breach any of the agreements **agreement** under which we license the use, development and commercialization rights to our product candidates or technology from third parties, we could lose license rights that are important to our business. Under our existing **or future** license and other agreements, we are **or may become** subject to various obligations, including diligence obligations such as development and commercialization obligations, as well as potential milestone payments and other obligations. If we fail to comply with any of these obligations or otherwise breach our license agreements, our licensing partners may have the right to terminate the applicable license in whole or in part , or convert an exclusive license to a non- exclusive license. Generally, the loss of any **such** one of our current licenses **license** , or **any** license exclusivity **thereunder** , or any other license we may acquire in the future , could materially harm our business, prospects, financial condition and results of operations. **If we are unable to** Confidentiality agreements with employees and third parties may not prevent unauthorized disclosure of trade secrets and other proprietary information, which would harm our competitive position **could be harmed** . In addition to patents, we rely on trade secrets, technical know- how and proprietary information concerning our discovery platform, business strategy and product candidates **, which can be difficult to protect,** in order to protect **maintain** our competitive position , which are difficult to protect . In the course of our research and development activities and our business activities, we often rely on confidentiality agreements to protect our proprietary information. Such confidentiality agreements are used, for example, when we talk to vendors of laboratory, manufacturing, pre- clinical development or clinical development goods or services or potential strategic collaborators. In addition, each of our employees and consultants is required to sign a confidentiality agreement and invention assignment agreement upon joining our company. Our employees, consultants, contractors, business partners or outside scientific collaborators might intentionally or inadvertently disclose our trade secret information in breach of these confidentiality agreements or our trade secrets may otherwise be misappropriated. Our collaborators might also have rights to publish data and we might fail to apply for patent protection prior to such publication. It is possible that a competitor will make use of such information, and that our competitive position will be compromised. In addition, to the extent that our employees, consultants or contractors use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know- how and inventions. Enforcing a claim that a third- party illegally obtained and is using any of our trade secrets is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the U. S. sometimes are less willing than U. S. courts to protect trade secrets. Moreover, our competitors may independently develop equivalent knowledge, methods and know- how. If we cannot maintain the confidentiality of our proprietary technology and other confidential information, then our ability to obtain patent protection or to protect our trade secret information would be jeopardized, which would adversely affect our competitive position. our common shares. In addition,we,or our licensors,may be subject to claims that former employees,collaborators or other third

parties have an interest in our owned or in- licensed patents,trade secrets,or other intellectual property as an inventor or co-inventor.For example,we,or our licensors,may have inventorship disputes arise from conflicting obligations of employees,consultants or others who are involved in developing our product candidates.Litigation may be necessary to defend against these and other claims challenging inventorship or our,or our licensors',ownership of our owned or in- licensed patents,trade secrets or other intellectual property.If we,or our licensors,fail in defending **against** any such claims,in addition to paying monetary damages,we may lose valuable intellectual property rights,such as exclusive ownership of,or right to use,intellectual property that is important to our product candidates.Even if we are successful in defending against such claims,litigation could result in substantial costs and be a distraction to management and other employees.Any of the foregoing could have a material adverse effect on our business,financial condition,results of operations **and prospects.** Changes in U. S. patent law, or laws in other countries, could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our ~~issued~~ patents, thereby impairing our ability to protect our product candidates **and future products** . Our success is heavily dependent on intellectual property, particularly patents. The patent positions of pharmaceutical and biopharmaceutical companies can be highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved. No consistent policy regarding the breadth of claims allowed in patents in these fields has emerged to date in the U. S. or other countries. In addition, Congress or other foreign legislative bodies may pass patent reform legislation that is unfavorable to us. For example, there have been recent changes regarding how patent laws are interpreted, and both the USPTO and Congress have recently made significant changes to the patent system. There have been U. S. Supreme Court decisions that now show a trend of the Supreme Court which is distinctly negative on some patents. The trend of these decisions along with resulting changes in patentability requirements being implemented by the USPTO could make it increasingly difficult for us to obtain ~~and~~ **,** maintain **and / or enforce** patents on our products. We cannot accurately predict future changes in the interpretation of patent laws or changes to patent laws which might be enacted into law. Those changes may materially affect our patents, our ability to obtain patents, the costs to prosecute our patent applications and enforce our patents and / or the patents and applications of our collaborators. The patent situation in these fields outside the U. S. also has uncertainties. Changes in either the patent laws or in interpretations of patent laws in the U. S. and other countries may diminish the value of our intellectual property or narrow the scope of our patent protection. Accordingly, we cannot predict the breadth of claims that may be allowed or enforced in the patents we own or to which we have a license or third- party patents. As an example, European patent applications ~~will soon~~ have the option, upon ~~grant~~ **issuance** of a patent, of becoming a Unitary Patent, which **is** ~~will be~~ subject to the jurisdiction of the Unitary Patent Court, or UPC. The option of a Unitary Patent ~~will be a~~ **and the creation of the UPC are** significant ~~change~~ **changes** in European patent practice. As the UPC is a new court system, there is ~~no~~ **little** precedent for the court, increasing the uncertainty of any litigation in the UPC **. Intellectual property litigation and administrative proceedings may lead to unfavorable publicity that harms our reputation and causes the market price of our common shares to decline. During the course of any intellectual property litigation or administrative proceeding, there could be public announcements of the initiation of the litigation or proceeding as well as results of hearings, rulings on motions, and other interim rulings in the litigation or proceeding. If securities analysts or investors regard these announcements as negative, the perceived value of our existing products, programs or intellectual property could be diminished. Accordingly, the market price of our common shares may decline. Such announcements could also harm our reputation or the market for our future products, which could have a material adverse effect on our business** . If we do not obtain protection under the Hatch- Waxman Act in the U. S. and similar **foreign** legislation ~~outside of the U. S.~~ by extending the patent terms for our product candidates, our business may be materially harmed. Depending upon the timing, duration and specifics of FDA marketing approval of our product candidates, if any, one or more U. S. patents may be eligible for limited patent term ~~restoration~~ **extension** under the Hatch- Waxman Act ~~. The Hatch- Waxman Act permits a patent restoration term of up to five years as compensation for patent term lost during clinical testing of the product and the subsequent FDA regulatory review process~~ . However, we may not be granted an extension because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than five years, or even less than we request if that number is less than five years. If we are unable to obtain patent term extension or ~~restoration or~~ the ~~term~~ **duration** of any such extension is less than we request, the period during which we will have the right to exclusively market our product may be shortened and our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced, possibly materially. ~~We have~~ **If our trademarks are** not ~~registered our corporate~~ **adequately protected, we may not be able to build** name **recognition** ~~as a trademark~~ in ~~all of~~ our ~~potential~~ markets **of interest** , **which** ~~and failure to secure those registrations~~ could adversely affect our business. Our **current and future trademarks, including our** corporate name, Xenon, has not been trademarked in each market where we operate and plan to operate. Our trademark applications for our corporate name or the name of our products may not be allowed for registration, and our registered trademarks may not be maintained or enforced. During trademark registration proceedings, we may receive rejections, which we may be unable to overcome in our responses. Third parties may also attempt to register trademarks utilizing the Xenon name on their products, and we may not be successful in preventing such usage. In addition, in the USPTO and in comparable ~~agencies~~ **patent officers** in many foreign ~~jurisdictions~~ **countries** , third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. **Our** ~~Opposition or cancellation proceedings may be filed against our trademarks, and our~~ trademarks may not survive such proceedings. If we do not secure registrations for our trademarks, we may encounter more difficulty in enforcing them against third parties than we otherwise would. ~~Intellectual property litigation may lead~~ **Moreover, any name we have proposed** to ~~unfavorable publicity~~ **use with our product candidates in the United States, regardless of whether we have registered it or applied to register it as a trademark, must be approved by the FDA. Similar requirements exist in Europe and other foreign countries. If the FDA (or an equivalent**

administrative body in a foreign country) objects to any of our proposed product names, we may need to identify a suitable substitute name, for example, that ~~harms our reputation and causes~~ **would qualify under applicable trademark laws, not infringe** the ~~market price~~ **existing rights** of ~~our common shares~~ **third parties, and be acceptable** to ~~decline. During~~ the ~~course of any intellectual property litigation~~ **FDA. This may require additional expense. In addition** , there could be ~~public announcements~~ **potential trademark infringement claims brought by owners** of ~~the~~ **other** ~~initiation~~ **registered trademarks that incorporate variations** of **our registered or unregistered trademarks. If we assert trademark infringement claims, a court may determine that** the ~~litigation~~ **marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement** ~~as~~ **has** ~~well as results of hearings~~ **superior rights to the marks in question. In this case** , ~~rulings~~ **we could ultimately be forced to cease use of such trademarks. If we are unable to establish name recognition based** on ~~motions, and other interim proceedings in the litigation. If securities analysts or~~ **our trademarks** ~~investors regard these announcements as negative~~ , **we may not** ~~the perceived value of our existing products, programs or intellectual property could~~ be ~~diminished. Accordingly~~ **able to compete effectively** , **and** ~~the market price of our common shares may decline. Such announcements could also harm our reputation or the market for our future products, which could have a material adverse effect on~~ our business **may be adversely affected** . Risks Related to Ownership of Our Common Shares Our common shares are listed on Nasdaq under the trading symbol " XENE. " The market price of our common shares has fluctuated in the past and is likely to be volatile in the future. As a result of this volatility, investors may experience losses on their investment in our common shares. The market price for our common shares may be influenced by many factors, including the following: • announcements by us or our competitors of new products, product candidates or new uses for existing products, significant contracts, commercial relationships or capital commitments and the timing of these introductions or announcements; • actions by any of our collaborators regarding our product candidates they are developing, including announcements regarding clinical or regulatory decisions or developments of our collaboration; • unanticipated serious safety concerns related to the use of any of our products and product candidates; • negative or inconclusive results from clinical trials of our product candidates, leading to a decision or requirement to conduct additional pre- clinical testing or clinical trials or resulting in a decision to terminate the continued development of a product candidate; • delays of clinical trials of our product candidates; • failure to obtain or delays in obtaining or maintaining product approvals or clearances from regulatory authorities; • adverse regulatory or reimbursement announcements; • announcements by us or our competitors of significant acquisitions, strategic collaborations, licenses, joint ventures or capital commitments; • the results of our efforts to discover or develop additional product candidates; • our dependence on third parties, including our collaborators, CROs, clinical trial sponsors and clinical investigators; • regulatory or legal developments in Canada, the U. S. or other countries; • developments or disputes concerning patent applications, issued patents or other proprietary rights; • the recruitment or departure of key personnel; • the level of expenses related to any of our product candidates or clinical development programs; • actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts; • actual or anticipated quarterly variations in our financial results or those of our competitors; • sales of common shares by us, our insiders or our shareholders in the future, as well as the overall trading volume of our common shares; • changes in the structure of healthcare payment systems; • commencement of, or our involvement in, litigation; • the impact of ~~the COVID- 19 pandemic~~ **pandemics , epidemics or other public health crises** on our business and the macroeconomic environment; • general economic, industry and market conditions; • market conditions in the pharmaceutical and biotechnology sectors and other factors that may be unrelated to our operating performance or the operating performance of our competitors, including changes in market valuations of similar companies; and • the other factors described in this " Risk Factors " section. In addition, the stock market in general, and Nasdaq and the biopharmaceutical industry in particular, have from time to time experienced volatility that often has been unrelated to the operating performance of the underlying companies. The COVID- 19 pandemic **and rising inflation and interest rates** , for example, resulted in significant volatility. These broad market and industry fluctuations may adversely affect the market price of our common shares, regardless of our operating performance. In several recent situations where the market price of a stock has been volatile, holders of that stock have instituted securities class action litigation against the company that issued the stock. If any of our shareholders were to bring a lawsuit against us, the defense and disposition of the lawsuit could be costly and divert the time and attention of our management and harm our operating results. The market price of our common shares could decline as a result of sales of a large number of our common shares or the perception that these sales could occur. These sales, or the possibility that these sales may occur, also might make it more difficult for us to sell equity securities in the future at a time and at a price that we deem appropriate. Pursuant to our equity incentive plans, our compensation committee (or a subset or delegate thereof) is authorized to grant equity- based incentive awards to our employees, directors and consultants. Future stock option grants and issuances of common shares under our share- based compensation plans will result in dilution to all shareholders and may have an adverse effect on the market price of our common shares. In addition, in the future, we may issue additional common shares, preferred shares, or other equity or debt securities convertible into common shares in connection with a financing, collaboration agreement, acquisition, litigation settlement, employee arrangements or otherwise. We may also issue additional common shares upon the exercise of pre- funded warrants that we have issued from time to time. Any such issuance, including any issuances pursuant to our " at- the- market " equity offering program under our sales agreement with Jefferies and Stifel, could result in substantial dilution to our existing shareholders and could cause the market price of our common shares to decline. We are governed by the corporate and securities laws of Canada which in some cases have a different effect on shareholders than the corporate laws of Delaware and U. S. securities laws. We are governed by the Canada Business Corporations Act, or CBCA, and other relevant laws, which may affect the rights of shareholders differently than those of a company governed by the laws of a U. S. jurisdiction, and may, together with our articles and by- laws, have the effect of delaying, deferring or discouraging another party from acquiring control of our company by means of a tender offer, a proxy contest or otherwise, or may affect the price an acquiring party would be willing to offer in such an instance. The material

differences between the CBCA and Delaware General Corporation Law, or DGCL, that may have the greatest such effect include, but are not limited to, the following: (i) for material corporate transactions (such as mergers and amalgamations, other extraordinary corporate transactions or amendments to our articles) the CBCA generally requires a two- thirds majority vote by shareholders, whereas DGCL generally only requires a majority vote; and (ii) under the CBCA **,** holders of 5 % or more of our shares that carry the right to vote at a meeting of shareholders can requisition a special meeting of shareholders, whereas such right does not exist under the DGCL. In addition, our board of directors is responsible for appointing the members of our management team and certain provisions of the CBCA and our articles and by- laws may frustrate or prevent any attempts by our shareholders to replace or remove our current management by making it more difficult for shareholders to replace members of our board of directors. Certain of these provisions include the following: • shareholders cannot amend our articles unless such amendment is approved by shareholders holding at least two- thirds of the shares entitled to vote on such approval; • shareholders must give advance notice to nominate directors or to submit proposals for consideration at shareholders' meetings; and • applicable Canadian corporate and securities laws generally require, subject to certain exceptions, a tender offer (also known as a take- over bid) to remain open for a minimum of 105 days and that more than 50 % of the outstanding securities not owned by the offeror be tendered before the offeror may take up the securities. Any provision in our articles, by- laws, under the CBCA or under any applicable Canadian securities law that has the effect of delaying or deterring a change in control could limit the opportunity for our shareholders to receive a premium for their common shares, and could also affect the price that some investors are willing to pay for our common shares, thereby depressing the market price of our common shares. U. S. civil liabilities may not be enforceable against us, our directors, or our officers. We are governed by the CBCA and our principal place of business is in British Columbia, Canada. Many of our directors and officers reside outside of the U. S., and all or a substantial portion of their assets as well as all or a substantial portion of our assets are located outside the U. S. As a result, it may be difficult for investors to effect service of process within the U. S. upon us and certain of our directors and officers or to enforce judgments obtained against us or such persons, in U. S. courts, in any action, including actions predicated upon the civil liability provisions of U. S. federal securities laws or any other laws of the U. S. Additionally, rights predicated solely upon civil liability provisions of U. S. federal securities laws or any other laws of the U. S. may not be enforceable in original actions, or actions to enforce judgments obtained in U. S. courts, brought in Canadian courts, including courts in the Province of British Columbia. We are at risk of securities class action litigation. ~~In the past, securities~~ **Securities** class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology companies have experienced significant share price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management' s attention and resources, which could harm our business. In addition, an increase in litigation against biotechnology companies may make it more difficult and more expensive for us to obtain director and officer liability insurance, and we may be required to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. Our management has broad discretion over the use of our cash and we may not use our cash effectively, which could adversely affect our results of operations. Our management has broad discretion in the application of our cash resources. Shareholders may not agree with our decisions, and our use of our cash resources may not improve our results of operation or enhance the value of our common shares. Our failure to apply these funds effectively could have a material adverse effect on our business, delay the development of our product candidates and cause the market price of our common shares to decline. In addition, pending their use, they may be placed in investments that do not produce significant income or that may lose value. We do not anticipate paying any cash dividends on our common shares in the foreseeable future. We do not currently intend to pay any cash dividends on our common shares in the foreseeable future. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. As a result, capital appreciation, if any, of our common shares may be investors' sole source of gain for the foreseeable future. Reports published by analysts, including projections in those reports that differ from our actual results, could adversely affect the price and trading volume of our common shares. The trading market for our common shares depends in part on the research and reports that industry or securities analysts publish about us or our business. If one or more of the analysts who cover us issues an adverse opinion about our company, our common share price would likely decline. If one or more of these analysts ceases research coverage of us or fails to regularly publish reports on us, we could lose visibility in the financial markets, which in turn could cause the price of our common shares or trading volume to decline. There is no public market for our outstanding pre- funded warrants. There is no public trading market for our outstanding pre- funded warrants and we do not expect a market to develop. In addition, we do not intend to list the outstanding pre- funded warrants on Nasdaq or any other national securities exchange or nationally recognized trading system. Without an active trading market, the liquidity of the outstanding pre- funded warrants will be limited. General Risk Factors Unstable market and economic conditions may have serious adverse consequences on our business and financial condition. Global credit and financial markets have at times experienced extreme disruptions, including ~~most recently~~ in connection with the COVID- 19 pandemic, characterized by increased market volatility, increased rates of inflation, declines in consumer confidence, declines in economic growth, increases in unemployment rates, and uncertainty about economic stability. Similarly, the current ~~conflict~~ **conflicts** between Ukraine and Russia **and in the Middle East,** ~~has~~ **as well as recent failures in the global banking sector, have** created volatility in the capital markets and ~~is~~ **are** expected to have further global economic consequences. **Limited liquidity, defaults, non- performance and other adverse developments affecting financial institutions or parties with which we do business, or perceptions regarding these or similar risks, have in the past and may in the future lead to market- wide liquidity problems. For example, in March 2023, Silicon Valley Bank was closed and placed into receivership and, subsequently, additional financial institutions have been placed into receivership. There is no guarantee that the U. S. government or governments in other jurisdictions will intervene to provide access to uninsured funds in the future in the event of the failure of other financial institutions, or that the U. S. government or governments in other jurisdictions would do so in a timely fashion.** If another

such disruption in credit and financial markets and deterioration of confidence in economic conditions occurs, our business may be adversely affected. If the equity and credit markets were to deteriorate significantly in the future, including as a result of a **pandemic** ~~resurgence of COVID- 19~~ , political unrest or war **, or further instability of the global banking sector** , it may make any necessary equity or debt financing more difficult to complete, more costly, and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our growth strategy, financial performance and the market price of our common shares and could require us to delay or abandon development or commercialization plans. In addition, there is a risk that one or more of our current collaborators, service providers, manufacturers and other partners would not survive or be able to meet their commitments to us under such circumstances, which could directly affect our ability to attain our operating goals on schedule and on budget. We have incurred, and expect to continue to incur, significant costs as a result of laws, regulations and investor- driven standards relating to corporate governance and other matters. Laws and regulations affecting public companies, including provisions of the Dodd- Frank Wall Street Reform and Consumer Protection Act, Sarbanes- Oxley Act of 2002, the CBCA, applicable Canadian securities laws, and rules adopted or proposed by the SEC, Nasdaq, Corporations Canada and applicable Canadian securities regulators have resulted in, and will continue to result in, significant compliance costs to us as we evaluate the implications of these rules and respond to their requirements. Compliance with the various reporting and other requirements applicable to public companies also requires considerable time and attention of management. In the future, if we are not able to issue an evaluation of our internal control over financial reporting, as required, or we or our independent registered public accounting firm determine that our internal control over financial reporting is not effective, this shortcoming could have an adverse effect on our business and financial results and the price of our common shares could be negatively affected. New rules could make it more difficult or more costly for us to obtain certain types of insurance, including director and officer liability insurance, and we may be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the coverage that is the same or similar to our current coverage. The impact of these events could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors and board committees, and as our executive officers. We cannot predict or estimate the total amount of the costs we may incur or the timing of such costs to comply with these rules and regulations. In addition, the SEC and applicable Canadian securities regulators **regularly pursue** ~~recently have been pursuing~~ various rulemaking efforts, including **recently** with respect to environmental, social and governance, or ESG, matters. A variety of organizations also measure the performance of companies on such ESG topics, and the results of these assessments are widely publicized. Investment in funds that specialize in companies that perform well in such assessments are increasingly popular, and major institutional investors have publicly emphasized the importance of such ESG measures to their investment decisions. If additional rules regarding ESG matters are adopted or if investors continue to increase their focus on ESG matters, we could incur substantially higher costs in our efforts to comply and cannot be certain that our efforts will be viewed as adequate **by regulators or by such investors** .