Risk Factors Comparison 2025-02-27 to 2024-02-29 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 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 substantially depends upon the successful development of ~~XEN1101~~ **azetukalner** . If we are unable to obtain regulatory approval for, and successfully commercialize, ~~XEN1101~~ **azetukalner** , 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 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 may be substantially harmed. • If 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. • 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, 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 neuroscience- focused biopharmaceutical company committed to improving the lives of people living with neurological and psychiatric disorders. We are advancing a novel product pipeline to address areas of high unmet medical need, including 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 treat a range of ~~neuroscience diseases~~ **neurological and psychiatric 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 ~~XEN1101 is~~ **Azetukalner Azetukalner,** a novel, **highly** potent **, selective** Kv7 potassium channel opener ~~being~~ **, represents the most advanced, clinically validated potassium channel modulator in late- stage clinical** ~~developed~~ **development** for the treatment of **multiple indications that include** epilepsy, **including focal onset seizures, or FOS, and primary generalized tonic- clonic seizures, or PGTCS, as well as neuropsychiatric disorders including** major depressive disorder, or MDD, and **bipolar depression,** ~~potentially other neurological disorders. XEN1101 for~~ **or BPD.** Epilepsy ~~(~~ **Programs** Focal Onset Seizures ~~) Our XEN1101~~ Phase 3 **azetukalner** ~~epilepsy program includes two identical Phase 3~~ clinical ~~trials, called~~ **studies in FOS (** X- TOLE2 and X- TOLE3 **) continue to advance** , ~~that are~~ **with the first topline data readout anticipated in the second half of 2025.** ~~designed~~ **Designed** closely after the Phase 2b X- TOLE clinical trial ~~. These~~ **, the Phase 3 X- TOLE clinical trials are** multicenter, randomized, double- blind, placebo- controlled **studies** ~~trials are~~ evaluating the clinical efficacy, safety, and tolerability of 15 mg or 25 mg of ~~XEN1101 azetukalner administered orally with food as adjunctive treatment in approximately~~ 360 patients ~~with FOS~~ 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 ~~12- week~~ double- blind period,or DBP,of ~~azetukalner~~ **XEN1101** compared to placebo. **Xenon anticipates patient enrollment** ~~Upon completion of the DBP~~ in **X-** ~~the Phase 3 FOS epilepsy studies,eligible patients may enter an OLE~~ **TOLE2** ~~study~~ **will be completed in late 2024 to early 2025.XEN1101** for **Epilepsy (** ~~up to three years.~~ Primary Generalized Tonic- Clonic Seizures ~~The~~ **) Our** Phase 3 X- ACKT clinical **trial** ~~study continues to enroll patients and~~ is intended to support potential regulatory submissions in an additional epilepsy indication of **primary generalized tonic- clonic seizures,or** PGTCS. **This** ~~X- ACKT is a~~ multicenter,randomized,double- blind,placebo- controlled study **is** evaluating the clinical efficacy,safety,and tolerability of 25 **mg of XEN1101 administered with food as adjunctive treatment in approximately** administered with food as adjunctive treatment in approximately 360 patients per study with focal onset..... 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 **12- week** DBP of ~~XEN1101~~ **azetukalner** compared to placebo. ~~XEN1101 for Epilepsy (Open- Label Extension)~~ Upon completion of the DBP in **the** ~~X- TOLE2, X- TOLE3, or~~ X- ACKT **study** , 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~~ **Azetukalner** Clinical Results in Epilepsy Phase 1: Phase 1 studies conducted in healthy subjects suggested that ~~XEN1101~~ **azetukalner** was generally well tolerated in the doses examined, and its 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. **In addition** ~~We completed a Phase 1 clinical trial that evaluated the safety~~ , ~~tolerability and 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 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 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~~ **azetukalner** ' 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~~ **azetukalner** 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. 6 %, or 50. 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~~ **azetukalner** . Summary of X- TOLE Efficacy Results in the DBP: The X- TOLE trial met its primary efficacy endpoint with ~~XEN1101~~ **azetukalner** 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~~ **Azetukalner** demonstrated a statistically significant reduction from baseline in monthly focal seizure frequency in pairwise comparisons to placebo for all three ~~XEN1101~~ **azetukalner** doses. The median percent reduction in monthly focal seizure frequency was 52. 8 % in the ~~XEN1101~~ **azetukalner** 25 mg group, 46. 4 % in the ~~XEN1101~~ **azetukalner** 20 mg group, and 33. 2 % in the ~~XEN1101~~ **azetukalner** 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~~ **azetukalner** 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~~ **azetukalner** 25 mg group, 43. 1 % in the ~~XEN1101~~ **azetukalner** 20 mg group, and 28. 3 % in the ~~XEN1101~~ **azetukalner** 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~~ **Azetukalner** 25 mg (~~N~~ **n** = 112) ~~XEN1101~~ **Azetukalner** 20 mg (~~N~~ **n** = 51) ~~XEN1101~~ **Azetukalner** 10 mg (~~N~~ **n** = 46) Placebo (~~N~~ **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~~ **Azetukalner** 25 mg Median reduction from baseline in monthly focal seizures frequency PlaceboOverall in X- TOLE 52. 8 % (~~N~~ **n** = 112) 18. 2 % (n = 114) Prior failed ASMs > 6 43. 2 % (n = 45) 14. 2 % (n = 47) Prior failed ASMs < 6 58. 3 % (n = 67) 20. 5 % (n = 67) Concomitant ASMs = 3 51. 3 % (n = 54) 20. 4 % (n = 56) Concomitant ASMs < 2 59. 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~~ **azetukalner** 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~~ **azetukalner** 25 mg group, which are shown in the table below: ~~XEN1101~~ **Azetukalner** 25 mg (~~N~~ **n** = 112) Placebo (~~N~~ **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~~ **azetukalner** 25 mg group was statistically significant in CGI- C and PGI- C, and the ~~XEN1101~~ **azetukalner** 20 mg group was statistically significant in PGI- C, while the ~~XEN1101~~ **azetukalner** 20 mg group in CGI- C and the ~~XEN1101~~ **azetukalner** 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~~ **Azetukalner** was generally well ~~-~~tolerated in the DBP with AEs **generally** 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~~ **azetukalner** 10 mg group, 68. 6 % of patients in the ~~XEN1101~~ **azetukalner** 20 mg group, and 85. 1 % of patients in the ~~XEN1101~~ **azetukalner** 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~~ **azetukalner** 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~~ **azetukalner** 10 mg group, 3. 9 % of patients in the ~~XEN1101~~ **azetukalner** 20 mg group, and 2. 6 % of patients in the ~~XEN1101~~ **azetukalner** 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~~ **azetukalner** 10 mg group, 13. 7 % of subjects in the ~~XEN1101~~ **azetukalner** 20 mg group, and 15. 8 % of subjects in the ~~XEN1101~~ **azetukalner** 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~~ **azetukalner** was associated with starting at an effective, therapeutic dose. There was a statistically significant reduction in median seizure frequency within one week for all doses compared with placebo. Rapid onset of efficacy of ~~XEN1101~~ **azetukalner** was seen at week 1, with a dose- dependent reduction from baseline in median weekly seizure frequency

of 39. 1 % (p < 0. 01, n = 46), 41. 5 % (p = 0. 04, n = 50) and 55. 4 % (p < 0. 001, n = 110) in the 10 mg, 20 mg, and 25 mg groups, respectively, compared to placebo (20. 2 %, n = 114). ~~Analyses of the~~ **The most recent** interim **data from the ongoing 7- year X- TOLE** OLE ~~data show XEN1101~~ **, in which participants received open - label azetukalner at a dose of 20 mg once daily with food, were presented in December 2024. For ongoing OLE patients, monthly MPC reductions in FOS frequency ranged from 61 % to 82 % during month 1 to OLE study month 24 and were maintained at 85 % at OLE study month 36. Patients who were receiving 1 to 2 anti- seizure medications, or ASMs, at baseline experienced higher monthly MPC reductions in FOS frequency from baseline at OLE study month 36 (100 % seizure reduction, n = 67), compared to those receiving 3 ASMs (80. 6 % seizure reduction, n = 80). For those participants who were treated for > 36 months in the OLE, 32. 7 % (48 / 147) achieved seizure freedom for a period of at least 12 months. Azetukalner** continues to be generally well ~~-~~ tolerated **in** ~~, yielding long- term efficacy at~~ the **OLE** ~~20 mg once- daily dose~~ , with ~~60 % retention at 24 months~~ **AEs generally consistent with prior results** in ~~the OLE, as of the analysis cutoff date of September 5, 2023. During OLE study months 18 to 30, there~~ -- **the** ~~was a sustained monthly reduction in seizure frequency (78 % – 95 % median percent change) from~~ double- blind period ~~baseline,~~ and **other** ~~higher reductions were observed for patients who were receiving one to two~~ ASMs **; no** ~~at baseline compared to those receiving three ASMs. Seizure freedom for ≥ 3- month, ≥ 6- month, and ≥ 12- month consecutive durations was achieved in 37. 5 %, 22. 2 %, and 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 **. A total of 182 participants were** ~~, and the clinical data analyzed to date indicates that XEN1101 continues to be generally well- tolerated~~ - **treated** in the OLE **for ≥ 12 months, 165 participants were treated for ≥ 24 months, and 143 participants were treated for ≥ 36 months at the time of the analysis cutoff (October 7, 2024). Retention rates** with ~~AEs consistent with prior results~~ **azetukalner at 12, 24,** and ~~AEs seen with~~ **36 months into** ~~other~~ -- **the** ~~anti- seizure medications. Based on the potential to continue to provide significant benefit to patients, we have extended the X- TOLE~~ OLE ~~from five to seven years~~ **study period were 66 %, 60 %, and 52 %, respectively** . 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, 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 **of action** important in polypharmacy, **and** are easy to take (for example, once- daily **and no dose titration**) ~~, and durable~~ . Based on our market research, we believe ~~XEN1101~~ **azetukalner** could offer a compelling value proposition to address FOS and PGTCS, if approved. ~~XEN1101~~ **Neuropsychiatric Programs We continue to explore the applicability of azetukalner in neuropsychiatric disorders based on establishing a strong scientific rationale, availability of preclinical and clinical data, and a determination of unmet medical needs. A Phase 3 program evaluating azetukalner in major depressive disorder, or MDD, is underway, and we recently announced plans** for **a Phase 3 program in bipolar depression, or BPD, with initiation of the first of two azetukalner clinical studies in bipolar I and bipolar II depression expected by mid- year.** Major Depressive Disorder ~~(~~ **Our Phase 3** MDD ~~)~~ **program includes three multicenter, randomized, double- blind, placebo- controlled clinical trials to evaluate the clinical efficacy, safety, and tolerability of 20 mg of azetukalner administered orally with food over the 6- week DBP as monotherapy treatment in approximately 450 patients with moderate- to- severe MDD per study. The primary efficacy endpoint is the change from baseline in the HAM- D17 score at week 6 in patients who received azetukalner compared to placebo. Upon completion of the DBP, eligible patients may enter an OLE study for up to 12 months. X- NOVA2, the first of three planned Phase 3 clinical trials evaluating azetukalner in patients with MDD, is currently enrolling patients, and X- NOVA3 is expected to initiate mid- year. In addition, patient enrollment in the investigator- sponsored Phase 2 proof- of- concept study of azetukalner in MDD led by Icahn School of Medicine at Mount Sinai is complete, and topline results are anticipated in the first half of 2025. Summary of Azetukalner Clinical Results in MDD Phase 2 Proof- of- Concept X- NOVA Clinical Trial:** In November 2023, we reported

topline results from the randomized, double- blind, placebo- controlled, Phase 2 proof- of- concept X- NOVA clinical trial, which evaluated the clinical efficacy, safety, and tolerability of 10 mg and 20 mg of ~~XEN1101~~ **azetukalner** taken once daily with food in 168 patients with moderate to severe ~~major depressive disorder, or~~ MDD. The primary objective was to assess the efficacy of ~~XEN1101~~ **azetukalner** 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- of- Phase 2 " meeting with the U. 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 trials, with the first Phase 3 study expected to begin in the second half of 2024. We are also evaluating other potential indications for the future development of XEN1101.~~ Summary of X- NOVA Efficacy Data in the DBP: 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~~ **azetukalner** 10 mg group and 16. 94 in the ~~XEN1101~~ **azetukalner** 20 mg group. A clear dose response and a clinically meaningful, but not statistically significant, 3. 04 difference between placebo and the ~~XEN1101~~ **azetukalner** 20 mg group (p = 0. 135) was observed. ~~Statistical~~ **A** ~~significance~~ **significantly different change** was achieved on the ~~pre~~ **following additional endpoints in the study: • 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~~ **azetukalner** 20 mg group (p = 0. 042) **; • Key** ~~. 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~~ **azetukalner** 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~~ **azetukalner** 20 mg group (p = 0. 047) demonstrating early onset of efficacy **; and • At** ~~. 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~~ **azetukalner** 20 mg group compared to placebo. Summary of X- NOVA Safety and Tolerability Data in the DBP: ~~XEN1101~~ **Azetukalner** was **generally** well tolerated with similar rates of adverse events reported across all treatment arms. The most commonly reported TEAEs in the ~~XEN1101~~ **azetukalner** 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~~ **azetukalner** 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~~ **azetukalner** treatment groups and there were two patients (3. 6 %) in the placebo group who experienced a treatment- emergent SAE. ~~XEN1101~~ **Azetukalner** 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~~ **Azetukalner** 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~~ **azetukalner** for the treatment of MDD in approximately 60 subjects. The primary objective of the study is to investigate the effect of ~~XEN1101~~ **azetukalner** 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~~ **azetukalner** compared to placebo on clinical measures of depression and anhedonia using the MADRS and SHAPS, respectively. About Major Depressive Disorder (MDD) MDD is a common, chronic neurological disorder characterized by low mood, inability to feel pleasure, 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 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- 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. Intellectual Property Related to ~~XEN1101~~ **Azetukalner** We have a comprehensive strategy in place to protect and expand the intellectual property portfolio that covers ~~XEN1101~~ **azetukalner** . Importantly, two U. S. patents were issued in 2021 with claims covering: (1) distinct crystalline forms of ~~XEN1101~~ **azetukalner** drug substance and related pharmaceutical compositions, along with methods for their preparation and use; and (2) various methods of orally administering ~~XEN1101~~ **azetukalner** 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 pipeline of product candidates, see " — Intellectual Property " below. ~~New~~ **Early- Stage** Pipeline **: Next Generation** ~~Opportunities Given our expertise in drug discovery, our efforts are concentrated on~~ **Ion** ~~the identification of~~ **Channel Modulators We continue to expand our portfolio by leveraging our extensive** ion channel ~~targets where~~ **expertise to discover and develop potassium and sodium channel therapeutics, with the goal of filing multiple investigational new drug applications, or INDs, or equivalent, in 2025. IND- enabling work is underway with multiple Kv7 development candidates, which** we believe ~~novel modulators might~~ **may have utility in a broad range of therapeutic indications including seizures, pain, and neuropsychiatric disorders, such as MDD and BPD. In addition, IND- enabling work is underway with a lead Nav1. 7 development candidate. Nav1. 7 is an important pain- related target, based on strong human genetic validation, that may** represent **a new class** ~~significant therapeutic advances. Expansion~~ of **medicines without** ~~our pipeline may come from our internal research efforts and through~~ the ~~acquisition~~ **limitations of opioids. We also expect a lead candidate within** ~~or~~ **our** ~~in~~ **Nav1. 1 program will enter IND - enabling studies in 2025** ~~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~~ **data suggests that targeting Nav1. 1 could potentially address the underlying cause and symptoms of Dravet Syndrome** . Our Partnered ~~Programs~~ **Program with Neurocrine Biosciences** ~~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. **As part** ~~Pursuant to the terms~~ of ~~the agreement~~ **this ongoing collaboration** , ~~we have the~~ **NBI- 921355, a Nav1. 2 / 1. 6 sodium channel inhibitor, has progressed into a Phase 1 first- in- human study as a** potential ~~to receive~~ **treatment for** certain ~~clinical~~ **types of epilepsy** , **triggering** ~~regulatory, and~~ **an** ~~commercial~~ **anticipated $ 7. 5 million** milestone ~~payments~~ **payment to Xenon** ~~, 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 being developed to treat pediatric patients with SCN8A developmental and epileptic encephalopathy, or SCN8A- DEE. 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. In December 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, **renamed** ~~now known~~ as NBI- 921352, and certain **pre-** ~~preclinical~~ --- **clinical** candidates ~~(~~**"** ~~,~~ **or** DTCs **,** ~~")~~ and research compounds which Neurocrine Biosciences will have the exclusive right to further develop and commercialize under the terms and conditions set forth in the Collaboration Agreement. Neurocrine Biosciences has an exclusive, royalty- bearing, sublicensable license to certain of our intellectual property rights for the research, development and commercialization of these 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. 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 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. Each party is solely responsible for all costs such party incurs to conduct its activities under the development and research plans, provided that, with respect to NBI- 921352 development and research 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 DTCs, Neurocrine Biosciences may make agreed- upon reimbursements. Except for the activities set forth in the development plans, Neurocrine Biosciences is solely responsible, at its sole cost and expense, for all development and manufacturing of the compounds and any pharmaceutical product that contains a compound, subject to the Co- Funding Option (as defined below). 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, 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~~ **February 27** , ~~2023~~ **2025** . 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~~ **common** ~~Shares~~ **shares** ~~(as defined below)~~ to Neurocrine Biosciences for an aggregate purchase price of $ 20. 0 million. **In January** ~~Based on the regulatory approval of a clinical trial application in Europe for NBI- 921352 for focal- onset seizures in adults, in September 2021~~ **2022 ,** 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 **U. S. Food and Drug Administration' s, or** FDA' s **,** acceptance of a protocol amendment to expand the study population of a clinical trial in pediatric patients with SCN8A- DEE **. In February 2025, NBI- 921355, a Nav1. 2 and Nav1. 6 sodium channel inhibitor in development for the potential treatment for certain types of epilepsy, has progressed into a Phase 1 clinical study in healthy adult participants, triggering an anticipated $ 7. 5 million milestone payment to us** . 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' 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. 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. 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. Share Purchase Agreements **In January 2022** ~~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~~ **258** , **986** ~~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. We entered into additional SPAs in September 2021 and January 2022 with Neurocrine Biosciences pursuant to which we issued and sold 275, 337 and 258, 986, respectively, of our Shares~~ to Neurocrine Biosciences in private placements for aggregate purchase ~~prices~~ **price** of ~~$ 5. 5 million ($ 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 announcements. 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~~ **azetukalner** (previously known as 1OP2198 **and XEN1101**). 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~~ **azetukalner** , 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~~ **Through December 31, 2024** , we **have paid** ~~made a payment of~~ $ **2.** 0 ~~. 3~~ million **based on progress against** ~~to 1st Order. In February 2023, an additional $ 1. 4 million was paid for the~~ **these** ~~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 and future products. 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, ~~2023~~ **2024** , we owned, co- owned or licensed ~~16~~ **21** U. S. issued patents ~~and 56~~ **, 78 issued** patents in foreign jurisdictions (exclusive of European patent national validations), and over ~~370~~ **355** pending patent applications. With regard to ~~XEN1101~~ **azetukalner** , as of December 31, ~~2023~~ **2024** , we owned ~~4~~ **7** U. S. issued patents, ~~29~~ **33** issued patents in foreign jurisdictions (exclusive of European patent national validations) and over ~~200~~ **175** pending patent applications. The issued patents, along with any patents issuing from these applications, are expected to expire between 2028 and ~~2044~~ **2045** (absent any extensions of term). With regard to ~~NBI- 921352 (formerly known as XEN901)~~ **our selective inhibitors of Nav1. 6 and / or Nav1. 2** , as of December 31, ~~2023~~ **2024** , we owned **10** ~~or co- owned 4~~ U. S. issued patents, ~~12~~ **43** issued patents in foreign jurisdictions (exclusive of European patent national validations), and over ~~18~~ **90** pending patent applications. The issued patents, along with any patents issuing from these

applications, are expected to expire between 2037 and 2044 (absent any extensions of term). **Pursuant to our collaboration with Neurocrine Biosciences, Neurocrine Biosciences controls the prosecution, maintenance and other matters relating to the patent portfolio for the selective Nav1. 6 inhibitors and dual Nav1. 2 / 1. 6 inhibitors subject thereto, although we have a right to comment.** With regard to our **development programs, including targets related to Kv7** ~~selective inhibitors of Nav1. 6 and / or Nav1. 2~~ (exclusive of **azetukalner** ~~NBI- 921352~~) **, Nav1. 1 and Nav1. 7** , as of December 31, ~~2023~~ **2024** , we owned ~~6~~ **4** U. S. issued patents ~~, 15 issued patents in~~ **and over 80 pending U. S. and** 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). 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 1 U. S. issued patent and over 20 pending patent applications. The issued patents, along with any patents issuing from these applications, are expected to expire between~~ 2036 and ~~2044~~ **2045** (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. If one or more of our proprietary or partnered product candidates ~~were~~ **is** approved for the treatment of epilepsy, we anticipate that they could potentially compete with other **anti-seizure medications, or** ASMs **,** or one another. ~~These currently commonly~~ **Commonly** prescribed ASMs ~~, among others,~~ include brivaracetam, carbamazepine, cenobamate, clobazam, eslicarbazepine acetate, ethosuximide, gabapentin, lacosamide, lamotrigine, levetiracetam, oxcarbazepine, perampanel, phenytoin, topiramate, and valproate. There are other ASMs in development that could potentially compete with our products, including product candidates in development from **AbbVie Inc.,** Biohaven Ltd. ~~, Cerevel Therapeutics Holdings, Inc., Equilibre Biopharmaceuticals Corp., Johnson & Johnson Innovative Medicine~~ , Neurona Therapeutics Inc., **NeuShen Therapeutics, Inc.,** Praxis Precision Medicines, Inc. **, QurAlis Corporation** , Rapport Therapeutics, Inc., SK Life Science Inc., 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., **Alto Neuroscience, Inc., Axsome Therapeutics, Inc.,** Biohaven Ltd., Intra-Cellular Therapies, Inc., Johnson & Johnson Innovative Medicine, Neumora Therapeutics, Inc., ~~Relmada~~ **and Neurocrine Biosciences, Inc. If one or more of our proprietary product candidates were approved for the treatment of depressive episodes associated with bipolar I or II disorder (bipolar depression), we anticipate that they could potentially compete with other generic antipsychotic and atypical antipsychotic medications. Patients with bipolar depression are typically treated with a variety of atypical antipsychotics as well as mood stabilizers and sometimes in combination with antidepressants. We are aware of several companies developing product candidates for the treatment of bipolar depression including Alto Neuroscience, Inc, Neumora** Therapeutics, Inc. ~~, Sage Therapeutics, Inc.~~ and **NRx Pharmaceuticals** ~~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. **The extensive regulatory requirements to which drugs are subject under the FD & C Act and other applicable statutes, regulations, and guidance are subject to change and often are revised or reinterpreted by the FDA and other regulatory authorities in ways that may have a significant impact on our business.** FDA approval of an ~~investigational new drug application, or~~ IND, 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. 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 sponsor to a variety of administrative or judicial sanctions. 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, restitution, disgorgement of profits, or civil or criminal investigations and penalties brought by FDA and the Department of Justice or other governmental entities. 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 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 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 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 does not undergo unacceptable deterioration over its labeled shelf life. Further, due to disasters and public health emergencies, we may be required to develop and implement additional clinical trial policies and procedures designed to help protect subjects. For example, the FDA has issued guidance on conducting clinical trials during major disruptions due to disasters and public health emergencies, which describes a number of considerations for sponsors of clinical trials impacted by these events, to ensure the 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 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 response letter, which typically describes all of the specific deficiencies in the application identified by the FDA. The deficiencies identified may be minor (e. g., requiring labeling changes) or major (e. g., requiring additional clinical studies). Additionally, the complete response letter may include recommended actions that the applicant might take to place the application in a condition for approval. If a complete 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, 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) a substantial amount of new data or new information not previously submitted to, or reviewed by, the FDA (e. g., a major new clinical safety or efficacy study report, a proposed REMS), 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 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 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. Fast Track Designation, Priority Review, Breakthrough Therapy Designation and Accelerated Approval The FDA has various programs, including fast 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. 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 track designation, the FDA must determine, based on the request of a sponsor, that a drug is intended to treat a 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 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 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. In addition, the fast track designation may be withdrawn by the FDA if it believes that the 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 priority review means that the goal for the FDA to review an application is six months, rather than the standard review of ten months under current PDUFA guidelines. 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 track designation are also likely to be considered appropriate to receive a priority review. Under the provisions of the new Food and Drug Administration Safety and Innovation Act, or FDASIA, enacted by Congress in 2012, a sponsor can request designation of a drug candidate as a " breakthrough therapy, " typically by the end of the 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 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. Orphan drug designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process. 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 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 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 drug has exclusivity or obtain approval for the same product but for a different indication for which the orphan drug has exclusivity. Orphan drug exclusivity also could block the approval of one of our 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 product candidate designated as an orphan drug receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan 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, 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 orphan drug exclusivity. On January 24, 2023, the FDA published a notice in the Federal Register to clarify that while the agency 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 orphan drug exclusivity.~~ 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 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 Act. The Hatch- Waxman Act permits a patent term extension of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. Patent term 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 extension and the application for the patent term extension must be submitted within 60 days of 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. Under the Hatch- Waxman 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 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 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 exclusivities and any Orange Book- listed patent term (s). This six- month exclusivity, which runs from the end of other exclusivity 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~~ **healthcare** ~~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, even if a firm complies with FDA and other requirements, new information regarding 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 an adverse way. Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the recall or discontinuation of our products; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business. 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. The requirements and 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 Clinical Trials Regulation EU No 536 / 2014, or the CTR, which replaced the Clinical Trials Directive, entered into application on January 31, 2022, harmonizes the procedures for the submission, assessment and monitoring of clinical drug trials in the EU, thus simplifying the current rules for clinical trial authorization and standards of performance. The CTR requires a clinical trial sponsor to obtain approval from the national competent authority (NCA) of each 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 an 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~~ **all clinical** trials **(including those** 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, 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 marketing exclusivity. If granted, data exclusivity prevents generic or biosimilar applicants from cross- referencing the innovator’ s preclinical and clinical trial data contained in the dossier of the reference medicinal product when applying for a generic or biosimilar MA until the data exclusivity period has expired. Even if a generic and a biosimilar 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 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, 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 accepted by any regulatory authority in the 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 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 ~~("~~ **, or** PIP ~~")~~, with the EMA' s Pediatric Committee **, or** ~~(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, and other organizations. These third- party payers may deny or limit coverage or reimbursement for a product. Within the U. S., coverage and reimbursement for drug products can differ significantly from payer to payer. One third- party 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 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 drugs. 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. While we cannot predict what cost- containment measures will be adopted or otherwise implemented in the future, new measures or any announcement of 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., for example, the Patient Protection and Affordable Care Act, as amended, or PPACA, is a sweeping law enacted in March of 2010 that expanded ~~health~~ **healthcare** ~~care~~ coverage through Medicaid expansion and the implementation of the individual mandate for health insurance coverage and which included changes to the coverage and reimbursement of drug products under government healthcare programs. Beyond the PPACA, there are ongoing and widespread ~~health~~ **healthcare** ~~care~~ reform efforts, a number of which have focused on regulation of prices or payment for drug products. ~~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 2021 eliminates~~ **eliminated** a statutory cap on Medicaid drug rebate program rebates effective January 1, 2024. As another example, the Inflation Reduction Act (IRA) of 2022 ~~contains various~~ **includes a number of changes intended to address rising prescription drug prices in Medicare Parts B and D. These changes, which have varying implementation dates, include caps on Medicare Part D out- of- pocket costs, Medicare Part B and Part D drug inflation rebates and a new Medicare Part D manufacturer discount drug program (replacing the PPACA Medicare Part D coverage gap discount program), and a** drug price negotiation **program** ~~, inflationary rebate, and pricing provisions with varying implementation dates. The IRA allows the federal government to negotiate a maximum fair price~~ for certain high- **spend** ~~priced single- source Medicare drugs, imposes penalties and excise tax for manufacturers that fail to comply with the drug price negotiation requirements, requires inflation rebates for all~~ Medicare Part B and ~~Part~~ D drugs ~~(with limited exceptions) if their drug prices increase faster than inflation, and redesigns Medicare Part D to reduce out- of- pocket prescription drug costs for beneficiaries, among other changes~~. The **IRA is likely to have a significant** impact ~~of the IRA~~ on ~~our business and~~ the ~~broader~~ pharmaceutical industry ~~remains uncertain~~ as implementation **proceeds** ~~is ongoing~~. As another example, in 2022, subsequent to the enactment of the IRA, the Biden administration ~~released~~ **announced its commitment to expanding certain IRA reforms. There have been significant** ~~an~~ **and wide- ranging reforms to federal policy and the federal government under the new Trump administration. Drug pricing and payment reform was a focus of the prior Trump administration, and that focus is likely to continue under the new Trump administration. Other potential healthcare reform efforts under the Trump administration may affect access to healthcare coverage or the funding of healthcare benefits. There is significant uncertainty regarding the nature or impact of any such reform implemented by the Trump administration through** executive **action** ~~order directing the HHS to report on how the Center for~~ **or by Congress** ~~Medicare and Medicaid Innovation (" CMMI ") could be leveraged to test new models for lowering drug costs for Medicare and Medicaid beneficiaries. The report was issued in 2023 and proposed various models that CMMI is currently developing which seek to lower the cost of drugs, promote accessibility and improve quality of care~~. These changes or 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. 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 have 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 if and when we have marketed products. Healthcare 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 eliminated the tax penalty established for 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 in litigation filed by various pharmaceutical manufacturers and industry groups. We expect that healthcare reform measures that have been or in the future may be adopted, 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 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. Complying with any new legislation and regulatory changes could be time- intensive and expensive, resulting in a material adverse effect on our business. 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 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 to 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, pharmaceutical manufacturers 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; regulate pricing of drugs and protect the privacy of individual information. These laws **, some of which may apply only if a pharmaceutical manufacturer has an approved product,** are enforced by various federal and state enforcement authorities, 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, and the Office of Inspector General, and state boards of pharmacy. We may be subject to various federal and state laws pertaining to ~~health~~ **healthcare** ~~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 federal ~~health~~ **healthcare** ~~care~~ programs (including Medicare and Medicaid) or, in some cases, commercial health plans. Anti- kickback 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 government and various states to regulate the sales and marketing practices of pharmaceutical manufacturers with marketed products. The laws and regulations generally limit financial interactions between manufacturers and ~~health~~ **healthcare** ~~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 and 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 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 and regulations, including extensive record- keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products. Federal and state consumer protection and unfair competition laws and regulations broadly regulate marketplace activities and that potentially harm consumers and could apply to the activities of pharmaceutical manufacturers. We may be subject to data privacy and security laws in 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, there has been an increasing focus on privacy and data protection issues that may affect our business. Efforts to ensure that our activities comply with applicable healthcare laws and regulations will involve substantial costs. Given the breadth of the laws and regulations, limited guidance for certain laws and regulations and evolving government interpretations of the laws and regulations, governmental authorities may possibly conclude that our business practices may not comply with such laws. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. Further, defending against any such 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 us, our

business may be impaired. 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, ~~2023~~ **2024** , we had ~~259~~ **327** employees, including ~~251~~ **316** full- time and part- time permanent employees, of which ~~179~~ **181** are located in Canada and ~~72~~ **135** are located in the U. S. Of our employees, ~~190~~ **239** were primarily engaged in research and development, ~~78~~ **98** of whom hold a Ph. D. or M. D. (or equivalent) degree, and ~~69~~ **88** 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. **For** ~~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 and benefits programs to attract and retain highly qualified personnel and to 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 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. 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 support our employees' further development through a variety of internal training and external professional development opportunities, including conference attendance and tuition reimbursement. We ~~are committed to diversity, equity, inclusion and accessibility, or DEIA, at all levels of our company, and we have established a joint management / employee committee to progress these important 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 are committed to diversity, equity, inclusion and accessibility at all levels of our company** . We currently rely, and expect to continue to rely, on 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. 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. 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 had one wholly- owned subsidiary as of December 31, ~~2023~~ **2024** , Xenon Pharmaceuticals USA Inc., which was incorporated in Delaware on December 2, 2016. Our principal executive offices are located at 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., 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~~ **sedarplus** . ~~com~~ **ca** . 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~~ **risk** ~~Factors~~ **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 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 $ **234. 3 million, $** 182. 4 million ~~,~~ **and** $ 125. 4 ~~million and $ 78. 9~~ million for the years ended December 31, **2024,** 2023 ~~,~~ **and** 2022 ~~and 2021~~ , respectively, and an accumulated deficit of $ ~~665~~ **899** . ~~1~~ **5** million as of December 31, ~~2023~~ **2024** , 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~~ **seek marketing authorization for** and **prepare for the potential commercial launch of azetukalner; • invest to further develop azetukalner for our current and future indications; • advance additional product candidates into** 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; • **require the manufacture of larger quantities of our product candidates for clinical development and potential commercialization; •** hire ~~and retain~~ additional ~~personnel~~ **commercial** , ~~such as~~ clinical, ~~quality assurance, regulatory,~~ scientific, ~~commercial~~ **management** and administrative personnel; • ~~seek to identify and validate additional product candidates; •~~ acquire or in- license other **assets** ~~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 **any** ~~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 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, 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 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 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 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 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 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 **and 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. **A portion** ~~As of December 31, 2023, approximately 3 %~~ of our cash and cash

equivalents and marketable securities ~~were~~ **are** denominated in Canadian dollars ~~. We~~ **, and 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 **, including as a result of trade relations between Canada and the United States,** 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 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. **If** ~~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-depressant medications, or ADs **. In addition, we plan to develop one or more proprietary products for the treatment of bipolar disorder, or BPD, and if any such products were approved for treatment of BPD, we anticipate that they could potentially compete with other anticonvulsant and antipsychotic medications** . 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 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. 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~~ **healthcare** ~~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. **In addition, Washington state enacted the My Health, My Data Act, a health- focused consumer privacy law, which took effect in March 2024. This law imposes obligations related to the collection and sharing of certain health- related information that is not subject to HIPAA and that does not fall within certain other exceptions in the law. Other states have enacted, or are in the process of enacting, similar health- focused consumer privacy laws.** Additional data privacy and security laws have been proposed **and enacted** at the federal, state, and local levels in recent years, which could further complicate compliance efforts **. For example, in June 2024, the Protecting Americans' Data from Foreign Adversaries Act of 2024 took effect. This law prohibits data brokers from making available certain personally identifiable sensitive data of U. S. individuals to " foreign adversary " countries, such as the People' s Republic of China, or the PRC, and entities controlled by such countries. Additionally, in January 2025, the U. S. Department of Justice published a final rule implementing President Biden' s Executive Order 14117, " Preventing Access to Americans' Bulk Sensitive Personal Data and United States Government- Related Data by Countries of Concern. " This final rule prohibits certain data brokerage transactions and transactions involving certain bulk human ' omic data, including human genomic data and biospecimens from which such data can be derived, with restricted persons and jurisdictions, such as the PRC. The final rule also places restrictions on certain vendor, employment and investment agreements with such jurisdictions. Most provisions of the final rule are scheduled to take effect in April 2025. These restrictions may affect our ability to engage in collaborations or license agreements with entities in restricted countries or with a nexus to such countries going forward** . 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 **have enacted and** 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 vendors and contractors, to acquire, transmit, store and otherwise process information in connection with our business activities. Our ability to effectively manage our business depends on the security, reliability and adequacy of our and our third- party contractors' and vendors' technology systems. Any incident, whether hostile or inadvertent, that adversely impacts the confidentiality, integrity or availability of our systems and / or data, 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 to access confidential information and widespread use of cloud- based applications hosted in remote data centers, 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. 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 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 **including as a result of trade relations between Canada and the United States** ; • economic weakness, including inflation, political instability or open conflict in particular foreign economies and markets; • differing and multiple 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; • 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 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 on our strategic partners, third- party manufacturers, suppliers and other third parties upon which we rely **; and • business interruptions resulting from increased government scrutiny on the use of certain foreign biotechnology service providers due to national security concerns, including the potential for legislation that restricts or prohibits the use of such third-party service providers** . If we are unable to successfully manage these risks associated with cross- border and international activities, our business could be materially harmed. U. S. holders of our common shares may suffer adverse tax consequences if we are characterized as a passive foreign investment company. **U. S. investors should be aware that based on our gross income and gross assets, we were a passive foreign investment company, or PFIC, for the taxable year ended December 31, 2024 and we may be a PFIC in 2025.** Generally, for any taxable year in which 75 % or more of our gross income is passive income, or at least 50 % of the **quarterly** 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. **For PFIC testing purposes** ~~Based on our gross income and gross assets~~ , **a range of factors can affect the determination, including the market price of our common shares and how** we **spend** ~~are deemed a PFIC for~~ - **or otherwise hold our cash** ~~the taxable year ending December 31, 2023 and may be a PFIC for subsequent taxable years~~ . ~~Our~~ **Thus, our** status as a PFIC is a fact- intensive determination made on an annual basis ~~,~~ and **the applicable law is subject to varying interpretation. In addition, a company' s PFIC status can be made only after the end of each taxable year. Accordingly,** 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 **in which a U. S. investor hold our shares** , **such** U. S. holders of our common shares may suffer adverse tax consequences **including in years after we cease to be classified as a PFIC** . Gains realized by **such** ~~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 Canadian federal net operating loss carryforwards which are limited in life, Canadian federal investment tax credit carryforwards and provincial investment tax credit carryforwards which 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 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,~~ **government pricing and** transparency, health information privacy and security, and other healthcare laws and regulations, **non- compliance with** 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 arrangements with healthcare providers, third- party payers, patients and other parties within the healthcare industry may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations 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. 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: • 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 healthcare programs, such as Medicare and Medicaid; • the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended, which imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and also establishes requirements related to the privacy, security, and 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 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 so- called federal" sunshine law" or Open Payments which requires manufacturers of drugs, devices, biologics, and medical supplies to report to the Centers for Medicare & Medicaid Services information related to payments and other transfers of value to teaching hospitals, physicians, and other healthcare practitioners, as well as ownership 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 and ~~health~~ **healthcare** ~~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 ~~;~~; 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. 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 clinical- stage product candidate, ~~XEN1101~~ **azetukalner** for the treatment of epilepsy, MDD **, BPD** and potentially other neurological disorders. Our future business success depends on the continued development and ultimate regulatory approval of ~~XEN1101~~ **azetukalner** . We will need to successfully enroll and complete our ~~XEN1101~~ **azetukalner** Phase 3 ~~epilepsy~~ clinical trials and any other future Phase 3 clinical trials. The future regulatory and commercial success of ~~XEN1101~~ **azetukalner** is subject to a number of risks, including: • successful patient enrollment in clinical trials and ultimate completion of clinical trials; • ~~successful~~ **safety and** efficacy data from our clinical programs that support acceptable risk- benefit profiles of ~~XEN1101~~ **azetukalner** 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~~ **azetukalner** ; • making arrangements with third- party manufacturers for both clinical and commercial supplies of ~~XEN1101~~ **azetukalner** ; • establishing sales, marketing and distribution capabilities and commercial launch of ~~XEN1101~~ **azetukalner** , if and when approved, whether alone or in collaboration with others; • successful commercial launch of ~~XEN1101~~ **azetukalner** , if and when approved; • acceptance of ~~XEN1101~~ **azetukalner** , if and when approved, by patients, the medical community and third- party payers; • obtaining and maintaining acceptable pricing, third- party insurance coverage and adequate reimbursement; • maintaining a continued acceptable safety profile of ~~XEN1101~~ **azetukalner** following approval; • effectively competing with other therapies; • enforcing and defending intellectual property rights and claims; and • raising sufficient funds to support regulatory approval and commercialization activities. Many of these risks are beyond our control, including the risks related to clinical development, the regulatory submission **and approval** 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~~ **azetukalner** 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~~ **azetukalner** 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~~ **azetukalner** . 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~~ **azetukalner** 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 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, 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 disorders for which no drugs have been developed previously and where the product candidates target novel mechanisms. Further, our product candidates may not be approved even if they achieve their primary ~~endpoint~~ **endpoints** 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 **or recommendations** for the approval of a product candidate **at any time in the future,** 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 **the** FDA or another regulatory authority, approval of an NDA or equivalent filing may be significantly delayed or **we may be unable to obtain approval of an NDA or equivalent filing because such studies** 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~~ **azetukalner** and NBI- ~~921352~~ **921355** (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~~ **azetukalner** in adult patients with focal epilepsy. In addition, in November 2023, we released topline data from our Phase 2 X- NOVA clinical trial of ~~XEN1101~~ **azetukalner** in patients with MDD. There can be no assurance that our ongoing ~~XEN1101~~ **azetukalner** Phase 3 ~~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~~ **azetukalner** . 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 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 and our collaborators' 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 collaborators' 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~~ **application** 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; ~~and~~ • governmental or regulatory delays **;** and **•** changes ~~in~~ **to the policies,** ~~regulatory~~ **regulations** ~~requirements, policy~~ and guidelines **of the FDA, EMA or other foreign regulators regarding development, approval, and marketing of biopharmaceutical products, including but not limited to, in the U. S., as a result of policies implemented by the new presidential administration that may, for example, render our clinical data insufficient for approval or restrict us from marketing our product candidates in the manner in which we anticipate** . 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. Challenges in enrolling and retaining patients in our clinical trials, including in our ~~XEN1101~~ **azetukalner** Phase 3 ~~epilepsy~~ clinical trials, whether as a result of 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 may not be adequate to support marketing approval. These clinical trials are lengthy and usually involve many hundreds to thousands of patients. Clinical trials can also be lengthy due to the challenge of identifying patients. 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 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. 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. 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 were generally mild or moderate in severity, there can be no guarantee that we will observe a similar tolerability profile of ~~XEN1101~~ **azetukalner** in our ongoing 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 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. **Such changes may also result in inventions** ~~For example, we have developed a pediatric formulation for NBI- 921352~~ that **result** ~~was included~~ in **additional patent protection** ~~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 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. **A statutory instrument to amend the Medicines for Human Use (Clinical Trials) Regulations 2004 was laid before parliament on December 12, 2024, and will come into force in early 2026 after a 12- month implementation period to address the research sector' s need for a more efficient, streamlined and adaptable regulatory framework for clinical trials.** 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~~ **azetukalner** Phase 3 ~~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 orphan drug designation has been granted in the United States and Europe to NBI- 921352 for the treatment of SCN8A- DEE, we may not be able to realize any value from such designations. NBI-921352, being developed by our collaborator Neurocrine Biosciences, has received orphan drug designation from the FDA and orphan medicinal product designation was granted by the European Commission for the treatment of SCN8A- DEE. Currently, 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 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 the FDA has granted rare pediatric disease, or 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 provide the drug any advantage in the regulatory review or approval process other than potential fee reductions, and priority review vouchers, nor does such designation increase the likelihood that the drug will receive marketing approval~~ . 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 ~~XEN1101~~ **azetukalner** , 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 ability to recruit and retain adequate numbers of qualified sales and marketing personnel or develop alternative sales channels; • the 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; • 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 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 healthcare 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 healthcare 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

manufacturers' communications on the subject of off- label use of their products **. The EU and other foreign jurisdictions also prohibit direct- to- consumer advertising for prescription- only medicines** . 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. We may in the future develop 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 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. If our 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. Any product candidates **for which** we ~~develop~~ **obtain approval** may become subject to unfavorable third- party coverage and reimbursement practices, as well as pricing regulations **, which may adversely affect demand for such products as well as our ability to obtain an appropriate return from the sale of the products** . 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 third- party payers, such as private health insurers, managed care plans, and other organizations. Government authorities and private third- party payers decide which 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. 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 **are** ~~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 payer coverage and reimbursement of newly approved products. Within the U. S., coverage and reimbursement varies from one third party payer to another. One third- party payer' s determination to provide coverage for a product candidate does not assure that other payers will also provide coverage for the product candidate. As a result, the coverage determination process is often time- consuming and costly. Factors 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. We may be required to provide scientific and clinical support for the use of our products to each third- party 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 healthcare 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 payers, and if covered, ~~whether~~ **that** 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 healthcare

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 **demanded by** private 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. In order to obtain and maintain acceptable reimbursement levels and access for patients at copay levels that are reasonable and customary, we may have to offer discounts or rebates from list prices or 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 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 or our collaborators' target patient populations may be in orphan or niche indications, such as 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 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 and 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. Beyond the ACA, there are ongoing and widespread ~~health~~ **healthcare** ~~care~~ reform efforts, a number of which have focused on regulation of prices or payment for drug products. Drug pricing and payment reform was a focus of the **first** Trump ~~Administration~~ **administration** and ~~has been a focus of~~ the Biden ~~Administration~~ **administration** . For example, federal legislation ~~enacted in 2021 eliminates~~ **eliminated** a statutory cap on Medicaid drug rebate program rebates effective January 1, 2024. As another example, the Inflation Reduction Act (IRA) of 2022 ~~contains various~~ **includes a number of changes intended to address rising prescription drug prices in Medicare Parts B and D. These changes, which have varying implementation dates, include caps on Medicare Part D out- of- pocket costs, Medicare Part B and Part D drug price inflation rebates, a new Medicare Part D manufacturer discount drug program (replacing the PPACA Medicare Part D coverage gap discount program) and a** drug price negotiation **program** ~~, inflationary rebate, and pricing provisions with varying implementation dates. The IRA allows the federal government to negotiate a maximum fair price~~ for certain high- **spend** ~~priced single- source Medicare drugs, impose penalties and excise tax for manufacturers that fail to comply with the drug price negotiation requirements, require inflation rebates for all~~ Medicare Part B and ~~Part~~ D drugs ~~(with limited exceptions) if their drug prices increase faster than inflation, and redesigns Medicare Part D to reduce out- of- pocket prescription drug costs for beneficiaries, among other changes~~ . The **IRA is likely to have a significant** impact ~~of the IRA~~ on ~~our business and~~ the ~~broader~~ pharmaceutical industry ~~remains uncertain~~ as implementation **proceeds** ~~is ongoing~~ . As another example, in 2022, subsequent to the enactment of the IRA, the Biden administration ~~released~~ **announced its commitment to expanding certain IRA reforms. Drug pricing** ~~an~~ **and payment reform was a focus of the prior Trump administration and that focus is likely to continue under the new Trump administration. Other potential healthcare reform efforts under the Trump administration may affect access to healthcare coverage or the funding of health care benefits. There is significant uncertainty regarding the nature or impact of any such reform implemented by the Trump administration through** executive **action** ~~order directing the HHS to report on how the Center for~~ **or by** ~~Medicare and Medicaid Innovation (" CMMI ") could be leveraged to test new models for lowering drug costs for Medicare and Medicaid beneficiaries. The report was issued in 2023 and proposed various models that CMMI is currently developing which seek to lower the cost of drugs, promote accessibility and improve quality of care. These changes or 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 states have 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 if and when we 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 **or other reform** legislation in the U. S. 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 and other third- party payers 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 **. The EU is undergoing a revision of its general pharmaceutical legislation to consolidate various legal instruments and achieve key policy objectives such as improving patient access to medicines, enhancing supply chain security, promoting innovation, ensuring environmental sustainability, and addressing antimicrobial resistance. The legislative proposal was considered by the European Parliament in April 2024 for a position to be adopted. The legislative process will take considerable time to complete as the proposal will require agreement by the European Parliament and the European Council** . 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. **Additionally, the U. S. Supreme Court' s June 2024 decision in Loper Bright Enterprises v. Raimondo overturned the longstanding Chevron doctrine, under which courts were required to give deference to regulatory agencies' reasonable interpretations of ambiguous federal statutes. The Loper decision could result in additional legal challenges to regulations and guidance issued by federal agencies, including the FDA, on which we rely. Any such legal challenges, if successful, could have a material impact on our business. Additionally, the Loper decision may result in increased regulatory uncertainty, inconsistent judicial interpretations, and other impacts to the agency rulemaking process, any of which could adversely impact our business and operations. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, our business could be materially harmed.** 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 **. Disruptions at the FDA and other government agencies caused by funding shortages could prevent our product candidates from being developed, approved, or commercialized in a timely manner, or at all, which could negatively impact our business. The ability of the FDA and foreign regulatory authorities to review or approve new product candidates can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory, and policy changes, the FDA' s or foreign regulatory authorities' ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA' s or foreign regulatory authorities' ability to perform routine functions. Average review times at the FDA and foreign regulatory authorities have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. For example, over the last several years, the U. S. federal government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities. If a prolonged government shutdown occurs, preventing the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Additionally, the Trump Administration has enacted several executive actions that could impose significant burdens on, or otherwise materially delay, the FDA' s ability to engage in routine regulatory and oversight activities. It is difficult to predict how these executive actions and executive actions that may be taken under the current Trump Administration may affect the FDA' s ability to exercise its regulatory authority. If these executive actions impose constraints on the FDA' s ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted** . 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. 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 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. **Our reliance on third parties to manufacture our product candidates may increase the risk that we will not have sufficient quantities of our raw materials, APIs or drug products when needed or at an acceptable cost.** We do not own or operate manufacturing **or testing** 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, 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, **test,** 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 **and time** 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~~ **azetukalner** 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. **Our use of foreign CROs and CMOs in some jurisdictions, such as China, may be or may become subject to U. S. legislation, sanctions, trade restrictions and other regulatory requirements which may increase the cost of, and cause delays for, our pre- clinical product candidates.** 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 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 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 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 issue with respect to our patent applications that are currently pending, and issued patents might later be found to be invalid or unenforceable, be interpreted in a manner that does not adequately protect our 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. In addition, the standards applied by the U. S. Patent and Trademark Office, or USPTO, and foreign patent offices in issuing patents are not always applied uniformly or predictably, and also may be subject to changing law. 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 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 offices outside of the U. S. in several stages over the lifetime of the patents and / or applications. The USPTO and foreign governmental patent 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 collaborators to effect compliance with respect to the patents and patent applications that we out- license. 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 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 own, co- own or may in- license; • others may independently develop similar or alternative technologies without infringing our intellectual property rights; • patents that we own, co- own or may in- 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, the term (s) may begin to run out prior to the commercial sale of the related product, **thereby limiting** 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 our future products. 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~~ **may** not protect intellectual property rights to the same extent as the 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 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 future products, 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 countries. The legal systems of some countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property 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 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 our intellectual property. We may be involved in lawsuits to enforce our patents or the patents of our 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. Competitors may infringe our patents or the patents of our licensors. To 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 is not valid or is not enforceable. In such ~~case~~ **cases ,** third parties may be able to use 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 from using the technology at issue on the ground that the other party' s activities are not covered by our patents **or that the legal requirements for imposing injunctive relief are not met** . In addition, third parties may affirmatively challenge our rights to, or the scope or validity of, our patents. An adverse result in any litigation or post- grant ~~proceedings~~ **proceeding** could put additional 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. Any 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 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, patent ineligibility, loss of priority claims, lack of written description, or lack of enablement. Grounds for an assertion of unenforceability could be an allegation that someone connected with prosecution of the patent withheld material information from the USPTO or an applicable foreign counterpart where such a duty to disclose exists, or made a misleading statement, during prosecution. For example, administrative proceedings such as derivation proceedings, entitlement proceedings, ex parte reexamination, inter partes review, ~~postgrant~~ **post- grant** review, or opposition proceedings, provoked by third parties or initiated by the USPTO or any foreign patent authority may be used to challenge inventorship, ownership, claim scope, or validity of our patents 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 administrative proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees **. Certain foreign countries may provide for compulsory licensing of our patent rights that would preclude us from enforcing our patents against a third party** . With respect to challenges to the validity of our patents or the patents of our licensors, for example, there might be 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 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 challenges is unpredictable. Even if a challenger does not prevail, our patent claims may be construed in a manner that would limit our ability to enforce such claims against the

challenger and others. The cost of defending such a challenge, particularly in a foreign 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. 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 future products are controlled by our collaborators, including licensees, sublicensees or licensors. 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 **certain** ~~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 collaborator with rights to file, prosecute, 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 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. 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, 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, without infringing the intellectual property rights or other proprietary rights of others. Third parties might allege that we, or our collaborators, are infringing, misappropriating, or otherwise violating their intellectual property rights. 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 were not 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. 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~~ **proceeding**, for example, derivation proceedings, entitlement proceedings, ex parte reexamination, inter partes review, ~~postgrant~~ **post- grant** review, or opposition proceedings, before the USPTO or **similar proceedings before** 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~~ **any** 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 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 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 be able to sustain the costs of complex intellectual property litigation or proceedings more effectively than we 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. 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 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 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. If we are found to infringe a third- party' s intellectual property rights, we could be forced, including by court order, to cease developing, manufacturing or commercializing the infringing product candidate or future product. 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, we may be required to pay substantial damage awards to the plaintiff, including up to treble damages and attorneys' fees if we are found to have willfully infringed a patent. As another alternative, we may be required to obtain a license from the intellectual property owner to continue our research and development programs or to market any resulting product. It is also possible that we may be required to modify or redesign our 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 we choose or are required to seek a license from a third- party, 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 as a result of actual or threatened litigation ~~, 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 developed or commercialized in a country without the third- party intellectual property ~~right~~ **rights** or, where it is decided that it would be useful to acquire such third- party ~~right~~ **rights** 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 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 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 license, or any license exclusivity thereunder, could materially harm our business, prospects, financial condition and results of operations. If we are unable to prevent unauthorized disclosure of trade secrets and other proprietary information, 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 maintain our competitive position. 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. 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 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, 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 have the option, upon issuance of a patent, of becoming a Unitary Patent, which is subject to the jurisdiction of the Unitary Patent Court, or UPC. The option of a Unitary Patent and the creation of the UPC are significant changes in European patent practice. As the UPC is a new court system, there is 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 by extending the patent terms for **patents covering** 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 extension under the Hatch- Waxman Act. However, we may not be granted an extension **if** ~~because of~~ , for example, ~~failing~~ **we fail** to apply within applicable deadlines, ~~failing~~ **fail** to apply prior to expiration of relevant patents or otherwise ~~failing~~ **fail** 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 the 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. If **any of our products are approved by the FDA, listing patents in the FDA' s Approved Drug Products with Therapeutic Equivalence Evaluations (Orange Book) is mandatory, and the decision to list or not list a given patent in the Orange Book could give rise to allegations of antitrust liability, from the Federal Trade Commission or private parties. In addition, we may be required by court order to delist patents from the Orange Book that are found to be improperly listed, which could impact our ability to take advantage of the benefits of the Hatch- Waxman Act, including the 30- month stay of generic approval. If** our trademarks are not adequately protected, we may not be able to build name recognition in our markets of interest, which 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 patent ~~officers~~ **offices** in many foreign countries, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. 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. Moreover, any name we have proposed to 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 would qualify under applicable trademark laws, not infringe the existing rights of third parties, and be acceptable to the FDA. This may require additional expense. In addition, there could be potential trademark infringement claims brought by owners of other registered trademarks that incorporate variations of **or allegedly cause confusion with** our registered or unregistered trademarks. If we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks. If we are unable to establish name recognition based on our trademarks, we may not be able to compete effectively, and 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 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. **Fluctuating** ~~The COVID- 19 pandemic and rising~~ inflation and interest rates, for example, **can** ~~resulted~~ -- **result** 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. 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 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. **The** ~~Similarly, the~~ current conflicts between Ukraine and Russia and in the Middle East, as well as recent failures in the global banking sector, have created volatility in the capital markets and 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, 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 various rulemaking efforts, including recently with respect to environmental, social and governance, or ESG, matters. **In March 2024, the SEC adopted climate- related disclosure rules but subsequently issued an order implementing a stay of its final rules.** 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 **formally** 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.