Filed Pursuant to Rule 424(b)(5)
Registration No. 333-260010

The information in this preliminary prospectus supplement is not complete and may be changed. A registration statement relating to these securities has been filed with the Securities and Exchange Commission and is effective. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities and they are not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED OCTOBER 4, 2021

PRELIMINARY PROSPECTUS SUPPLEMENT
(To Prospectus dated October 4, 2021)

$250,000,000

Common Shares

We are offering up to $250,000,000 of our common shares in this offering.

Our common shares are listed on the Nasdaq Global Market under the symbol “XENE.” Based on assumed public offering price of $31.50 per share, the last reported sale price of our common shares on the Nasdaq Global Market on October 4, 2021, we would expect to offer approximately 7,936,507 common shares hereby.

Investing in our common shares involves a high degree of risk. See “Risk Factors” beginning on page S-7 of this prospectus supplement and under similar headings in the documents incorporated by reference into this prospectus supplement and the accompanying prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement or the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

	Per Common Share	Total
Public Offering Price	$	$
Underwriting Discounts and Commissions (1)	$	$
Proceeds to Xenon Pharmaceuticals Inc., before expenses	$	$

(1) See “Underwriting” beginning on page S-61 of this prospectus supplement for additional information regarding underwriters’ compensation.

Delivery of the common shares is expected to be made on or about October , 2021. We expect to grant the underwriters an option for a period of 30 days to purchase up to an additional $37,500,000 of common shares. If the underwriters exercise the option in full, the total underwriting discounts and commissions will be $, and the total proceeds to us, before expenses, will be $.

Joint Book-Running Managers

Jefferies **SVB Leerink** **Stifel** **RBC Capital Markets**

Prospectus Supplement dated October , 2021

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Prospectus Supplement

Prospectus

ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus dated October 4, 2021 form part of an automatic shelf registration statement that we filed with the Securities and Exchange Commission, or the SEC, as a "well-known seasoned issuer" as defined in Rule 405 under the Securities Act of 1933, as amended, or the Securities Act. This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of this securities offering and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference herein. The second part, the accompanying prospectus, provides more general information. Generally, when we refer to this prospectus supplement, we are referring to both parts of this document combined. To the extent there is a conflict between the information contained in this prospectus supplement and the information contained in the accompanying prospectus or any document incorporated by reference therein filed prior to the date of this prospectus supplement, you should rely on the information in this prospectus supplement; provided that if any statement in one of these documents is inconsistent with a statement in another document having a later date, for example, a document incorporated by reference in the accompanying prospectus, the statement in the document having the later date modifies or supersedes the earlier statement.

Neither we nor the underwriters have authorized anyone to provide any information other than that contained or incorporated by reference in this prospectus supplement, the accompanying prospectus or in any free writing prospectus prepared by or on behalf of us or to which we have referred you. We and the underwriters take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus supplement and the accompanying prospectus or any free writing prospectus do not constitute an offer to sell, or a solicitation of an offer to purchase, the securities offered by this prospectus supplement and the accompanying prospectus or any free writing prospectus in any jurisdiction to or from any person to whom or from whom it is unlawful to make such offer or solicitation of an offer in such jurisdiction. The information contained in this prospectus supplement or the accompanying prospectus, or incorporated by reference herein or therein or any free writing prospectus is accurate only as of the respective dates thereof, regardless of the time of delivery of this prospectus supplement and the accompanying prospectus or any free writing prospectus or of any sale of our common shares. It is important for you to read and consider all information contained in this prospectus supplement and the accompanying prospectus, including the documents incorporated by reference herein and therein or any free writing prospectus, in making your investment decision. You should also read and consider the information in the documents to which we have referred you in the sections entitled "Where You Can Find More Information" and "Information Incorporated by Reference" in this prospectus supplement and in the accompanying prospectus.

We are offering to sell, and seeking offers to buy, securities only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement and the accompanying prospectus or any free writing prospectus and the offering of the securities in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus supplement and the accompanying prospectus or any free writing prospectus must inform themselves about, and observe any restrictions relating to, the offering of the securities and the distribution of this prospectus supplement and the accompanying prospectus or any free writing prospectus outside the United States.

Unless the context requires otherwise, references in this prospectus supplement to "Xenon," "the Company," "we," "us" and "our" refer to Xenon Pharmaceuticals Inc. and its subsidiary.

PROSPECTUS SUPPLEMENT SUMMARY

This summary description about us and our business highlights selected information contained elsewhere in this prospectus supplement or incorporated by reference in this prospectus supplement and the accompanying prospectus. This summary does not contain all of the information that you should consider before deciding to invest in our securities. You should carefully read this entire prospectus supplement, the accompanying prospectus and any related free writing prospectus, including each of the documents incorporated herein or therein by reference, before making an investment decision. Investors should carefully consider the information set forth under "Risk Factors" in this prospectus supplement beginning on page S-7 and in any related free writing prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus supplement and the accompanying prospectus. You also should carefully read the information incorporated by reference into this prospectus supplement and the accompanying prospectus, including our financial statements, other information and the exhibits to the registration statement of which the accompanying prospectus is a part.

Overview

We are a clinical stage biopharmaceutical company committed to developing innovative therapeutics to improve the lives of patients with neurological disorders. We are advancing a novel product pipeline of neurology-focused therapies to address areas of high unmet medical need, with a focus on epilepsy. In addition to our proprietary product candidates, we also have partnered programs with several pharmaceutical companies, including Neurocrine Biosciences, Inc., or Neurocrine Biosciences, and Flexion Therapeutics, Inc., or Flexion.

Our proprietary product candidates include:

- XEN1101 is a differentiated Kv7 potassium channel modulator being developed for the treatment of epilepsy, major depressive disorder, or MDD, and potentially other neurological disorders. Designed as a randomized, double-blind, placebo-controlled, multicenter study, our 'X-TOLE' Phase 2b clinical trial was designed to evaluate the clinical efficacy, safety, and tolerability of XEN1101 administered as adjunctive treatment in adult patients with focal epilepsy. We reported positive topline results from the Phase 2b X-TOLE clinical trial on October 4, 2021. See "Recent Developments" for additional information.

  We also continue to evaluate opportunities to develop XEN1101 in neurological indications outside of epilepsy that could be well suited to its unique mechanism of action. Our collaborators at the Icahn School of Medicine at Mount Sinai are conducting an investigator-sponsored Phase 2 proof-of-concept, randomized, parallel-arm, placebo-controlled clinical trial of XEN1101 for the treatment of MDD and anhedonia, with enrollment expected to start in October 2021. In parallel, we are planning a company-sponsored clinical study in MDD supported by promising pre-clinical data with XEN1101 and clinical data generated from both an open-label study and a randomized, placebo-controlled clinical trial that explored the targeting of KCNQ channels as a treatment for MDD using ezogabine.

- XEN496, a Kv7 potassium channel modulator, is a proprietary pediatric formulation of the active ingredient ezogabine being developed for the treatment of KCNQ2 developmental and epileptic encephalopathy, or KCNQ2-DEE. We received Fast Track designation and Orphan Drug Designation, or ODD, for XEN496 for the treatment of seizures associated with KCNQ2-DEE from the U.S. Food and Drug Administration, or FDA, as well as orphan medicinal product designation from the European Commission. A Phase 3 randomized, double-blind, placebo-controlled, parallel group, multicenter clinical trial, called the "EPIK" study, is underway to evaluate the efficacy, safety, and tolerability of XEN496 administered as adjunctive treatment in approximately 40 pediatric patients aged one month to less than six years with KCNQ2-DEE.

- XEN007 (active ingredient flunarizine) is a CNS-acting Cav2.1 and T-type calcium channel modulator that is being studied in treatment-resistant absence seizures and potentially other neurological disorders. Recently, the FDA granted ODD and rare pediatric disease, or RPD, designation for the treatment of childhood absence epilepsy, or CAE, with XEN007. The FDA grants the RPD designation for serious or life-threatening diseases that primarily affect children 18 years old or younger and affect fewer than 200,000 people nationwide. An investigator-led Phase 2 proof-of-concept study is ongoing to examine the potential clinical efficacy, safety, and tolerability of XEN007 as an adjunctive treatment in pediatric patients diagnosed with treatment-resistant absence seizures, including CAE and juvenile absence epilepsy, or JAE. A presentation of promising interim data collected from a small number of patients was presented at the virtual annual meeting of the American Epilepsy Society in December 2020. The lead investigator has expanded the study to include an additional site, which is currently screening patients, and is also evaluating the addition of other sites. Additional results from a larger data set are anticipated by the end of this year, which will inform our decision regarding the future development of XEN007.

Our clinical stage partnered programs include:

- We have an ongoing collaboration with Neurocrine Biosciences to develop treatments for epilepsy. Neurocrine Biosciences has an exclusive license to XEN901, now known as NBI-921352, a selective Nav1.6 sodium channel inhibitor. Neurocrine Biosciences is currently advancing NBI-921352 through Phase 2 development in adolescent patients (aged 12 years and older) with SCN8A developmental and epileptic encephalopathy, or SCN8A-DEE, and, in parallel, in adult patients with focal-onset seizures. Based on the regulatory approval of a clinical trial application in Europe for NBI-921352 for focal-onset seizures in adults, we received an aggregate milestone payment of $10.0 million in the form of cash and an equity investment in September 2021. Upon FDA acceptance of a protocol amendment for NBI-921352 in pediatric patients (aged 2-11 years) with SCN8A-DEE, we are eligible to receive an aggregate payment of $15.0 million in the form of 45% cash and a 55% equity investment in our common shares at a 15% premium to our 30-day trailing volume weighted average price at that time.

- Flexion acquired the global rights to develop and commercialize XEN402, a Nav1.7 inhibitor also known as funapide. Flexion's FX301 consists of XEN402 formulated for extended release from a thermosensitive hydrogel. The initial development of FX301 is intended to support administration as a peripheral nerve block for control of post-operative pain. On March 31, 2021, Flexion announced the treatment of the first patient in a Phase 1b proof-of-concept trial evaluating the safety and tolerability of FX301 administered as a single-dose, popliteal fossa block (a commonly used nerve block in foot and ankle-related surgeries) in patients undergoing bunionectomy. Flexion anticipates data from the Phase 1b trial of FX301 in late 2021. Pursuant to the terms of the agreement, we are eligible to receive certain clinical, regulatory, and commercial milestone payments, as well as future sales royalties.

In addition to current product candidates in development and our partnered programs, we intend to expand our pipeline from our internal research efforts and may expand our pipeline through the acquisition or in-licensing of other product candidates.

Recent Developments

On October 4, 2021, we announced positive topline data from our 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 XEN1101 administered as an adjunctive treatment for adult patients with focal epilepsy. The trial met its primary efficacy endpoint with XEN1101 demonstrating a statistically significant and dose-dependent reduction from baseline in monthly (defined as 28 days) focal seizure frequency when compared to placebo (monotonic dose response; $p<0.001$). Additional primary and secondary efficacy measures 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 was generally well-tolerated in this study with adverse events consistent with other anti-seizure medicines. We intend to gather input from the FDA and other regulatory agencies to continue planning the future clinical development of XEN1101. In addition, the X-TOLE open-label extension, which has been expanded to three years, is expected to continue to generate important long-term data for XEN1101.

Risk Factor Summary

Our business is subject to numerous risks and uncertainties, including those highlighted in the section of this prospectus supplement 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 likely need to raise additional funding, which may not be available on acceptable terms, if at all. Failure to obtain this necessary capital when needed may force us to delay, limit or terminate our product development efforts or other operations;

- Clinical drug development involves a lengthy and expensive process with uncertain timelines and uncertain outcomes. If clinical trials are prolonged, delayed, not completed, unsuccessful or inconclusive, we could experience material harm to our business and the market price of our common shares. In addition, we, or our collaborators, may be unable to commercialize our product candidates on a timely basis or at all;

- 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 studies, including for ultra-orphan, orphan or niche indications, which could delay or prevent clinical studies of our product candidates;

- The regulatory approval processes of the FDA, EMA, Health Canada and regulators in other jurisdictions are lengthy, time-consuming and inherently unpredictable. If we, or our collaborators, are unable to obtain regulatory approval for our product candidates in a timely manner, or at all, our business will be substantially harmed;
- If, in the future, we are unable to establish our own sales, marketing and distribution capabilities or enter into agreements for these purposes, we may not be successful in independently commercializing any future products;
- Our prospects for successful development and commercialization of our partnered products and product candidates are dependent upon the research, development and marketing efforts of our collaborators;
- We depend on our collaborative relationship with Neurocrine Biosciences to further develop and commercialize NBI-921352, and if our relationship is not successful or is terminated, we may not be able to effectively develop and/or commercialize NBI-921352, which could have a material adverse effect on our business;
- We intend to rely on third-party manufacturers to produce our clinical product candidates and commercial supplies. Any failure by a third-party manufacturer to produce acceptable supplies for us may delay or impair our ability to initiate or complete our clinical trials, gain regulatory approvals or commercialize approved products;
- We rely on third parties to conduct our pre-clinical studies and clinical trials. If these third parties do not successfully carry out their contractual duties including to comply with applicable laws and regulations or meet expected deadlines, our business could be substantially harmed;
- We could be unsuccessful in obtaining or maintaining adequate patent protection for one or more of our products or product candidates;
- 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 information security incident such as a cybersecurity breach, system failure, or other compromise of our systems or those of a contractor or vendor;
- Health pandemics or epidemics, including the COVID-19 pandemic and other public health crises may materially and adversely affect our business, financial condition and results of operations;
- The 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, preferred shares, or rights to purchase common shares, including warrants or pursuant to our equity incentive plans, could cause shareholders to incur dilution and could cause the market price of our common shares to fall; and
- We are at risk of securities class action litigation.

About Xenon

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, 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, 2020, Xenon Pharmaceuticals USA Inc., which was incorporated in Delaware on December 2, 2016. Our principal executive offices are located at 200 – 3650 Gilmore Way, Burnaby, British Columbia, Canada V5G 4W8, and our telephone number is (604) 484-3300. We are a reporting issuer in British Columbia, Alberta and Ontario, but our shares are not listed on any recognized Canadian stock exchange. Our common shares trade on the Nasdaq Global Market under the symbol “XENE.” Our website address is *www.xenon-pharma.com*. The information contained in, or that can be accessed through, our website is not incorporated by reference into this prospectus supplement and should not be considered to be a part of this prospectus supplement.

“Xenon,” the Xenon logo and other trademarks or service marks of Xenon appearing in this prospectus supplement are trademarked and are the property of Xenon Pharmaceuticals Inc. This prospectus supplement contains references to our trademarks and service marks and to those belonging to other entities. Solely for convenience, trademarks and trade names referred to in this prospectus supplement, including logos, artwork and other visual displays, may appear without the ® or ™ symbols, but such references are not intended to indicate in any way that we will not assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensor to these trademarks and trade names. We do not intend our use or display of other entities’ trade names, trademarks or service marks to imply a relationship with, or endorsement or sponsorship of us by, any other entity.

THE OFFERING

Common shares offered by us	shares (common shares if the underwriters' option to purchase additional common shares is exercised in full).
Option to purchase additional common shares	We expect to grant the underwriters an option to purchase up to additional common shares. This option is exercisable, in whole or in part, for a period of 30 days from the date of this prospectus supplement.
Common shares to be outstanding after this offering	common shares (common shares if the underwriters' option to purchase additional common shares is exercised in full).
Use of proceeds	We estimate that the net proceeds to us from this offering, after deducting underwriting discounts and commissions and estimated offering expenses payable by us, based on an assumed public offering price of $31.50 per share, which is the last reported sale price of our common shares on the Nasdaq Global Market on October 4, 2021, will be approximately $234.7 million, or approximately $269.9 million if the underwriters exercise their option to purchase additional common shares from us in full. We currently expect to use the net proceeds to us from this offering for external and personnel-related expenses associated with the clinical development of our XEN1101 and XEN496 product candidates as well as other programs entering clinical development; to fund our pre-clinical and discovery activities; and for working capital, capital expenditures and other general corporate purposes. See "Use of Proceeds" on page S-49 of this prospectus supplement.
Risk factors	An investment in our common shares involves a high degree of risk. See "Risk Factors" beginning on page S-7 of this prospectus supplement and the similarly titled sections in the documents incorporated by reference into this prospectus supplement.
Nasdaq Global Market symbol	Our common shares are listed on the Nasdaq Global Market under the symbol "XENE".

Outstanding Shares

The number of common shares to be outstanding after this offering is based on 42,133,568 common shares outstanding as of June 30, 2021 which number includes 1,016,000 common shares issuable upon the conversion of 1,016,000 of our Series 1 Preferred Shares outstanding as of June 30, 2021, and excludes:

- 5,771,051 common shares issuable upon the exercise of outstanding options to purchase common shares as of June 30, 2021, at a weighted average exercise price of $12.04 per common share;
- 275,337 common shares sold subsequent to June 30, 2021 pursuant to our license and collaboration agreement with Neurocrine Biosciences;
- 2,557,246 common shares reserved for future issuance as of June 30, 2021 under our Amended and Restated 2014 Equity Incentive Plan;
- 40,000 common shares issuable upon the exercise of warrants outstanding as of June 30, 2021, at a weighted-average exercise price of $9.79 per share; and
- pre-funded warrants to purchase up to 1,081,081 common shares outstanding as of June 30, 2021, at an exercise price of $0.0001 per share.

Except as otherwise indicated herein, all information in this prospectus supplement, including the number of common shares that will be outstanding after this offering, reflects an assumed public offering price of $31.50 per share, which is the last reported sale price of our common shares on the Nasdaq Global Market on October 4, 2021, and assumes no exercise by the underwriters of their option to purchase additional common shares.

RISK FACTORS

Investing in our common shares involves a high degree of risk. You should carefully consider the risks described below, as well as all other information included in this prospectus supplement, the accompanying prospectus and in our other filings with the SEC incorporated by reference into this prospectus supplement before you decide to purchase common shares. If any of the following risks actually occurs, our business, financial condition, operating results, prospects and ability to accomplish our strategic objectives could be materially harmed. As a result, the trading price of our common shares could decline and you could lose all or part of your investment. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our business operations and the market price of our common shares.

Risks Related to Our Financial Condition and Capital Requirements

We have incurred significant losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future.

We do not expect to have sustained profitability for the foreseeable future. We had a net loss of $37.9 million for the six months ended June 30, 2021 and an accumulated deficit of $316.4 million as of June 30, 2021, 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 have devoted most of our financial resources to research and development, including our clinical and pre-clinical development activities. To date, we have financed our operations primarily through the sale of equity securities, funding received from our licensees and collaborators, and debt financing. We do not generate any revenue from product sales and our product candidates will require substantial additional investment before they may provide us with any revenue.

We expect to incur significant expenses and increasing operating losses for the foreseeable future as we:

- continue our research and pre-clinical and clinical development of our product candidates;
- expand the scope of our clinical studies for our current and prospective product candidates;
- initiate additional pre-clinical, clinical or other studies for our product candidates;
- change or add additional manufacturers or suppliers and manufacture drug supply and drug product for clinical trials and commercialization;
- seek regulatory and marketing approvals for any of our product candidates that successfully complete clinical studies;
- seek to identify and validate additional product candidates;
- acquire or in-license other product candidates and technologies;
- make milestone or other payments under our in-license or other agreements, including, without limitation, payments to Memorial University of Newfoundland, 1st Order Pharmaceuticals, Inc. and other third parties;
- maintain, protect and expand our intellectual property portfolio;
- establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval;
- create additional infrastructure and incur additional costs to support our operations and our product development and planned future commercialization efforts; and
- experience any delays or encounter issues with any of the above.

Our expenses could increase beyond expectations for a variety of reasons, including if we are required by the FDA, the European Medicines Agency, or EMA, Health Canada, or other regulatory agencies, domestic or foreign, to perform clinical and other studies including post-approval commitments in addition to those that we currently anticipate. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our shareholders' equity.

We do not generate any royalty or other revenue from product sales and may never become profitable on a U.S. GAAP basis.

Our ability to generate meaningful revenue and achieve profitability on a U.S. GAAP basis depends on our ability, alone or with strategic collaborators, to successfully complete the development of, and obtain the regulatory approvals necessary to commercialize, our product candidates. Substantially all of our revenue since inception has consisted of upfront and milestone payments associated with our collaboration and license agreements. Revenue from these agreements is dependent on successful development of our product candidates by us or our collaborators. We do not generate any royalty or other revenue from product sales, and do not otherwise anticipate generating revenue from product sales for the foreseeable future, if ever. 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. Our ability to generate future revenue from product sales depends heavily on our success, and the success of our collaborators, in:

- completing research, pre-clinical and clinical development of our product candidates;
- seeking and obtaining regulatory and marketing approvals for product candidates for which we complete clinical studies;
- commercializing products for which we obtain regulatory and marketing approval, either with a collaborator or, if launched independently, by establishing sales, marketing and distribution infrastructure;
- negotiating favorable terms in any collaboration, licensing or other arrangements into which we may enter;
- obtaining market acceptance of products for which we obtain regulatory and marketing approval as therapies;
- addressing any competing technological and market developments;
- establishing and maintaining supply and manufacturing relationships with third parties that can provide adequate (in amount and quality) products and services to support clinical development and the market demand for any approved products in the future;
- developing sustainable, scalable, reproducible, and transferable manufacturing processes for any of our products approved in the future;
- maintaining, protecting, expanding and enforcing our portfolio of intellectual property rights, including patents, trade secrets and know-how;
- implementing additional internal systems and infrastructure, as needed; and
- attracting, hiring and retaining qualified personnel.

The scope of our future revenue will also depend upon the size of any markets in which our product candidates receive approval and the availability of insurance coverage and the availability and amount of reimbursement from third-party payers for future products, if any. If we are unable to achieve 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.

We will likely need to raise additional funding, which may not be available on acceptable terms, if at all. Failure to obtain this necessary capital when needed may force us to delay, limit or terminate our product development efforts or other operations.

Since our inception, we have dedicated most of our resources to the discovery and development of our pre-clinical and clinical product candidates, and we expect to continue to expend substantial resources doing so for the foreseeable future. These expenditures will include costs associated with research and development, potential milestone payments and royalties to third parties, manufacturing of product candidates and products approved for sale, conducting pre-clinical experiments and clinical trials and obtaining and maintaining regulatory approvals, as well as commercializing any products later approved for sale. During the six months ended June 30, 2021, we incurred $34.7 million of costs associated with research and development, exclusive of costs incurred by our collaborators in developing our product candidates.

Our current cash and cash equivalents and marketable securities are not expected to be sufficient to complete clinical development of any of our product candidates and prepare for commercializing any product candidate which receives regulatory approval. Accordingly, we will likely require substantial additional capital to continue our clinical development and potential commercialization activities. Our future capital requirements depend on many factors, including but not limited to:

- the number and characteristics of the future product candidates we pursue either from our internal research efforts or through acquiring or in-licensing other product candidates or technologies;
- the scope, progress, results and costs of independently researching and developing any of our future product candidates, including conducting pre-clinical research and clinical trials;

- whether our existing collaborations generate substantial milestone payments and, ultimately, royalties on future approved products for us;
- the timing of, and the costs involved in, obtaining regulatory approvals for any future product candidates we develop independently;
- the timing and magnitude of potential milestone payments and royalties under our product acquisition and in-license agreements;
- the cost of pre-commercial activities in advance of product commercialization as well as the cost of commercializing any future products we develop independently that are approved for sale;
- the cost of manufacturing our future product candidates and products, if any;
- our ability to maintain existing collaborations and to establish new collaborations, licensing or other arrangements and the financial terms of such agreements;
- the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing patents, including litigation costs and the outcome of such litigation; and
- the timing, receipt and amount of sales of, or royalties on, our future products, if any.

We are unable to estimate the funds we will actually require to complete research and development of our product candidates or the funds required to commercialize any resulting product in the future.

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 our most recent Quarterly Report on Form 10-Q 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, through public or private equity or debt financings, government or other third-party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements or a combination of these approaches. 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.

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 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.

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. For example, in November 2019, we entered into the November 2019 sales agreement with Jefferies LLC, or Jefferies, and Stifel, Nicolaus & Company, Incorporated, or Stifel, to sell up to $50.0 million of our common shares, from time to time, through an "at-the-market" equity offering program under which Jefferies and Stifel acted as sales agents. As of January 2020, we had sold an aggregate of 3,252,330 common shares for proceeds of $48.5 million, net of commissions paid and transaction expenses. In January 2020, we completed an underwritten public offering of 3,750,000 of our common shares at a public offering price of $16.00 per share for proceeds of $56.3 million, net of underwriting discounts, commissions and offering expenses. In February 2020, the underwriters of the January 2020 public offering exercised their option to purchase an additional 562,500 of our common shares at a public offering price of $16.00 per share, raising additional proceeds of $8.4 million, net of underwriting discounts, commissions and offering expenses. Further, in August 2020, we entered into the August 2020 sales agreement with Jefferies and Stifel to sell up to $100.0 million of our common shares, from time to time, through an "at-the-market" equity offering program under which Jefferies and Stifel are acting as sales agents. As of June 30, 2021, we had sold an aggregate of 733,000 common shares for proceeds of $10.7 million, net of commissions paid and transaction expenses. In March 2021, we completed an underwritten public offering of 5,135,135 of our common shares, including 810,810 shares sold upon the full exercise of the underwriters' option to purchase additional shares, and pre-funded warrants to purchase 1,081,081 common shares. The common shares were offered at a public offering price of $18.50 per common share and the pre-funded warrants were offered at a price of $18.4999 per pre-funded warrant, for proceeds of $107.9 million, net of underwriting discounts, commissions and offering expenses. In September 2021, pursuant to the terms of our collaboration agreement with Neurocrine Biosciences, we issued 275,337 common shares to Neurocrine Biosciences for an aggregate purchase price of $5.5 million.

We were also party to an amended and restated loan and security agreement with Silicon Valley Bank pursuant to which we had borrowed an aggregate principal amount of $15.5 million. The restated loan and security agreement was secured by substantially all of our assets except intellectual property and required compliance with various affirmative and negative covenants. In May 2020, we repaid the total outstanding term loan balance ahead of the maturity date and all encumbrances were removed by Silicon Valley Bank. 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 arrangements with collaborators or otherwise at an earlier stage than otherwise would be desirable resulting in the loss of rights to some of our product candidates or other unfavorable terms, any of which may have a material adverse effect on our business, operating results and prospects. In addition, any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates.

We are subject to risks associated with currency fluctuations which could impact our results of operations.

As of June 30, 2021, approximately 5% of our cash and cash equivalents and marketable securities were denominated in Canadian dollars. We incur significant expenses in Canadian dollars in connection with our operations in Canada. We do not currently engage in foreign currency hedging arrangements for our Canadian dollar expenditures, and, consequently, foreign currency fluctuations may adversely affect our earnings; however, in the future, we may engage in exchange rate hedging activities in an effort to mitigate the impact of exchange rate fluctuations. Any hedging technique we implement may fail to be effective. If our hedging activities are not effective, changes in currency exchange rates may have a more significant impact on the market price of our common shares.

We have historically financed our cash needs through a combination of sources including debt financing, which arrangements can contain operating and financial covenants that may restrict our business and financing activities.

We have historically financed our cash needs through a combination of collaboration agreements, equity and debt financings. Debt financings may require a security interest in substantially all of our assets and may also restrict our ability, among other things, to:

- sell, transfer or otherwise dispose of any of our business assets or property, subject to limited exceptions;
- make material changes to our business;
- enter into transactions resulting in significant changes to the voting control of our common shares;
- make certain changes to our organizational structure;
- consolidate or merge with other entities or acquire other entities;

- incur additional indebtedness or create encumbrances on our assets;
- pay dividends, other than dividends paid solely in our common shares, or make distributions on and, in certain cases, repurchase our common shares;
- enter into certain transactions with our affiliates;
- repay subordinated indebtedness; or
- make certain investments.

For example, in August 2018, we entered into an amended and restated loan and security agreement with Silicon Valley Bank providing for a term loan to us with an aggregate principal amount of $15.5 million. Borrowings under this amended and restated loan and security agreement were secured by substantially all of our assets except intellectual property and also subjected us to certain affirmative and restrictive covenants. In May 2020, we repaid our borrowings and terminated the amended and restated loan agreement; however, we may consider similar debt financing arrangements in the future. Any such debt financing we seek in the future may restrict our ability to finance our operations, engage in business activities or expand or fully pursue our business strategies.

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.

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, EMA, Health Canada or other 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.

To the extent that we are unable to compete effectively against one or more of our competitors in these areas, our business will not grow and our financial condition, results of operations and the market price of our common shares may suffer.

For example, if more than one of our proprietary or partnered products were approved for the treatment of epilepsy, we anticipate that they could potentially compete with one another and other anti-seizure medications, or ASMs. Currently prescribed ASMs, among others, include phenytoin, levetiracetam, brivaracetam, carbamazepine, cenobamate, clobazam, lamotrigine, valproate, oxcarbazepine, topiramate, lacosamide, ethosuximide, perampanel, cannabidiol, eslicarbazepine acetate, gabapentin and fenfluramine. The FDA has not yet approved any drug products specifically for KCNQ2 developmental and epileptic encephalopathy (otherwise known as KCNQ2-DEE or EIEE7) or for SCN8A developmental and epileptic encephalopathy (otherwise known as SCN8A-DEE or EIEE13), an early infantile epileptic encephalopathy due to gain-of-function mutations in the SCN8A gene that encodes the Nav1.6 sodium channel. There are other ASMs in clinical development that could potentially compete with our products, including products in development from Angelini Pharma, Eisai Co., Ltd., Jazz Pharmaceuticals plc, Knopp Biosciences LLC, Longboard Pharmaceuticals Inc., Marinus Pharmaceuticals, Inc., Neurocrine Biosciences, Ovid Therapeutics Inc., Praxis Precision Medicines, Inc., Sage Therapeutics, SK Life Science Inc., Stoke Therapeutics Inc., Supernus Pharmaceuticals, Inc., Takeda Pharmaceutical Company Ltd., UCB, Inc., Upsher-Smith Laboratories, Inc., Zogenix Inc., and Zynerba Pharmaceuticals, Inc.

We have no marketed proprietary products and have not yet completed clinical development beyond Phase 2 clinical trials, which makes it difficult to assess our ability to develop our future product candidates and commercialize any resulting products independently.

As a company, we have no previous experience in completing a Phase 3 clinical trial or in completing clinical trials in pediatric indications, and related regulatory requirements or the commercialization of products. We have not yet demonstrated our ability to independently and repeatedly conduct clinical development after Phase 2, conduct a pivotal clinical trial, obtain regulatory approval, manufacture drug product on a 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:

- 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;
- 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, acquiring or in-licensing product candidates in addition to XEN496, XEN1101 and XEN007, our ability to expand our business and achieve our strategic objectives may be impaired.

We have built a product development pipeline by identifying product candidates either from our internal research efforts or through acquiring or in-licensing other product candidates or technologies. To date, our internal discovery efforts have yielded multiple development candidates, including XEN901, which we licensed to Neurocrine Biosciences and is now known as NBI-921352, and XEN402, which has been acquired by Flexion to use in its product candidate FX301. 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 senior management 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.

We could experience difficulties attracting and retaining qualified employees as competition for qualified personnel in the biotechnology and pharmaceutical field is intense. We are highly dependent upon our senior management, particularly Mr. Ian Mortimer, our President and Chief Executive Officer, as well as other employees. The loss of services of one or more of our members of senior management 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 regulatory standards and requirements and insider trading.

We are exposed to the risk of fraud or other misconduct by our employees, collaborators, vendors, principal investigators, consultants and commercial partners. Misconduct by these parties could include intentional failures to comply with the regulations of the FDA, EMA, Health Canada and other regulators, provide accurate information to the FDA, EMA, Health Canada and other regulators, comply with data privacy and security and healthcare fraud and abuse laws and regulations in the U.S. and abroad, report financial information or data accurately or disclose unauthorized activities to us. 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, laws regarding data privacy and security, including the 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, the General Data Protection Regulation (EU) 2016/679, or GDPR, and the Personal Information Protection and Electronic Documents Act, or PIPEDA, as well as comparable laws in other jurisdictions, may impose obligations with respect to safeguarding the privacy, use, security and transmission of individually identifiable health information such as genetic material or information we have obtained through our direct-to-patient web-based recruitment approach for identifying patients with rare or extreme phenotypes or patients identified for clinical trials.

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 of information obtained in the course of clinical studies, 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 lawsuits stemming from a failure to comply with these laws and regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions, exclusion from participation in government healthcare programs, or the curtailment or restructuring of our operations.

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 who have not worked together as a group previously. 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.

Our business and operations could suffer in the event of an information security incident such as a cybersecurity breach, system failure, or other compromise of our systems or those of a contractor or vendor.

To meet business objectives, we rely on both internal information technology systems and networks, and those of third parties and their vendors and contractors, to process and store sensitive data, including confidential research, business plans, financial information, intellectual property, and personal data that may be subject to legal protection. Computer system, network or telecommunications failures due to events such as damage from malware, unauthorized access, public health pandemics or epidemics (including, for example, the COVID-19 pandemic), terrorism, war, or natural disasters could interrupt our internal or partner operations. We are increasingly dependent upon our technology systems to operate our business with a growing remote workforce and our ability to effectively manage our business depends on the security, reliability and adequacy of our or our third-party contractors' or vendors' technology systems and data. A breakdown, invasion, corruption, destruction or breach of our or our third-party contractors' or vendors' technology systems, including cloud technologies, and/or unauthorized access to our data and information and cyberattacks such as phishing, social engineering, ransomware and other malware attacks could subject us to liability and increased costs or negatively impact the operation of our business. In addition, the loss of or alteration or other damage to pre-clinical trial data, data from completed or ongoing clinical trials for our product candidates or other confidential information could result in delays in our regulatory filings and development efforts, significantly increase our costs and result in other adverse impacts to our business. To the extent that any disruption or cybersecurity breach was to result in a loss of or alteration or other damage to our data, or inappropriate disclosure of confidential, personal or proprietary information, we could incur liability and other remediation costs, could suffer harm to our reputation and the development of our product candidates could be delayed.

To date, we have not experienced any material impact to our business, financial position or operations resulting from information security incidents or cyberattacks such as phishing, social engineering, ransomware or malware attacks; however, because of the 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. This impact could result in reputational, competitive, operational or other business harm as well as financial costs and regulatory action. Moreover, the prevalent use of mobile devices that access confidential information and ability to work remotely increases the risk of data security breaches, which could lead to the loss of confidential information, trade secrets or other intellectual property. These risks may be heightened due to the increasing number of our and our 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 any information security vulnerabilities. While we have implemented security measures and, to date, have not detected a cybersecurity breach of our systems nor experienced a material system failure, our computer systems and the external systems and services used by our third-party contract manufacturers, or CMOs, third-party contract research organizations, or CROs, or other contractors, vendors, consultants, directors and partners remain potentially vulnerable to these events.

A variety of risks associated with international operations could materially adversely affect our business.

As we engage in significant cross-border and international activities, we will be subject to risks related to international operations, including:

- different regulatory requirements for initiating clinical trials and maintaining approval of drugs in foreign countries;
- reduced protection for intellectual property rights in certain countries;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, political instability or open conflict in particular foreign economies and markets;
- differing and multiple payor 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;
- controlled substance legislation differs between countries and legislation in certain countries may restrict or limit our ability to manufacture and/or transport our product candidates;

- likelihood of 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, which likelihood 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 the collection, use and retention of data, including clinical data and genetic material, may apply in jurisdictions outside of North America;
- business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters including earthquakes, typhoons, floods and fires; and
- supply and other disruptions resulting from the impact of public health epidemics, including the COVID-19 pandemic, on our strategic partners, third-party manufacturers, suppliers and other third parties upon which we rely.

If any of these issues were to occur, our business could be materially harmed.

Health pandemics or epidemics, including the COVID-19 pandemic and other public health crises may materially and adversely affect our business, financial condition and results of operations.

The COVID-19 pandemic and other public health crises may materially and adversely affect our business, financial condition and results of operations in several ways. For example, because our supply chain for raw materials, drug substance and drug product is worldwide, it could be subject to significant disruptions. There may be related restrictions on the export, import or shipment of raw materials, drug substance or drug product that could materially delay our business or clinical trials.

Certain of our research and development efforts are also conducted globally, including our ongoing Phase 3 XEN496 (EPIK) clinical trial, which includes investigative sites in North America and Australia, and is expected to include sites in Europe and Asia. For example, we previously experienced a significant reduction in the rate of new patient enrollment in our Phase 2b XEN1101 (X-TOLE) clinical trial due to the COVID-19 pandemic. While we were able to complete recruitment for this trial, we cannot be certain that the ongoing COVID-19 pandemic or related variants will not negatively impact ongoing or future clinical trials. Our EPIK trial is dependent upon our ability to initiate clinical sites and enroll patients despite the ongoing COVID-19 pandemic.

We continue to provide many of our employees the option to work from home and implemented a halt of non-essential business travel since March 2020. As some of our employees have transitioned back to our premises, there is a risk that COVID-19 infections could break out at our offices or laboratory facilities and significantly affect our operations. Additionally, if any of our critical vendors are impacted, our business could be affected if we become unable to timely procure essential equipment, clinical trial drug product, supplies or services.

There continues to be uncertainty around the ultimate impact of the COVID-19 pandemic on public health, business operations and the overall economy; therefore, the negative impact on our financial position, operating results and liquidity cannot be reasonably estimated at this time, but the impact may be material.

U.S. holders of our common shares may suffer adverse tax consequences if we are characterized as a passive foreign investment company.

Generally, for any taxable year in which 75% or more of our gross income is passive income, or at least 50% of the average quarterly value of our assets (which may be determined in part by the market value of our common shares, which is subject to change) are held for the production of, or produce, passive income, we would be characterized as a passive foreign investment company, or PFIC, for U.S. federal income tax purposes. Based on the price of our common shares and the composition of our gross income and gross assets, we do not believe we were a PFIC for the taxable years ended December 31, 2020 and 2019 but we could be a PFIC in subsequent years. Our status as a PFIC is a fact-intensive determination made on an annual basis, and we cannot provide any assurance regarding our PFIC status for the current taxable year or future taxable years.

If we are a PFIC for any year, U.S. holders of our common shares may suffer adverse tax consequences. Gains realized by non-corporate U.S. holders on the sale of our common shares would be taxed as ordinary income, rather than as capital gain, and the preferential tax rate applicable to dividends received on our common shares would be lost. Interest charges would also be added to taxes on gains and dividends realized by all U.S. holders. U.S. holders should consult their own tax advisors with respect to their particular circumstances.

A U.S. holder may avoid these adverse tax consequences by timely making a qualified electing fund election. For each year that we would meet the PFIC gross income or asset test, an electing U.S. holder would be required to include in gross income its pro rata share of our net ordinary income and net capital gains, if any. A U.S. holder may make a qualified electing fund election only if we commit to provide U.S. holders with their pro rata share of our net ordinary income and net capital gains. We will provide, upon request, our U.S. holders with the information that is necessary in order for them to make a qualified electing fund election and to report their common 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.

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 United States, 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, joint ventures 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, joint ventures, 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, joint venture 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 joint ventures or acquisitions, or the effect that any such transactions might have on our operating results.

If product liability lawsuits are brought against us, we may incur substantial liabilities 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 of $10,000,000 per occurrence and $10,000,000 aggregate limit. We believe our product liability insurance coverage is 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 may 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.

Our current and future operations in the U.S. and elsewhere will be subject, directly or indirectly, to applicable federal and state anti-kickback, fraud and abuse, false claims, transparency, health information privacy and security, and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, administrative burdens, and diminished profits and future earnings.

Healthcare providers, physicians and third-party payers in the U.S. and elsewhere play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our current arrangements with health care providers and our future arrangements with third-party payers and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations, including, without limitation, the federal Anti-Kickback Statute and the federal False Claims Act and similar laws in foreign jurisdictions in which we conduct business, that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any products for which we obtain marketing approval. In addition, we may be subject to transparency laws and patient privacy regulation by the federal government and by the U.S. states and foreign jurisdictions in which we conduct our business. The applicable federal, state and foreign healthcare laws and regulations that may affect our ability to operate include the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service for which payment may be made under federal and state healthcare programs such as Medicare and Medicaid;
- federal civil and criminal false claims laws, including the federal False Claims Act, which can be enforced through civil whistleblower, or qui tam actions, as well as civil monetary penalty laws can impose criminal and civil penalties, assessment, and exclusion from participation for various forms of fraud and abuse involving the federal health care programs, such as Medicare and Medicaid;
- HIPAA, which imposes criminal and civil liability for, among other things, executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters;
- the federal Physicians Payment Sunshine Act, also referred to as the CMS Open Payments, which requires applicable manufacturers of certain drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to CMS, information related to: certain payments or other transfers of value made to physicians, as defined by such law, and teaching hospitals and ownership or investment interests held by such healthcare professionals and their immediate family members; effective January 1, 2022, for data collected in 2021 and reported to CMS in 2022, these reporting obligations are extended to include payments and transfers of value made and ownership interests held during the previous year to certain non-physician providers, including physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists and anesthesiologist assistants, and certified nurse midwives; 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 require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers; state and foreign laws that require drug manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures; state and local laws requiring the registration of pharmaceutical sales representatives; and state and foreign laws governing the collection, export, privacy, use and security of biological materials and health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations may involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, including, without limitation, damages, fines, disgorgement, imprisonment, exclusion from participation in government healthcare programs, such as Medicare and Medicaid, integrity oversight and reporting obligations, and the curtailment or restructuring of our operations, which could have a material adverse effect on our business. If any of the physicians or other providers or entities with whom we expect to do business, including our collaborators, is found not to be in compliance with applicable laws, it may be subject to criminal, civil or administrative sanctions, including exclusions from participation in government healthcare programs, which could also materially affect our business.

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 Development, Clinical Testing and Regulatory Approval of Our Product Candidates

The regulatory approval processes of the FDA, EMA, Health Canada and regulators in other jurisdictions are lengthy, time-consuming and inherently unpredictable. If we, or our collaborators, are unable to obtain regulatory approval for our product candidates in a timely manner, or at all, our business will be substantially harmed.

The regulatory approval process is expensive and the time required to obtain approval from the FDA, EMA, Health Canada or other 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, Health Canada or other 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, Health Canada or other 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, Health Canada or other 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, Health Canada or 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, Health Canada or other 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, Health Canada or other 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 a New Drug Application, or NDA, or other submission or to obtain regulatory approval in the U.S. or elsewhere;
- the FDA, EMA, Health Canada or other 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 manufacturing, clinical sites or clinical service providers, conducted by regulatory authorities may identify errors or omissions that may results in the product candidate not being approved; and
- the approval policies or regulations of the FDA, EMA, Health Canada or other 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, 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.

Clinical drug development involves a lengthy and expensive process with uncertain timelines and uncertain outcomes. If clinical trials are prolonged, delayed, not completed, unsuccessful or inconclusive, we could experience material harm to our business and the market price of our common shares. In addition, we, or our collaborators, may be unable to commercialize our product candidates on a timely basis or at all.

Clinical testing of product candidates is expensive and, depending on the stage of development, can take a substantial period of time to complete. Clinical trial outcomes are inherently uncertain, and failure can occur at any time during the clinical development process and can have a material impact on our business and the market price of our common shares.

Clinical trials can be halted or delayed for a variety of reasons, including those related to:

- side effects or adverse events in study participants presenting an unacceptable safety risk;
- inability to reach agreement with prospective CROs and clinical trial sites, or the breach of such agreements;
- failure of third-party contractors, such as CROs, or investigators to comply with regulatory requirements, including good clinical practices, or GCPs;
- 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;
- 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;
- inability to enroll sufficient patients to complete a protocol, particularly in orphan diseases or disorders;
- difficulty in having patients complete a trial, adhere to the trial protocol, or return for post-treatment follow-up;
- clinical sites deviating from trial protocol or dropping out of a trial;
- problems with investigational medicinal product storage, stability and distribution;
- our inability to add new or additional clinical trial sites;
- 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;
- unforeseen disruptions, caused by man-made or natural disasters or public health pandemics or epidemics or other business interruptions, including, for example, the COVID-19 pandemic; and
- governmental or regulatory delays and changes in regulatory requirements, policy and guidelines.

These risks and uncertainties could impact any of our or our collaborators' clinical programs and any of the clinical, regulatory or operational events described above could change our or our collaborators' planned clinical and regulatory activities. For example, we previously experienced a significant reduction in the rate of new patient enrollment in our X-TOLE trial due to the COVID-19 pandemic. While we were able to complete recruitment for this trial, we cannot be certain that the ongoing COVID-19 pandemic or related variants will not negatively impact other trials in the future. In addition, due to the impact of the COVID-19 pandemic, we have experienced an impact on the initiation of clinical sites in our EPIK trial which includes investigative sites in North America and Australia, and is expected to include clinical sites in Europe and Asia. COVID-19 may continue to impact the enrollment of patients in our XEN496 EPIK clinical trial.

The results of any Phase 3 or other pivotal clinical trial, including without limitation our EPIK trial, may not be adequate to support marketing approval. These clinical trials are lengthy and, with respect to non-orphan indications, usually involve many hundreds to thousands of patients. With respect to orphan indications like KCNQ2-DEE, SCN8A-DEE or childhood or juvenile absence epilepsy, or CAE or JAE, clinical trials can also be lengthy due to the challenge of identifying and recruiting patients. In addition, if the FDA, EMA, Health Canada or another regulator disagrees with our or our collaborators' choice of the key testing criterion, or primary endpoint, 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, Health Canada or other 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, Health Canada or other 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, Health Canada or other 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.

We may also be required to develop and implement additional clinical trial policies and procedures designed to support remote clinical trial activities which have and are expected to continue to increase the cost and complexity of our clinical trials. Since March 2020, the FDA, EMA and Health Canada have issued various guidance documents and related guidance updates describing a number of considerations for sponsors conducting clinical trials during the COVID-19 pandemic. FDA has also issued COVID-19 related guidance addressing resuming normal drug and biologics manufacturing operations; manufacturing, supply chain, and inspections; and statistical considerations for clinical trials during the COVID-19 public health emergency, among others. In view of the spread of the COVID-19 variants, FDA and other regulatory authorities may issue additional guidance and policies that may materially impact our business and clinical development timelines. Changes to existing policies and regulations can increase our compliance costs or delay our clinical plans.

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. Any of these occurrences may harm our business, financial condition and prospects significantly. In addition, many of the factors that cause or lead to a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our or our collaborators' product candidates.

XEN496 targets an ultra-orphan indication of KCNQ2-DEE and the FDA has indicated that a single, small pivotal trial may be sufficient to demonstrate effectiveness and safety in KCNQ2-DEE provided that no new or unexpected safety issues arise during drug development. However, other regulatory authorities may require additional data. Further, even though we believe the safety and efficacy profile of ezogabine, the active ingredient in XEN496, in pediatric patients with KCNQ2-DEE generated to date by others appears promising based on published clinical case reports, we do not yet know if the pediatric-specific formulation of XEN496 will have the same or similar safety, pharmacokinetic and/or efficacy profile in pediatric patients with KCNQ2-DEE as the original formulation of ezogabine. If we are unable to replicate the published clinical case reports, due to the new formulation or any other factors, the clinical development of XEN496 may not be successful and the FDA or other regulatory authorities may require additional data in more patients or we may not be able to generate sufficient data for approval in this patient population.

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.

Our and our collaborators' clinical product candidates, which include XEN1101, XEN496, XEN007, NBI-921352 (being developed by our collaborator Neurocrine Biosciences), and FX301 (being developed by Flexion), 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 products, we or our collaborators must demonstrate through lengthy, complex and expensive pre-clinical testing and clinical trials that the 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, on October 4, 2021 we released topline data from our X-TOLE Phase 2b clinical trial of XEN1101 in adult patients with focal epilepsy. Even though the topline data from our X-TOLE Phase 2b clinical trial are positive, there can be no assurance that we will be able to successfully advance development of this product candidate into later stage clinical trials or obtain regulatory approval of XEN1101. Any of the foregoing outcomes would materially and adversely impact our business, product candidate pipeline and future prospects.

If our or our collaborators' product candidates are not shown to be both safe and effective in clinical trials, such product candidates will be unable to obtain regulatory approval or be successfully commercialized. In addition, our or our collaborators' failure to demonstrate positive results in clinical trials in any indication for which we or our collaborators are developing clinical product candidates could adversely affect development efforts in other indications. In such case, we would need to develop other compounds and conduct associated pre-clinical testing and clinical trials, as well as potentially seek additional financing, all of which would have a material adverse effect on our business, growth prospects, operating results, financial condition and results of operations.

We or our collaborators may find it difficult to enroll patients in our clinical studies, including for ultra-orphan, orphan or niche indications, which could delay or prevent clinical studies of our product candidates.

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 studies in a timely manner, or at all. Patient enrollment for clinical trials for ultra-orphan, orphan and niche indications and for more prevalent conditions is affected by factors including:

- severity of the disease or disorder under investigation;
- design of the study protocol;

- size of the patient population and geographic dispersion;
- identification of patients;
- eligibility criteria for the study in question;
- perceived risks and benefits of the product candidate under study;
- proximity and availability of clinical study sites for prospective patients;
- availability of competing therapies and clinical studies;
- efforts to facilitate timely enrollment in clinical studies; and
- patient referral practices of physicians.

The limited patient populations in ultra-orphan, orphan and niche indications, such as KCNQ2-DEE, SCN8A-DEE, other early infantile epileptic encephalopathies, as well as potential orphan indications for the future development of XEN007 including alternating hemiplegia of childhood, or AHC, hemiplegic migraine, or HM, CAE and JAE, present significant recruitment challenges for clinical trials and a full understanding of the size of these populations is still relatively unknown. Many of these patients may not be suitable or available to participate in our or our collaborators' clinical trials. This means that we or our collaborators will generally have to run multi-site and potentially multi-national trials, which can be expensive and require close coordination and supervision. If we or our collaborators' experience delays in completing our clinical trials, such delays could result in increased costs, delays in advancing our product development, delays in testing the effectiveness of our product candidates or termination of the clinical studies altogether. Even if we or our collaborators' are successful in receiving regulatory approval, the limited patient populations in ultra-orphan, orphan and niche indications may impact the successful commercialization of our or our collaborators' product candidates and reimbursement rates, which could impact revenue and our ability to achieve profitability.

If we fail to obtain or maintain orphan drug designation or other regulatory exclusivity for some of our product candidates, our competitive position would be harmed.

Although we have pending provisional and non-provisional patent applications related to XEN496 and XEN007, these product candidates are not currently covered by any issued patents and we may have to rely solely on orphan drug designation to gain market exclusivity for these product candidates. Currently, this 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 (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.

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. XEN007, a drug we are evaluating for potential development in CAE, JAE, HM, or AHC, has received orphan drug designation from the FDA for CAE, HM and AHC. We have also received orphan drug designation from the FDA and orphan medicinal product designation was granted by the European Commission to XEN496 as a treatment of KCNQ2-DEE. If we seek orphan drug designations for other indications or in other jurisdictions, we may fail to receive such orphan drug designations and, even if we succeed, such orphan drug designations may fail to result in or maintain orphan drug exclusivity upon approval, which would harm our competitive position. Further, not all jurisdictions, such as Canada, have orphan drug designations. Neither orphan drug designation, nor RPD designation gives the drug any advantage in the regulatory review or approval process other than potential fee reductions, and in the case of RPD, priority review vouchers.

Although the FDA has granted RPD designation to XEN007 for the treatment of CAE and AHC and RPD designation to NBI-921352 for the treatment of SCN8A-DEE, we may not be able to realize any value from such designation.

Our product candidate XEN007 has received RPD designation from the FDA for the treatment of CAE and AHC and 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 a new drug application, 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 we or 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 we or Neurocrine Biosciences obtain approval for XEN007 in CAE or AHC or NBI-921352 in SCN8A-DEE, respectively, and qualify for such a priority review voucher, the program may no longer be in effect at the time of approval of either of these product candidates. 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 were to sell a priority review voucher to a third party. In addition, as part of the Coronavirus Response and Relief Supplemental Consolidated Appropriations Act of 2021, Congress extended FDA authorization to operate the RPD Priority Review Voucher Program through fiscal year 2024. RPD Designation does not lead to faster development or regulatory review of the product, or increase the likelihood that it will receive marketing approval.

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 the requirements of the FDA, EMA, Health Canada or foreign regulatory authorities.

The results of pre-clinical studies, either generated by us, such as for XEN901 (which we licensed to Neurocrine Biosciences and is now known as NBI-921352) or XEN402 (which was acquired by Flexion for use in its product candidate FX301), by our CROs or by other third parties from which we have in-licensed or acquired a product candidate, may not be predictive of results in clinical testing. Moreover, pre-clinical results can often be difficult to compare across different studies for a variety of reasons, including differences in experimental protocols and techniques, personnel, equipment and other factors, which may make the pre-clinical results less reliable and predictive of clinical trial results. In addition, published clinical data or case reports from third parties or early clinical trial data of our product candidates may not be predictive of the results of later-stage clinical trials. Interpretation of results from early, usually smaller, studies that suggest a clinically meaningful response in some patients, requires caution. Results from later stages of clinical trials enrolling more patients may fail to show the desired safety and efficacy results or otherwise fail to be consistent with the results of earlier trials of the same product candidate. Later clinical trial results may not replicate earlier clinical trials for a variety of reasons, including differences in trial design, different trial endpoints (or lack of trial endpoints in exploratory studies), patient population, number of patients, patient selection criteria, trial duration, drug dosage and formulation and lack of statistical power in the earlier studies. These uncertainties are enhanced where the diseases or disorders under study lack established clinical endpoints, validated measures of efficacy, as is often the case with orphan diseases or disorders for which no drugs have been developed previously and where the product candidates target novel mechanisms. For example, to our knowledge, NBI-921352 is the first selective Nav1.6 sodium channel inhibitor being developed for the treatment of epilepsy and therefore standard pre-clinical models may not be predictive of clinical efficacy due to its novel molecular mechanism.

Further, our product candidates may not be approved even if they achieve their primary endpoint in our Phase 3 clinical trials. The FDA, EMA, Health Canada or foreign regulatory authorities may disagree with our trial design and our interpretation of data from pre-clinical studies and clinical trials. In addition, any of these regulatory authorities may change its requirements for the approval of a product candidate even after reviewing and providing comments or advice on a protocol for a pivotal clinical trial that, if successful, would potentially form the basis for an application for approval by the FDA, EMA, Health Canada or another regulatory authority. Furthermore, any of these regulatory authorities may also approve our product candidates for a narrower indication than we request or may grant approval contingent on the performance of costly post-marketing clinical trials.

Our approach to drug discovery is unproven, and we do not know whether we will be able to develop any products of commercial value.

Our approach to drug discovery may not reproducibly or cost-effectively result in the discovery of product candidates and development of commercially viable products that safely and effectively treat human disease.

Our drug discovery efforts may initially show promise in identifying additional potential product candidates yet fail to yield viable product candidates for clinical development or commercialization. Such failure may occur for many reasons, including the following: 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 any product candidate may 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.

Changes in methods of product candidate manufacturing or formulation may result in additional costs or delay.

As product candidates are developed through pre-clinical to late stage clinical trials towards approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods and formulations, are altered along the way in an effort to optimize products, processes and results, to extend patent protection and/or to target different populations. For example, XEN496 is a pediatric-specific formulation of ezogabine and we have also developed a pediatric formulation for NBI-921352 that was included in the license to Neurocrine Biosciences. Any of these changes could cause our product candidates to perform differently and not provide the same drug exposure profile in children and/or cause side effects different to those observed with formulations previously tested in adults. 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.

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, Health Canada 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.

Even if a product is approved, the FDA, EMA, Health Canada, or another applicable regulatory authority, as the case may be, may limit the indications for which the product may be marketed, require extensive 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 United States as conditions of approval to help ensure that the benefits of the drug outweigh the potential risks. REMS can include medication guides, communication plans for health care professionals, and elements to assure safe use, or ETASU. ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries. The requirement for a REMS can materially affect the potential market and profitability of the drug. Moreover, product approval may require substantial post-approval testing and surveillance to monitor the drug's safety or efficacy. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing. In many countries outside the U.S., a product candidate must be approved for reimbursement before it can be approved for sale in that country. In some cases, the price that we intend to charge for a product is also subject to approval.

Regulatory authorities in countries outside of the U.S., Canada and the EU also have their own requirements for approval of product candidates with which we must comply prior to marketing in those countries. Obtaining foreign regulatory approvals and compliance with such foreign regulatory requirements could result in significant delays, difficulties and costs for us or our collaborators and could delay or prevent the introduction of our current and any future products, in certain countries.

If we or our collaborators fail to receive applicable marketing approvals or comply with the regulatory requirements in international markets, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed and our business will be adversely affected.

Risks Related to Commercialization

If, in the future, we are unable to establish our own sales, marketing and distribution capabilities or enter into agreements for these purposes, we may not be successful in independently commercializing any future products.

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 and/or commercial markets, including XEN496 and XEN1101, we are evaluating commercial partners for markets outside of North America and 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.

To develop internal sales, distribution and marketing capabilities in North America, we will have to invest significant amounts of financial and management resources, some of which will need to be committed prior to any confirmation that any of our product candidates will be approved. We have no prior experience as a company in the marketing, sale and distribution of biopharmaceutical products and there are significant risks involved in building and managing a commercial organization. For any future products for which we decide to perform sales, marketing and distribution functions ourselves, we could face a number of additional risks, including:

- the maintenance of existing or the establishment of new supply arrangements with third-party logistics providers and secondary packagers;
- the maintenance of existing or the establishment of new scaled production arrangements with third-party manufacturers to obtain finished products that are appropriately packaged for sale;
- a continued acceptable safety profile following any marketing approval;
- our inability to recruit and retain adequate numbers of qualified sales and marketing personnel or develop alternative sales channels;
- the inability of our products to secure acceptance from physicians, healthcare providers, patients, third-party payers and the medical community including identifying an adequate number of physicians and patients, especially for ultra-orphan, orphan or niche indications;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines;
- unforeseen costs and expenses associated with creating and maintaining an independent sales and marketing organization; and
- our ability to compete with other therapies.

Where and when appropriate, we may elect to utilize contract sales forces, distribution partners or collaborators that have sales, marketing and distribution capabilities to assist in the commercialization of or 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.

Any regulatory approvals that we receive for the product candidates we commercialize, alone or with a collaborator, will be subject to limitations on the approved indicated uses for which the product may be marketed or subject to certain conditions of approval and may contain requirements for potentially costly post-approval trials, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the marketed product and compliance with the approved package insert. 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 United States) which will result in additional complexity in manufacturing, supply chain, licensing, import/export and distribution.

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, 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, 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 with third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- additional restrictions on the marketing or manufacturing of the product, withdrawal of the product from the market or voluntary or mandatory product recalls;
- fines, warning letters or holds on any post-approval clinical trials;
- refusal by the FDA, EMA, Health Canada or another applicable regulatory authority to approve pending applications or supplements to approved applications filed by us or our collaborators, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the release, import or export of products; and
- injunctions or the imposition of civil or criminal penalties.

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 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 and other foreign regulators do restrict manufacturer's communications on the subject of off-label use of their products.

If the market opportunities for our product candidates are smaller than we believe they are, our revenue may be adversely affected, and our business may suffer. Because the target patient populations for some of our product candidates are small, we must be able to successfully identify patients and acquire a significant market share to achieve profitability and growth.

Some of our product candidates focus on treatments for rare and ultra-rare disorders. Given the small number of patients who have some of the disorders that we are targeting, our profitability and growth depend on successfully identifying patients with these rare and ultra-rare disorders. Currently, most reported estimates of the prevalence of these disorders are based on studies of small subsets of the population in specific geographic areas, which are then extrapolated to estimate the prevalence of the disorders in the U.S. or elsewhere. Our projections of both the number of people who have these disorders, as well as the subset of people with these disorders who have the potential to benefit from treatment with our product candidates, are based on our internal estimates. These estimates have been derived from a variety of sources, including scientific literature, surveys of clinics, patient foundations, and market research, and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these disorders, and, as a result, the number of patients with these disorders may turn out to be lower than expected.

Our effort to identify patients with diseases or disorders we seek to treat is in early stages, and we cannot accurately predict the number of patients for whom treatment might be possible. Additionally, the potentially addressable patient population for some of our product candidates may be limited or may not be amenable to treatment with our product candidates, and new patients may become increasingly difficult to identify or gain access to, which would adversely affect our results of operations and our business. Finally, even if we obtain significant market share for our product candidates focused on treatments for rare and ultra-rare disorders, because the potential target populations are very small, we may never achieve profitability despite obtaining such significant market share.

Even if we or our collaborators receive approval to commercialize our products, unfavorable pricing regulations and challenging third-party coverage and reimbursement practices could harm our business.

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, private health insurers, managed care plans, and other organizations. Government authorities and third-party payers, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the U.S. healthcare industry is cost containment. Government authorities and third-party payers have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payers are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that coverage and reimbursement will be available for any product that we or our collaborators commercialize and, if reimbursement is available, the level of reimbursement. In addition, coverage and reimbursement may impact the demand for, or the price of, any product candidate for which we or a collaborator obtains marketing approval. If coverage and reimbursement are not available or reimbursement is available only to limited levels, we or our collaborators may not be able to successfully commercialize any product candidate for which marketing approval is obtained.

There may be significant delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA, EMA, Health Canada or other regulatory authorities. Moreover, eligibility for coverage and reimbursement does not imply that a drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution expenses. Interim reimbursement levels for new drugs, if applicable, may also be insufficient to cover our and our collaborators' costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or 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. Third-party payers often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Our or our collaborators' inability to promptly obtain coverage and profitable payment rates from both government-funded and private payers for any approved products that we or our collaborators develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

Some of our and our collaborators' target patient populations in orphan and niche indications, such as KCNQ2-DEE, SCN8A-DEE, CAE and JAE. In order for therapies that are designed to treat smaller patient populations to be commercially viable, the pricing, coverage and reimbursement for such therapies needs to be higher, on a relative basis, to account for the lack of volume. Accordingly, we will need to implement pricing, coverage and reimbursement strategies for any approved product that accounts for the smaller potential market size. If we are unable to establish or sustain coverage and adequate reimbursement for our 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.

Recently enacted and future legislation may increase the difficulty and cost for us to commercialize any products that we or our collaborators develop and affect the prices we may obtain.

The U.S. and some foreign jurisdictions are considering or have enacted a number of legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to sell any of our products profitably, once such products are approved for sale. Among policy makers and payers in the U.S. and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the U.S., the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives.

For example, in 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, collectively, the PPACA, was enacted and includes measures that have significantly changed the way healthcare is financed by both governmental and private insurers. Since its enactment, there have been legislative and judicial efforts to repeal, replace, or change some or all of the PPACA. For example, various portions of the PPACA have been the subject of legal and constitutional challenges. In June 2021, the United States Supreme Court held that Texas and other challengers had no legal standing to challenge the PPACA, dismissing the case without specifically ruling on the constitutionality of the PPACA. Accordingly, the PPACA remains in effect in its current form. It is unclear how this Supreme Court decision, future litigation, and healthcare measures promulgated by the Biden administration will impact the implementation of the PPACA, our business, financial condition and results of operations. Complying with any new legislation or changes in healthcare regulation could be time-intensive and expensive, resulting in a material adverse effect on our business.

In addition, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for pharmaceutical products. For example, HHS and CMS issued final rules in November and December of 2020 that are expected to impact, among others, price reductions from pharmaceutical manufacturers to plan sponsors under Part D, fee arrangements between pharmacy benefit managers and manufacturers, prescription drug importation, manufacturer price reporting requirements under the Medicaid Drug Rebate Program, including regulations that affect manufacturer-sponsored patient assistance programs subject to pharmacy benefit manager accumulator programs and Best Price reporting related to certain value-based purchasing arrangements. Multiple lawsuits have been brought against the HHS challenging various aspects of these new rules. In January 2021, the Biden administration issued a "regulatory freeze" memorandum that directs department and agency heads to review new or pending rules of the prior administration. Under the American Rescue Plan Act of 2021, effective January 1, 2024, the statutory cap on Medicaid Drug Rebate Program rebates that manufacturers pay to state Medicaid programs will be eliminated. Elimination of this cap may require pharmaceutical manufacturers to pay more in rebates than it receives on the sale of products, which could have a material impact on our business. In July 2021, the Biden administration released an executive order, "Promoting Competition in the American Economy," with multiple provisions aimed at increasing competition for prescription drugs. In response to Biden's executive order, on September 9, 2021, HHS released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and potential legislative policies that Congress could pursue to advance these principles. In addition, Congress is considering legislation that, if passed, could have significant impact on prices of prescription drugs covered by Medicare, including limitations on drug price increases. The impact of these regulations and any future healthcare measures and agency rules implemented by the Biden administration on us and the pharmaceutical industry as a whole is currently unknown.

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. Further, a number of states are considering or have recently enacted state drug price transparency and reporting laws that could substantially increase our compliance burdens and expose us to greater liability under such state laws once we begin commercialization. These and other health reform measures that are implemented may have a material adverse effect on our operations.

We are unable to predict the future course of federal or state healthcare legislation in the United States directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. These and any further changes in the law or regulatory framework could reduce our ability to generate revenue in the future or increase our costs, either of which could have a material and adverse effect on our business, financial condition and results of operations. It is also possible that additional governmental action will be taken to address the COVID-19 pandemic. The continuing efforts of the government, insurance companies, managed care organizations, and other payors of healthcare services and medical products to contain or reduce costs of healthcare and/or impose price controls may adversely affect the demand for our product candidates, if approved, and our ability to achieve or maintain profitability.

In the EU, similar political, economic and regulatory developments may affect our or our collaborators' ability to profitably commercialize our current or any future products. In addition to continuing pressure on prices and cost containment measures, legislative developments at the EU or member state level may result in significant additional requirements or obstacles that may increase our operating costs. In international markets, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. Our future products, if any, might not be considered medically reasonable and necessary for a specific indication or cost-effective by third-party payers. An adequate level of reimbursement might not be available for such products and third-party payers' reimbursement policies might adversely affect our or our collaborators' ability to sell any future products profitably.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-approval testing and other requirements.

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.

Foreign governments tend to impose strict price controls, which may adversely affect our future profitability.

In most foreign countries, particularly those in the EU and Canada, prescription drug pricing and/or reimbursement is subject to governmental control. In those countries that impose price controls, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. 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. As of October 2021, Canada is in the midst of implementing new drug pricing regulations and additional pricing guidance that will affect the price at which patented medicines can be sold, with the implementation date delayed until January 2022 to provide additional time for the industry to adapt to new reporting obligations. Such regulations, as well as future regulations on drug pricing and reporting obligations, will increase manufacturers' compliance burden, which can be expensive and time consuming.

Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we or our collaborators might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenue that is generated from the sale of the product in that country. If reimbursement of such products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, or if there is competition from lower priced cross-border sales, our profitability will be negatively affected.

Risks Related to Our Dependence on Third Parties

Our prospects for successful development and commercialization of our partnered products and product candidates are dependent upon the research, development and marketing efforts of our collaborators.

We 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 and Flexion, to fund and conduct the research and any clinical development of product candidates under our agreements with each of them, and for the successful regulatory approval, marketing and commercialization of one or more of such products or product candidates. Such success will be subject to significant uncertainty.

Our ability to recognize revenue from successful collaborations may be impaired by multiple factors including:

- a collaborator may shift its priorities and resources away from our programs due to a change in business strategies, or a merger, acquisition, sale or downsizing of its company or business unit;
- a collaborator may cease development in therapeutic areas which are the subject of our strategic alliances;
- a collaborator may change the success criteria for a particular program or product candidate thereby delaying or ceasing development of such program or candidate;
- a significant delay in initiation of certain development activities by a collaborator will also delay payment of milestones tied to such activities, thereby impacting our ability to fund our own activities;
- a collaborator could develop a product that competes, either directly or indirectly, with our current or future products, if any;
- a collaborator with commercialization obligations may not commit sufficient financial or human resources to the marketing, distribution or sale of a product;
- a collaborator with manufacturing responsibilities may encounter regulatory, resource or quality issues and be unable to meet demand requirements;
- a collaborator may exercise its rights under the agreement to terminate our collaboration;
- a dispute may arise between us and a collaborator concerning the research or development of a product candidate, commercialization of a product or payment of royalties or milestone payments, any of which could result in a delay in milestones, royalty payments or termination of a program and possibly resulting in costly litigation or arbitration which may divert management attention and resources;
- a collaborator may not adequately protect the intellectual property rights associated with a product or product candidate;
- a collaborator may use our proprietary information or intellectual property in such a way as to invite litigation from a third party; and
- disruptions caused by man-made or natural disasters or public health pandemics or epidemics or other business interruptions, including, for example, the COVID-19 pandemic.

If our collaborators do not perform in the manner we expect or fulfill their responsibilities in a timely manner, or at all, the clinical development, regulatory approval and commercialization efforts could be delayed, terminated or be commercially unsuccessful. Conflicts between us and our collaborators may arise. In the event of termination of one or more of our collaboration agreements, it may become necessary for us to assume the responsibility of any terminated product or product candidates at our own expense or seek new collaborators. In that event, we could be required to limit the size and scope of one or more of our independent programs or increase our expenditures and seek additional funding which may not be available on acceptable terms or at all, and our business could be materially and adversely affected.

We depend on our collaborative relationship with Neurocrine Biosciences to further develop and commercialize NBI-921352, and if our relationship is not successful or is terminated, we may not be able to effectively develop and/or commercialize NBI-921352, which could have a material adverse effect on our business.

We depend on Neurocrine Biosciences to collaborate with us to develop and commercialize NBI-921352. Under the agreement and subject to input from the joint steering committee, Neurocrine Biosciences controls all decision-making with respect to the clinical development and commercialization for NBI-921352.

As a result of our collaboration with Neurocrine Biosciences, the eventual success or commercial viability of NBI-921352 is largely beyond our control. The financial returns to us, if any, depend in large part on the achievement of development and commercialization milestones, plus a share of any revenue from sales. Therefore, our success, and any associated financial returns to us and our investors, will depend in part on Neurocrine Biosciences' performance under the agreement.

We are subject to a number of additional specific risks associated with our dependence on our collaborative relationship with Neurocrine Biosciences, including:

- adverse decisions by Neurocrine Biosciences regarding the development and commercialization of NBI-921352;
- Neurocrine Biosciences' failure to collect all data required by FDA or any other regulatory authority to support an Investigational New Drug application, or IND, or equivalent or any amendments thereof, address any deficiencies or compliance issues raised by FDA or any other regulatory authority, or comply with all regulatory requirements in order to advance clinical development of NBI-921352 to approval;
- possible disagreements as to the timing, nature and extent of development plans, including clinical trials or regulatory strategy;
- loss of significant rights if we fail to meet our obligations under the agreement;
- changes in key management personnel at Neurocrine Biosciences, including in members of the joint steering committee; and
- possible disagreements with Neurocrine Biosciences regarding the agreement, for example, with regard to ownership of intellectual property rights.

For example, following Neurocrine Biosciences' submission of the IND for NBI-921352, the FDA requested additional non-clinical data to support dose justification in the proposed pediatric study of NBI-921352 in pediatric SCN8A-DEE patients. Based on this feedback, Neurocrine Biosciences is advancing a Phase 2 clinical trial in adolescent patients (aged 12 years and older) with SCN8A-DEE and intends to amend the trial protocol to include younger pediatric patients (aged 2-11 years) with SCN8A-DEE following the FDA's review and approval of the additional non-clinical information. In connection with this announcement, we and Neurocrine Biosciences amended our collaboration agreement to restructure the terms of potential payments owed to us upon achievement of certain development milestones, including deferring the milestone payment owing to us for the SCN8A-DEE trial until the FDA has approved the protocol amendment to include younger pediatric patients (aged 2-11 years). The terms of our amended collaboration agreement with Neurocrine Biosciences are described in greater detail in the section of our Annual Report on Form 10-K filed with the SEC on March 1, 2021 titled "Business — Collaborations, Commercial and License Agreements — License and Collaboration Agreement with Neurocrine Biosciences, Inc." If Neurocrine Biosciences does not provide the FDA with sufficient additional non-clinical data to support a protocol amendment, we would not qualify for the milestone tied to the SCN8A-DEE development program. In addition, although we have previously announced that Neurocrine Biosciences is advancing clinical plans to develop NBI-921352 for the treatment of adult focal epilepsy and expects to initiate a Phase 2 clinical trial later this year, we cannot be certain that Neurocrine Biosciences will continue to pursue this indication and we may not qualify for additional payments under our collaboration agreement.

If either we or Neurocrine Biosciences fail to perform our respective obligations, any clinical trial, regulatory approval or development progress could be significantly delayed or halted, could result in costly or time-consuming litigation or arbitration and could have a material adverse effect on our business.

Decisions by Neurocrine Biosciences to emphasize other drug candidates currently in its portfolio ahead of our product candidates, or to add competitive agents to its portfolio could result in a decision to terminate the agreement, in which event, among other things, we may be responsible for paying any remaining costs of all ongoing or future clinical trials, including expending additional time and resources needed to address any prior deficiencies or regulatory noncompliance issues that we may inherit from Neurocrine Biosciences upon any such termination.

Any of the above discussed scenarios could adversely affect the timing and extent of the development and commercialization activities related to NBI-921352, which could materially and adversely impact our business.

We may not be successful in establishing new collaborations or maintaining our existing alliances, which could adversely affect our ability to develop product candidates and commercialize products.

In the ordinary course, we engage with other biotechnology and pharmaceutical companies to discuss potential in-licensing, out-licensing, alliances and other strategic transactions. We may seek to enter into these types of transactions to enhance and accelerate the development of our current or future product candidates and the commercialization of any resulting products. 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 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 will bear all of the risk related to the development of any such product candidates; and
- the competitiveness of any product that is commercialized could be reduced.

We intend to rely on third-party manufacturers to produce our clinical product candidates and commercial supplies. Any failure by a third-party manufacturer to produce acceptable supplies for us may delay or impair our ability to initiate or complete our clinical trials, gain regulatory approvals or commercialize approved products.

We do not currently own or operate any manufacturing facilities nor do we have significant in-house manufacturing experience or personnel. We rely on our collaborators, either directly or through CMOs, to manufacture product candidates licensed to them or work with multiple CMOs to produce sufficient quantities of materials required for the manufacture of our product candidates for pre-clinical testing and clinical trials and intend to do so for the commercial manufacture of our products. 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 materially harm our business.

Reliance on third-party manufacturers entails risks to which we would not be subject if we manufactured product candidates ourselves, including reliance on the third party 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) and the possibility of termination or nonrenewal of the agreement by the third party at a time that is costly or damaging to us. In addition, the FDA, EMA, Health Canada and other 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, Health Canada and other regulatory agencies. They are also subject to pre-approval inspections and periodic unannounced inspections by the FDA, EMA, Health Canada and other 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, 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.

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 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, XEN007 is currently being evaluated under a physician-led, multi-center, Phase 2 proof-of-concept study as an adjunctive treatment in pediatric patients diagnosed with treatment-resistant absence epilepsy, including CAE and JAE. In addition, a Phase 2 proof-of-concept clinical trial examining XEN1101 in major depressive disorder and anhedonia is being conducted in partnership with academic collaborators at the Icahn School of Medicine at Mount Sinai, with enrollment expected to start in October 2021.

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, Health Canada or other 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, Health Canada, 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 nonclinical studies and clinical trials may be deemed unreliable and our submission of marketing applications may be delayed or the FDA, EMA, Health Canada or another regulatory authority may require us to perform additional clinical trials before approving our marketing applications. Upon inspection, the FDA, EMA, Health Canada or another 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, Health Canada and other 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.

If any of our clinical trial sites terminates for any reason, we may experience the loss of follow-up information on patients enrolled in our ongoing clinical trials unless we are able to transfer the care of those patients to another qualified clinical trial site. Further, if our relationship with any of our CROs or CMOs is terminated, we may be unable to enter into arrangements with alternative CROs or CMOs on commercially reasonable terms, or at all.

Switching or adding CROs, CMOs or other suppliers can involve substantial cost and require extensive management time and focus. In addition, there is a natural transition period when a new CRO, CMO or supplier commences work. As a result, delays may occur, which can materially impact our ability to meet our desired clinical development timelines. If we are required to seek alternative supply arrangements, the resulting delays and potential inability to find a suitable replacement could materially and adversely impact our business.

We work with outside scientists and their institutions in executing our business strategy of developing product candidates. These scientists may have other commitments or conflicts of interest, which could limit our access to their expertise and harm our ability to develop viable product candidates.

We work with scientific advisors and collaborators at academic institutions and other research institutions. These scientists and collaborators are not our employees; rather, they serve as either independent contractors or the primary investigators under research collaboration agreements that we have with their sponsoring academic or research institution. Such scientists and collaborators may have other commitments that would limit their availability to us. Although our scientific advisors generally agree not to do competing work, if an actual or potential conflict of interest between their work for us and their work for another entity arises, we may lose their services. It is also possible that some of our valuable proprietary knowledge may become publicly known through these scientific advisors if they breach their confidentiality agreements with us, which would cause competitive harm to our business.

Risks Related to Intellectual Property

We could be unsuccessful in obtaining or maintaining adequate patent protection for one or more of our products or product candidates.

Our commercial success will depend, in large part, on our ability to obtain and maintain patent, trademark and trade secret protection of our product candidates, their respective components, formulations, methods used to manufacture them and methods of treatment, as well as successfully defending these patents against third-party challenges. We evaluate our global patent portfolio in the ordinary course of business to enhance patent protection in areas of our strategic focus and in key markets for our potential products and may abandon existing patents or patent applications related to terminated development programs, areas, or markets of low strategic importance. For example, as of October 4, 2021, we owned (a) two issued U.S. patents directed to XEN1101 and certain related compounds and methods of using the same for the treatment of seizure disorders which are expected to expire between 2028 and 2029 (absent any extensions of term); (b) a U.S. patent with claims directed to four distinct crystalline forms of XEN1101, pharmaceutical compositions comprising the same, and methods of preparing and using the same which is expected to expire in 2040 (absent any extensions of term); and (c) an allowed U.S. patent application with claims directed to methods of enhancing the bioavailability of XEN1101 by oral administration with, or in temporal proximity to, consuming food which is expected to expire in 2039 (absent any extensions of term). We also filed in July 2021 a U.S. continuation application of the aforementioned crystalline form patent and in October 2021 a U.S. continuation application of the aforementioned bioavailability enhancement patent application. In addition, as of October 4, 2021, we have two pending U.S. non-provisional patent applications directed to (1) methods of using XEN1101 for the treatment of depressive disorders; and (2) methods of using XEN1101 for the treatment of pain disorders. While there is no guarantee that patents will issue from these two pending U.S. patent applications, any patents that that may issue are expected to expire in 2040 (absent any patent term adjustments or extensions). While we believe that these pending patent applications may provide us with additional intellectual property protection for XEN1101, we cannot be certain that such protection will be sufficient or that competitors will not challenge the scope, validity or enforceability of such patents.

Patents might not be issued or granted with respect to our patent applications that are currently pending, and issued or granted patents might later be found to be invalid or unenforceable, be interpreted in a manner that does not adequately protect our current product or any future products, or fail to otherwise provide us with any competitive advantage. The patent position of biotechnology and pharmaceutical companies is generally uncertain because it involves complex legal and factual considerations. The standards applied by the U.S. Patent and Trademark Office, or USPTO, and foreign patent offices in granting patents are not always applied uniformly or predictably. For example, there is no uniform worldwide policy regarding patentable subject matter or the scope of claims allowable in biotechnology and pharmaceutical patents. Consequently, patents may not issue from our pending patent applications, or we may end up with patent claims of different scope in different jurisdictions. As such, we do not know the degree of future protection that we will have on our proprietary products and technology, if any, and a failure to obtain adequate intellectual property protection with respect to our product candidates and proprietary technology could have a material adverse impact on our business.

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or applications will be due to be paid to the USPTO and various governmental patent agencies outside of the U.S. in several stages over the lifetime of the patents and/or applications. The USPTO and various non-US governmental patent agencies 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, and we rely upon our licensors or our other collaborators to effect compliance with respect to the patents and patent applications that we license. In some cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. However, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, our competitors might be able to enter the market and this circumstance would have a material adverse effect on our business.

Our intellectual property rights will not necessarily provide us with competitive advantages.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business, or may not permit us to maintain our competitive advantage.

The following examples are illustrative:

- others may be able to make compounds that are similar to our product candidates but that are not covered by the claims of the patents that we or our collaborators own or have exclusively licensed;
- others may independently develop similar or alternative technologies without infringing our intellectual property rights;
- issued patents that we own or have exclusively licensed may not provide us with any competitive advantages, or may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- we may obtain patents for certain compounds many years before we obtain marketing approval for products containing such compounds, and because patents have a limited life, which may begin to run out prior to the commercial sale of the related product, the commercial value of our patents may be limited;
- 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;
- 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 marketing one or more of our product candidates for one or more indications.

Any of the aforementioned threats to our competitive advantage could have a material adverse effect on our business.

We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting, enforcing and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the U.S. can be less extensive than those in the U.S. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the U.S. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the U.S., or from offering to sell, selling, using, making or importing products made using our inventions in and into the U.S. or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the U.S. These products may compete with our current or future products, if any, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions 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 and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Our patents covering one or more of our products or product candidates could be found invalid or unenforceable if challenged.

Any of our intellectual property rights could be challenged or invalidated despite measures we take to obtain patent and other intellectual property protection with respect to our product candidates and proprietary technology. For example, if we were to initiate legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that our patent is invalid and/or unenforceable. In patent litigation in the U.S. and in some other jurisdictions, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, for example, lack of novelty, obviousness, broken priority, lack of written description, insufficient or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld material information from the USPTO or the applicable foreign counterpart, or made a misleading statement, during prosecution. A litigant or the USPTO itself could challenge our patents on this basis even if we believe that we have conducted our patent prosecution in accordance with the duty of candor and in good faith. The outcome following such a challenge is unpredictable.

With respect to challenges to the validity of our patents, for example, there might be invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on a product candidate. Even if a defendant does not prevail on a legal assertion of invalidity and/or unenforceability, our patent claims may be construed in a manner that would limit our ability to enforce such claims against the defendant and others. The cost of defending such a challenge, particularly in a foreign jurisdiction, and any resulting loss of patent protection could have a material adverse impact on one or more of our product candidates and our business.

Enforcing our intellectual property rights against third parties may also cause such third parties to file other counterclaims against us, which could be costly to defend, particularly in a foreign jurisdiction, and could require us to pay substantial damages, cease the sale of certain products or enter into a license agreement and pay royalties (which may not be possible on commercially reasonable terms, or at all). Any efforts to enforce our intellectual property rights are also likely to be costly and may divert the efforts of our scientific and management personnel.

Patent protection and patent prosecution for some of our product candidates is dependent on, and the ability to assert patents and defend them against claims of invalidity is maintained by, third parties.

There have been and may be times in the future when certain patents that relate to our product candidates or any approved products are controlled by our licensees, sublicensees, licensors or other collaborators. Although we may, under such arrangements, have rights to consult with our collaborators on actions taken as well as back-up rights of prosecution and enforcement, we have in the past and may in the future relinquish rights to prosecute and maintain patents and patent applications within our portfolio as well as the ability to assert such patents against infringers. For example, currently the rights relating to the patent portfolio for XEN901 (now known as NBI-921352), other selective Nav1.6 inhibitors and dual Nav1.2/1.6 inhibitors are exclusively licensed to Neurocrine Biosciences and the rights to the patent portfolio for XEN402 (which was acquired by Flexion for use in its product candidate FX301) were sold to Flexion.

If any current or future licensee, sublicensee, licensor or other collaborators with rights to prosecute, assert or defend patents related to our product candidates 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 are asserted against infringers or defended against claims of invalidity or unenforceability in a manner which adversely affects such coverage, our ability to develop and commercialize any such product candidate may be adversely affected and we may not be able to prevent competitors from making, using, importing, offering for sale, and/or selling competing products.

We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time consuming and unsuccessful.

Competitors may infringe our patents or the patents of our licensors. To counter 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 of ours or one of our licensors is not valid or is unenforceable or may refuse to stop the other party in such infringement proceeding from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated, held unenforceable or interpreted narrowly, and could put any of our patent applications at risk of not yielding an issued patent.

Interference proceedings, derivation proceedings, entitlement proceedings, ex parte reexamination, inter partes review, post-grant review, and opposition proceedings provoked by third parties or brought by the USPTO or any foreign patent authority may be used to challenge inventorship, ownership, claim scope, or validity of our patent applications. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms, if any license is offered at all. Litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees.

We may not be able to prevent, alone or with our licensors, misappropriation of our trade secrets or confidential information, particularly in countries where the laws may not protect those rights as fully as in the U.S. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the market price of our common shares.

In addition, we or our licensors may be subject to claims that former employees, collaborators or other third parties have an interest in our owned or in-licensed patents, trade secrets, or other intellectual property as an inventor or co-inventor. For example, we or our licensors may have inventorship disputes arise from conflicting obligations of employees, consultants or others who are involved in developing our product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship or our or our licensors' ownership of our owned or in-licensed patents, trade secrets or other intellectual property. If we or our licensors fail in defending 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.

Claims that our product candidates or the sale, offer for sale, importation, manufacture, or use of our future products infringe the patent or other intellectual property rights of third parties could result in costly litigation or could require substantial time and money to resolve, even if litigation is avoided.

Our commercial success depends upon our ability to develop product candidates and commercialize products that may be approved in the future, using our proprietary technology without infringing the intellectual property rights of others. Our product or product candidates or any uses of them may now and in the future infringe third-party patents or other intellectual property rights. Third parties might allege that we or our collaborators are infringing their patent rights or that we have misappropriated their trade secrets, or that we are otherwise violating their intellectual property rights, whether with respect to the manner in which we have conducted our research or to the composition, use or manufacture of the compounds we have developed or are developing with our collaborators. Such third parties might resort to litigation against us or other parties we have agreed to indemnify, which litigation could be based on either existing intellectual property or intellectual property that arises in the future.

It is possible that relevant patents or patent applications held by third parties will cover our product candidates at the time of launch and we may also fail to identify, relevant patents or patent applications held by third parties that cover our product candidates. For example, U.S. applications filed before November 29, 2000, and certain applications filed after that date that will not be filed outside the U.S. remain confidential until patents issue. Other patent applications in the U.S. and several other jurisdictions are published approximately 18 months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Furthermore, publication of discoveries in the scientific or patent literature often lags behind actual discoveries. Therefore, we cannot be certain that we or our collaborators were the first to invent, or the first to file patent applications on our product candidates or for their uses, or that our product candidates will not infringe patents that are currently issued or that will be issued in the future. In the event that a third party has also filed a patent application covering one of our product candidates or a similar invention, we may have to participate in an adversarial proceeding, known as an interference or derivation proceeding, declared by the USPTO or its foreign counterpart to determine priority of invention. Additionally, pending patent applications and patents which have been published can, subject to certain limitations, be later amended in a manner that could cover our current or future products, if any, or their use.

Defending against claims of patent infringement, misappropriation of trade secrets or other violations of intellectual property rights could be costly and time consuming, regardless of the outcome. Thus, even if we were to ultimately prevail, or to settle at an early stage, such litigation 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 our product candidates or the selling, using, making, offering to sell, or importing, of our future products infringe, misappropriate or otherwise violate third-party intellectual property rights could therefore have a material adverse impact on our business.

Most of our competitors are larger than we are and have substantially greater financial resources. They are, therefore, likely to be able to sustain the costs of complex intellectual property litigation longer than we could. In addition, the uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to conduct our clinical trials, continue our internal research programs, in-license needed technology, or enter into strategic collaborations that would help us bring our product candidates to market.

In addition, any future intellectual property litigation, interference or other administrative proceedings will result in additional expense and distraction of our personnel. An adverse outcome in such litigation or proceedings may expose us or any future strategic collaborators to loss of our proprietary position, expose us to significant liabilities, or require us to seek licenses that may not be available on commercially acceptable terms, if at all, each of which could have a material adverse effect on our business.

Unfavorable outcomes in intellectual property litigation could limit our research and development activities and/or our ability to commercialize certain products.

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 products. Prohibitions against using certain technologies, or prohibitions against commercializing certain products, could be imposed by a court or by a settlement agreement between us and a plaintiff. In addition, if we are unsuccessful in defending against allegations that we have infringed, misappropriated or otherwise violated patent or other intellectual property rights of others, we may be forced to pay substantial damage awards to the plaintiff. There is inevitable uncertainty in intellectual property litigation, and we could lose, even if the case against us is weak or flawed. If litigation leads to an outcome unfavorable to us, we may be required to obtain a license from the intellectual property owner in order to continue our research and development programs or to market any resulting product. It is possible that the necessary license will not be available to us on commercially acceptable terms, or at all. Alternatively, we may be required to modify or redesign our current 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.

In order to avoid or settle potential claims with respect to any patent or other intellectual property rights of third parties, we may choose or be required to seek a license from a third party and be required to pay license fees or royalties or both, which could be substantial. These licenses may not be available on acceptable terms, or at all. Even if we or any future collaborators were able to obtain a license, the rights may be nonexclusive, which could result in our competitors gaining access to the same intellectual property. Ultimately, we could be prevented from commercializing a product, or be forced, by court order or otherwise, to cease some or all aspects of our business operations, if, as a result of actual or threatened patent or other intellectual property claims, we are unable to enter into licenses on acceptable terms. Further, we could be found liable for significant monetary damages as a result of claims of intellectual property infringement. In the future, we may receive offers to license and demands to license from third parties claiming that we are infringing their intellectual property or owe license fees and, even if such claims are without merit, we could fail to successfully avoid or settle such claims.

If Neurocrine Biosciences, Flexion or other collaborators license or otherwise acquire rights to intellectual property controlled by a third party in various circumstances, for example, where a product could not be legally developed or commercialized in a country without the third-party intellectual property right or, where it is decided that it would be useful to acquire such third-party right to develop or commercialize the product, they are eligible under our collaboration agreements to decrease payments payable to us on a product-by-product basis and, in certain cases, on a country-by-country basis. Any of the foregoing events could harm our business significantly.

If we breach any of the agreements under which we license the use, development and commercialization rights to our product candidates or technology from third parties, we could lose license rights that are important to our business.

Under our existing license and other agreements, including those associated with the XEN007 program, we are 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 one of our current licenses, or license exclusivity, or any other license we may acquire in the future, could materially harm our business, prospects, financial condition and results of operations.

Confidentiality agreements with employees and third parties may not prevent unauthorized disclosure of trade secrets and other proprietary information, which would harm our competitive position.

In addition to patents, we rely on trade secrets, technical know-how and proprietary information concerning our discovery platform, business strategy and product candidates in order to protect our competitive position, which are difficult to protect. In the course of our research and development activities and our business activities, we often rely on confidentiality agreements to protect our proprietary information. Such confidentiality agreements are used, for example, when we talk to vendors of laboratory, manufacturing, pre-clinical development or clinical development goods or services or potential strategic collaborators. In addition, each of our employees and consultants is required to sign a confidentiality agreement and invention assignment agreement upon joining our company. Our employees, consultants, contractors, business partners or outside scientific collaborators might intentionally or inadvertently disclose our trade secret information in breach of these confidentiality agreements or our trade secrets may otherwise be misappropriated. Our collaborators might also have rights to publish data and we might fail to apply for patent protection prior to such publication. It is possible that a competitor will make use of such information, and that our competitive position will be compromised. In addition, to the extent that our employees, consultants or contractors use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions. Enforcing a claim that a third party illegally obtained and is using any of our trade secrets is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the U.S. sometimes are less willing than U.S. courts to protect trade secrets. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how. If we cannot maintain the confidentiality of our proprietary technology and other confidential information, then our ability to obtain patent protection or to protect our trade secret information would be jeopardized, which would adversely affect our competitive position.

Recent court decisions could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued 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. There have been recent changes regarding how patent laws are interpreted, and both the USPTO and Congress have recently made significant changes to the patent system. There have been U.S. Supreme Court decisions that now show a trend of the Supreme Court which is distinctly negative on some patents. The trend of these decisions along with resulting changes in patentability requirements being implemented by the USPTO could make it increasingly difficult for us to obtain and maintain 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.

If we do not obtain protection under the Hatch-Waxman Act in the U.S. and similar legislation outside of the U.S. by extending the patent terms for our product candidates, our business may be materially harmed.

Depending upon the timing, duration and specifics of FDA marketing approval of our product candidates, if any, one or more U.S. patents may be eligible for limited patent term restoration under the Hatch-Waxman Act. The Hatch-Waxman Act permits a patent restoration term of up to five years as compensation for patent term lost during clinical testing of the product and the subsequent FDA regulatory review process. However, we may not be granted an extension because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than five years, or even less than we request if that number is less than five years.

If we are unable to obtain patent term extension or restoration or the term of any such extension is less than we request, the period during which we will have the right to exclusively market our product may be shortened and our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced, possibly materially.

We have not registered our corporate name as a trademark in all of our potential markets, and failure to secure those registrations could adversely affect our business.

Our corporate name, Xenon, has not been trademarked in each market where we operate and plan to operate. Our trademark applications for our corporate name or the name of our products may not be allowed for registration, and our registered trademarks may not be maintained or enforced. During trademark registration proceedings, we may receive rejections, which we may be unable to overcome in our responses. Third parties may also attempt to register trademarks utilizing the Xenon name on their products, and we may not be successful in preventing such usage. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. If we do not secure registrations for our trademarks, we may encounter more difficulty in enforcing them against third parties than we otherwise would.

Intellectual property litigation may lead 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, there could be public announcements of the initiation of the litigation as well as results of hearings, rulings on motions, and other interim proceedings in the litigation. 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.

Risks Related to Ownership of Our Common Shares

The market price of our common shares may be volatile, and purchasers of our common shares could incur substantial losses.

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 scientific or management personnel;
- our ability to successfully commercialize our future product candidates we develop independently, if approved;
- 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;
- any change to the composition of our board of directors or key personnel;
- sales of common shares by us or our shareholders in the future, as well as the overall trading volume of our common shares;
- failure to comply with covenants or make required payments under loan agreements;
- changes in the structure of healthcare payment systems;
- commencement of, or our involvement in, litigation;
- the impact of the COVID-19 pandemic on our business and the macroeconomic environment;
- general economic, industry and market conditions in the pharmaceutical and biotechnology sectors and other factors that may be unrelated to our operating performance or the operating performance of our competitors, including changes in market valuations of similar companies; and
- the other factors described in this “Risk Factors” section.

In addition, the stock market in general, and Nasdaq and the biopharmaceutical industry in particular, have from time to time experienced volatility that often has been unrelated to the operating performance of the underlying companies. The COVID-19 pandemic, for example, resulted in significant volatility. These broad market and industry fluctuations may adversely affect the market price of our common shares, regardless of our operating performance. In several recent situations where the market price of a stock has been volatile, holders of that stock have instituted securities class action litigation against the company that issued the stock. If any of our shareholders were to bring a lawsuit against us, the defense and disposition of the lawsuit could be costly and divert the time and attention of our management and harm our operating results.

Future sales of our common shares in the public market could cause the market price of our common shares to fall.

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.

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. Any such issuance, including any issuances pursuant to our “at-the-market” equity offering program under our August 2020 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.

Provisions in our corporate charter documents and Canadian law could make an acquisition of us, which may be beneficial to our shareholders, more difficult and may prevent attempts by our shareholders to replace or remove our current management and/or limit the market price of our common shares.

Provisions in our articles and our by-laws, as well as certain provisions under the Canada Business Corporations Act, or CBCA, and applicable Canadian securities laws, may discourage, delay or prevent a merger, acquisition, tender offer or other change in control of us that shareholders may consider favorable, including transactions in which they might otherwise receive a premium for their common shares. These provisions could also limit the price that investors might be willing to pay in the future for our common shares, thereby depressing the market price of our common shares. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions 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. Among other things, 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 securities laws generally require, subject to certain exceptions, a tender offer to remain open for 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.

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 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 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, U.S. and U.S. securities laws.

We are governed by the 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 charter documents, 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.

We are a smaller reporting company, and any decision on our part to comply only with certain reduced reporting and disclosure requirements applicable to such companies could make our common shares less attractive to investors.

We are a "smaller reporting company," as defined under the Securities Exchange Act of 1934, as amended, or the Exchange Act. For as long as we continue to be a smaller reporting company, we may choose to take advantage of exemptions from various reporting requirements applicable to other public companies that are not smaller reporting companies, including, but not limited to, two years of audited financial statements in our annual reports.

Investors could find our common shares less attractive if we choose to rely on these disclosure exemptions. If some investors find our common shares less attractive as a result of any choices to reduce future disclosure, there may be a less active trading market for our common shares and the market price of our common shares may be more volatile.

Effective December 31, 2021, we will be a large accelerated filer and no longer qualify as a smaller reporting company, which will increase our costs and demands on management.

As a result of our public float (the market value of our common shares held by non-affiliates) as of June 30, 2021, we will become a large accelerated filer as of December 31, 2021 and therefore no longer qualify as a "smaller reporting company" as defined under the Exchange Act. Our ability to rely on the reduced disclosure requirements available to smaller reporting companies will cease after the filing of our Annual Report on Form 10-K for the year ended December 31, 2021, including those portions of our definitive proxy statement relating to our 2022 annual meeting of shareholders that will be incorporated by reference into Part III of the Annual Report on Form 10-K.

As a smaller reporting company, we have had the option to take advantage of certain exemptions from various reporting requirements that are applicable to other public companies, including, but not limited to, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements.

As a non-accelerated filer and smaller reporting company, we have availed ourselves of the exemption from the requirement that our independent registered public accounting firm attest to the effectiveness of our internal control over financial reporting under Section 404. However, we may no longer avail ourselves of this exemption when we become a large accelerated filer.

When our independent registered public accounting firm is required to undertake an assessment of our internal control over financial reporting, the cost of our compliance with Section 404 will correspondingly increase. We expect to incur significant expense and devote substantial management effort toward ensuring compliance with Section 404 in preparation for and once we are a large accelerated filer. We currently do not have an internal audit group, and we will need to continue to hire additional accounting and financial staff with appropriate public company experience and technical accounting knowledge, and it may be difficult to recruit and maintain such personnel. Implementing any appropriate changes to our internal control over financial reporting may require specific compliance training for our directors, officers and employees and take a significant period of time to complete. Such changes may not, however, be effective in maintaining the adequacy of our internal control over financial reporting, and any failure to maintain that adequacy, or consequent inability to produce accurate financial statements or other reports on a timely basis, could increase our operating costs and could materially impair our ability to operate our business.

Future sales and issuances of our common shares, preferred shares, or rights to purchase common shares, including warrants or pursuant to our equity incentive plans, could cause shareholders to incur dilution and could cause the market price of our common shares to fall.

As of June 30, 2021, stock options to purchase 5,771,051 of our common shares with a weighted-average exercise price of $12.04 per common share were outstanding, a warrant to purchase 40,000 of our common shares with a weighted-average exercise price of $9.79 per common share was outstanding, 1,016,000 of our Series 1 Preferred Shares were outstanding, which are convertible into our common shares on a one-for-one basis at the option of the holder, subject to certain ownership limitations following a requested conversion, and pre-funded warrants to purchase 1,081,081 of our common shares with an exercise price of $0.0001 per share. The exercise of any of these stock options or warrants or conversion of the remaining Series 1 Preferred Shares would result in dilution to current common shareholders. Further, because we anticipate the need to raise additional capital to fund our clinical development programs, we may in the future sell substantial amounts of common shares, preferred shares, pre-funded warrants or other securities convertible into or exchangeable for common shares. 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 may have an adverse effect on the market price of our common shares.

Any future issuances of common shares, preferred shares, or securities such as warrants, notes, or preferred shares that are convertible into, exercisable or exchangeable for, our common shares, would have a dilutive effect on the voting and economic interests of our existing shareholders.

We are at risk of securities class action litigation.

In the past, 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 team has broad discretion as to the use of the net proceeds from public and private equity and debt financings and the investment of these proceeds may not yield a favorable return. We may invest the proceeds in ways with which our shareholders disagree.

We have broad discretion in the application of any net proceeds we have received or may receive pursuant to this offering, our March 2021 public offering of common shares and pre-funded warrants to purchase common shares, our August 2020 "at-the-market" equity offering program with Jefferies and Stifel, our January 2020 public offering of common shares, as well as the net proceeds to us from previous equity and debt financings. Shareholders may not agree with our decisions, and our use of the proceeds and our existing cash and cash equivalents and marketable securities 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, until the net proceeds are used, 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. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common shares may be investors' sole source of gain for the foreseeable future.

There is no public market for our outstanding pre-funded warrants or our Series 1 Preferred Shares.

There is no public trading market for our outstanding pre-funded warrants or our Series 1 Preferred Shares and we do not expect a market to develop. In addition, we do not intend to list the outstanding pre-funded warrants or our Series 1 Preferred Shares on the Nasdaq Global Market or any other national securities exchange or nationally recognized trading system. Without an active trading market, the liquidity of the outstanding pre-funded warrants and our Series 1 Preferred Shares will be limited.

General Risk Factors

Unstable market and economic conditions may have serious adverse consequences on our business and financial condition.

Global credit and financial markets have at times experienced extreme disruptions, including most recently in connection with the novel coronavirus, or COVID-19 pandemic, characterized by increased market volatility, declines in consumer confidence, declines in economic growth, increases in unemployment rates, and uncertainty about economic stability. 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, 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 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.

If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, shareholders could lose confidence in our financial and other public reporting, which would harm our business and the market price of our common shares.

Effective internal control over financial reporting is necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations.

We are required to disclose changes made in our internal controls and procedures on a quarterly basis and our management is required to assess the effectiveness of these controls annually. We may also be required to obtain an independent assessment of the effectiveness of our internal controls which could detect problems that our management's assessment might not. Going forward, even if our management concludes that our internal control over financial reporting is effective, our independent registered public accounting firm may conclude that there are material weaknesses or significant deficiencies with respect to our internal controls or the level at which our internal controls are documented, designed, implemented or reviewed. If we or our independent registered public accounting firm identifies deficiencies in our internal control over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements, investors may lose confidence in our reported financial information, which could cause the market price of our common shares to decline and we could be subject to sanctions or investigations by the SEC or other regulatory authorities, which would require additional financial and management resources. Irrespective of compliance with Section 404, any failure of our internal control over financial reporting could have a material adverse effect on our stated operating results and harm our reputation.

Environmental, social and governance matters may impact our business and reputation.

Companies are increasingly being judged by their performance on a variety of environmental, social and governance, or ESG, matters, which are considered to contribute to the long-term sustainability of companies' performance.

A variety of organizations measure the performance of companies on such ESG topics, and the results of these assessments are widely publicized. In addition, 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. Topics taken into account in such assessments include, among others, the role of the company's board of directors in supervising various ESG issues and board diversity.

In light of investors' increased focus on ESG matters, there can be no certainty that we will manage such issues successfully, or that we will successfully meet expectations as to our proper role. Any failure or perceived failure by us in this regard could have a material adverse effect on our reputation and on our business, share price, financial condition, or results of operations, including the sustainability of our business over time.

If securities or industry analysts do not publish research reports about our business, or if they issue an adverse opinion about our business, the market price of our common shares and the trading volume of our common shares could decline.

The trading market for our common shares is influenced by the research and reports that securities or industry analysts publish about us or our business. If too few securities or industry analysts cover our company, the market price of our common shares would likely be negatively impacted. If securities and industry analysts who cover us downgrade our common shares or publish inaccurate or unfavorable research about our business, the market price of our common shares would likely decline. If one or more of these analysts cease coverage of our company or fail to publish reports on us regularly, demand for our common shares could decrease, which might cause the market price of our common shares and the trading volume of our common shares to decline.

An active trading market for our common shares may not be maintained.

Our common shares are currently traded on Nasdaq, but we can provide no assurance that we will be able to maintain an active trading market on Nasdaq or any other exchange in the future. If an active market for our common shares is not maintained, it may be difficult for our shareholders to sell the common shares they have purchased without depressing the market price for the common shares or at all. Further, an inactive market may also impair our ability to raise capital by selling additional common shares and may impair our ability to enter into strategic collaborations or acquire companies or products by using our common shares as consideration.

Nasdaq may delist our securities from its exchange, which could limit investors' ability to make transactions in our securities and subject us to additional trading restrictions.

Our common shares are listed on Nasdaq under the trading symbol "XENE." Our securities may fail to meet the continued listing requirements to be listed on Nasdaq. If Nasdaq delists our common shares from trading on its exchange, we could face significant material adverse consequences, including:

- significant impairment of the liquidity for our common shares, which may substantially decrease the market price of our common shares;
- a limited availability of market quotations for our securities;

- a determination that our common shares qualify as a “penny stock” which will require brokers trading in our common shares to adhere to more stringent rules and possibly resulting in a reduced level of trading activity in the secondary trading market for our common shares;
- a limited amount of news and analyst coverage for our company; and
- a decreased ability to issue additional securities or obtain additional financing in the future.

Risks Related to this Offering

We will have broad discretion in the use of proceeds from this offering and our existing cash and cash equivalents and marketable securities, and may invest or spend the proceeds in ways with which you do not agree and in ways that may not yield a return.

We will have broad discretion in the application of the net proceeds to us from this offering, including for any of the purposes described in the section of this prospectus supplement entitled “Use of Proceeds,” and our existing cash and cash equivalents and marketable securities. You may not agree with our decisions, and our use of the proceeds and our existing cash and cash equivalents and marketable securities may not improve our results of operations or enhance the value of our common shares. You will be relying on the judgment of our management regarding the application of the proceeds of this offering. The results and effectiveness of the use of proceeds are uncertain, and we could spend the proceeds in ways that you do not agree with or that do not improve our results of operations 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 price of our common shares to decline.

New investors in our common shares will experience immediate and substantial dilution after this offering.

Since the public offering price for our common shares in this offering is substantially higher than the net tangible book value per share of our common shares outstanding prior to this offering, you will suffer immediate and substantial dilution in the net tangible book value of the common shares you purchase in this offering. If the underwriters exercise their option to purchase additional common shares, you will experience additional dilution. See the section entitled “Dilution” below for a more detailed discussion of the dilution you will incur if you purchase shares in this offering.

The issuance of additional common shares could be dilutive to shareholders if they do not invest in future offerings. In addition, we have a significant number of options to purchase our common shares outstanding. If these options are exercised, you may incur further dilution. Moreover, to the extent that we issue additional options to purchase, or securities convertible into or exchangeable for, common shares in the future and those options or other securities are exercised, converted or exchanged, shareholders may experience further dilution.

FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the information incorporated by reference in this prospectus supplement and the accompanying prospectus contain certain statements that constitute “forward-looking statements” within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act, and Canadian securities laws.

Our forward-looking statements include, but are not limited to, statements about:

- our ability to identify additional products or product candidates either from our internal research efforts or though acquiring or in-licensing other product candidates or technologies;
- the initiation, timing, cost, progress and success of our research and development programs, pre-clinical studies, and clinical trials;
- our ability to advance product candidates into, and successfully complete, clinical trials;
- our ability to recruit sufficient numbers of patients for our current and future clinical trials for orphan or more common indications;
- the direct and indirect impact of COVID-19 on our business and operations, including supply chain, manufacturing, research and development costs, clinical trial conduct, clinical trial data and employees;
- our ability to achieve profitability;
- our ability to obtain funding for our operations;
- our ability to receive milestones, royalties and sublicensing fees under our collaborations, and the timing of such payments;
- the timing and magnitude of potential milestone payments under our product acquisition and in-licensing agreements;
- the implementation of our business model and strategic plans;
- our ability to develop and commercialize product candidates for orphan and niche indications or more common indications independently;
- our ability to advance XEN007 and potentially other future product candidates directly into Phase 2 or later stage clinical trials;
- our pre-commercial, commercialization, marketing and manufacturing capabilities and strategy;
- our ability to identify drug targets;
- our ability to protect our intellectual property and operate our business without infringing upon the intellectual property rights of others;
- our expectations regarding federal, state and foreign regulatory requirements;
- the therapeutic benefits, effectiveness and safety of our product candidates;
- the accuracy of our estimates of the size and characteristics of the markets that may be addressed by our products and product candidates and our ability to obtain suitable pricing and receive reimbursements from health agencies;
- the rate and degree of market acceptance and clinical utility of any future products;
- the timing of, and our and our collaborators’ ability to obtain and maintain regulatory approvals for our product candidates;
- our ability to maintain and establish collaborations;
- our expectations regarding market risk, including interest rate changes and foreign currency fluctuations;
- our belief in the sufficiency of our cash, cash equivalents and marketable securities to meet our needs for at least the next 12 months;
- our expected use of the net proceeds to us from this offering;
- our ability to engage and retain the employees required to grow our business;
- our future financial performance and projected expenditures;

- developments relating to our competitors and our industry, including the success of competing therapies that are or become available; and
- estimates of our expenses, future revenue, capital requirements and our needs for additional financing.

The words “believe,” “may,” “will,” “potentially,” “estimate,” “continue,” “anticipate,” “intend,” “could,” “would,” “project,” “plan,” “expect” and the negative and plural forms of these words and similar expressions are intended to identify forward-looking statements, but are not the exclusive means of identifying such statements. Those statements appear in this prospectus supplement, the accompanying prospectus and the documents incorporated herein and therein by reference, particularly in the sections titled “Prospectus Supplement Summary,” “Prospectus Summary,” “Risk Factors,” “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and “Business,” and include statements regarding the intent, belief or current expectations of the Company and management that are subject to known and unknown risks, uncertainties and assumptions.

This prospectus supplement and the accompanying prospectus and the information incorporated by reference in this prospectus supplement and the accompanying prospectus also contain statements that are based on the current expectations of our Company and management. You are cautioned that any such forward-looking statements are not guarantees of future performance and involve risks and uncertainties, and that actual results may differ materially from those projected in the forward-looking statements as a result of various factors.

The factors and assumptions used by us to develop the forward-looking statements contained herein include, but are not limited to, the assumption that regulatory requirements for the approval of marketing authorization applications/new drug approvals will be maintained, the assumption that the time required to analyze and report the results of our clinical studies will be consistent with past timing, the assumption that market data and reports reviewed by us are accurate, the assumption relating to the availability of capital on terms that are favorable to us, and the assumptions relating to the feasibility of future clinical trials.

Because forward-looking statements are inherently subject to risks and uncertainties (including the risks outlined under the section “Risk Factors” beginning on page S-7 of this prospectus supplement, on page 4 of the accompanying prospectus and the documents incorporated by reference herein), some of which cannot be predicted or quantified, you should not rely upon forward-looking statements as predictions of future events. The events and circumstances reflected in the forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Except as required by applicable law, including the securities laws of the United States and Canada and the rules and regulations of the SEC, we do not plan to publicly update or revise any forward-looking statements contained herein after we distribute this prospectus supplement, whether as a result of any new information, future events or otherwise.

In addition, statements that “we believe” and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this prospectus supplement, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and investors are cautioned not to unduly rely upon these statements.

USE OF PROCEEDS

We estimate that the net proceeds to us from this offering will be approximately $234.7 million, or approximately $269.9 million if the underwriters exercise in full their option to purchase additional common shares, based on an assumed public offering price of $31.50 per share, which is the last reported sale price of our common shares on the Nasdaq Global Market on October 4, 2021, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

A $1.00 increase or decrease in the assumed public offering price of $31.50 per share, which is the last reported sale price of our common shares on the Nasdaq Global Market on October 4, 2021, would increase or decrease, as applicable, the net proceeds to us by approximately $7.5 million, assuming that the number of shares offered by us (based on the assumed public offering price of $31.50 per share)remains the same and after deducting the estimated underwriting commissions and estimated offering expenses payable by us. We may also increase or decrease the number of shares we are offering. An increase or decrease of 1,000,000 in the number of shares we are offering would increase or decrease, as applicable, the net proceeds to us from this offering by approximately $29.6 million, assuming that the assumed public offering price remains the same and after deducting the estimated underwriting commissions and estimated offering expenses payable by us.

We currently expect to use the net proceeds from this offering, together with our existing cash and cash equivalents and marketable securities, as follows:

- for external and personnel-related expenses associated with the clinical development of our XEN1101 and XEN496 product candidates as well as other programs entering clinical development;
- to fund our pre-clinical and discovery activities; and
- for working capital, capital expenditures and other general corporate purposes.

Additionally, we may use a portion of the net proceeds to us from this offering to expand our business by in-licensing or acquiring, as the case may be, commercial products, product candidates, technologies, compounds, other assets or complementary businesses, using cash or common shares. However, we have no current commitments or obligations to complete any such transactions.

This expected use of our net proceeds from this offering represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress of our product candidate development, the status of and results from clinical trials, as well as any collaborations that we may enter into with third parties for our product candidates, and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of our net proceeds from this offering, and investors will be relying on the judgment of our management regarding the application of our net proceeds from this offering. The timing and amount of our actual expenditures will be based on many factors, including receipt of potential milestone payments pursuant to our ongoing collaborations; competitive and technological developments; and the anticipated growth of our business. Pending these uses, we plan to invest these net proceeds in treasury bills, corporate bonds, commercial paper, term deposits, bankers acceptances or deposit-based investments including, but not limited to, interest savings accounts. The goal with respect to the investment of these net proceeds is capital preservation and liquidity so that such funds are readily available to fund our operations.

The key business objective that we intend to meet with the net proceeds to us from this offering is the advancement and development of our product candidates, programs and research activities described above. The estimated costs and timing to reach regulatory approval, if ever, and commercial production with respect to such product candidates, programs and research activities will depend on a number of factors, including those listed under the heading “Risk Factors” in this prospectus supplement and the accompanying prospectus and the documents incorporated by reference herein and therein.

We believe, based on our current operating plan and expected expenditures, that our existing cash and cash equivalents, and marketable securities, together with the proceeds from this offering, will be sufficient to meet our anticipated cash and capital expenditure requirements for at least the next 12 months. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect.

DIVIDEND POLICY

We have never declared or paid any cash dividends on our common shares or any other securities. We currently anticipate that we will retain all available funds and any future earnings, if any, in the foreseeable future for use in the operation of our business and do not currently anticipate paying cash dividends in the foreseeable future. Payment of future cash dividends, if any, will be at the discretion of the board of directors, subject to applicable law and will depend on various factors, including our financial condition, operating results, current and anticipated cash needs, the requirements of any debt instruments and other factors the board of directors deems relevant.

DILUTION

If you invest in our common shares your interest will be diluted immediately to the extent of the difference between the public offering price per common share you will pay in this offering and the as adjusted net tangible book value per common share after this offering. Net tangible book value per common share represents our total tangible assets less total liabilities, divided by the number of common shares outstanding, as adjusted to reflect the assumed conversion of our outstanding Series 1 Preferred Shares as discussed below.

As of June 30, 2021, our net tangible book value was $257.0 million, or $6.10 per common share. After giving effect to our issuance and sale of 7,936,507 common shares in this offering at the assumed public offering price of $31.50 per common share, which is the last reported sale price of our common shares on the Nasdaq Global Market on October 4, 2021, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, the as adjusted net tangible book value as of June 30, 2021 would have been $491.7 million, or $9.82 per common share. This represents an immediate increase in as adjusted net tangible book value to existing shareholders of $3.72 per common share and an immediate dilution to new investors purchasing common shares in this offering of $21.68 per common share.

The following table illustrates this per common share dilution to the new investors purchasing common shares in this offering:

Assumed public offering price per common share		$ 31.50
Net tangible book value per common share at June 30, 2021	$ 6.10	
Increase in net tangible book value per common share attributable to new investors purchasing common shares in this offering	3.72	
As adjusted net tangible book value per common share after this offering	$ 9.82	
Dilution per common share to new investors in this offering		$ 21.68

If the underwriters exercise their option to purchase an additional 1,190,476 common shares in full, at the assumed public offering price of $31.50 per common share, the as adjusted net tangible book value per share after giving effect to this offering would be $10.28 per common share, representing an immediate increase in net tangible book value (after deducting estimated underwriting discounts and commissions and estimated expenses payable by us) to existing shareholders of $4.18 per common share and immediate dilution in net tangible book value of $21.22 per common share to new investors.

A $1.00 increase (decrease) in the assumed public offering price of $31.50 per share, which is the last reported sale price of our common shares on the Nasdaq Global Market on October 4, 2021, would increase (decrease) the as adjusted net tangible book value as of June 30, 2021 by approximately $7.5 million, or approximately $0.15 per share, and increase (decrease) the dilution per share to new investors by approximately $0.85 per share, assuming that the number of shares offered by us (based on the assumed public offering price of $31.50 per share) remains the same and after deducting the estimated underwriting commissions and estimated offering expenses payable by us. An increase (decrease) of 1,000,000 in the number of shares we are offering would increase (decrease) the as adjusted net tangible book value by approximately $29.6 million, or $0.39 per share, and would decrease (increase) the dilution per share to new investors by approximately $0.39 per share, assuming that the assumed public offering price remains the same and after deducting the estimated underwriting commissions and estimated offering expenses payable by us. The as adjusted information discussed above is illustrative only and will adjust based on the actual public offering price and other terms of this offering determined at pricing.

The foregoing table and calculations are based on 42,133,568 common shares outstanding as of June 30, 2021 which number includes 1,016,000 common shares issuable upon the conversion of 1,016,000 of our Series 1 Preferred Shares outstanding as of June 30, 2021, and excludes:

- 5,771,051 common shares issuable upon the exercise of outstanding options to purchase common shares as of June 30, 2021, at a weighted average exercise price of $12.04 per common share;
- 275,337 common shares sold subsequent to June 30, 2021 pursuant to our license and collaboration agreement with Neurocrine Biosciences;
- 2,557,246 common shares reserved for future issuance as of June 30, 2021 under our Amended and Restated 2014 Equity Incentive Plan;
- 40,000 common shares issuable upon the exercise of warrants outstanding as of June 30, 2021, at a weighted-average exercise price of $9.79 per share; and
- pre-funded warrants to purchase up to 1,081,081 common shares outstanding as of June 30, 2021, at an exercise price of $0.0001 per share.

MATERIAL INCOME TAX CONSIDERATIONS

U.S. Federal Income Tax Information for U.S. Holders

The following summary describes the material U.S. federal income tax consequences of the ownership and disposition of common shares purchased in this offering. The discussion set forth below is applicable to U.S. Holders (as defined below). This summary deals only with common shares held as capital assets, meaning generally, assets held for investment.

The term “U.S. Holder” means a beneficial owner of a common share that is, for U.S. federal income tax purposes:

- an individual citizen or resident of the U.S.;
- a corporation (or other entity treated as a corporation for U.S. federal income tax purposes) created or organized in or under the laws of the U.S., any state thereof or the District of Columbia;
- an estate, the income of which is subject to U.S. federal income taxation regardless of its source; or
- a trust if it (a) is subject to the primary supervision of a court within the U.S. and one or more U.S. persons have the authority to control all substantial decisions of the trust or (b) has a valid election in effect under applicable U.S. Treasury regulations to be treated as a U.S. person.

This summary does not describe all of the U.S. federal income tax consequences applicable to a U.S. Holder if such U.S. Holder is subject to special treatment under U.S. federal income tax laws, including if such U.S. Holder is:

- a dealer in securities or currencies;
- a financial institution;
- a regulated investment company;
- a real estate investment trust;
- an insurance company;
- a tax-exempt organization;
- a person holding our common shares as part of a hedging, integrated or conversion transaction, a constructive sale or a straddle;
- a trader in securities that has elected the mark-to-market method of accounting for its securities;
- a person who owns, directly, indirectly or constructively, or is deemed to own 10% or more of our equity, by vote or value;
- a partnership or other pass-through entity for U.S. federal income tax purposes;
- a person whose “functional currency” is not the U.S. dollar;
- a person that received common shares as compensation for the performance of services; or
- a person holding our common shares in connection with a trade or business conducted outside the United States.

If a partnership (or any other entity or arrangement treated as a partnership for U.S. federal income tax purposes) holds our common shares, the tax treatment of a partner will generally depend upon the status of the partner and the activities of the partnership. Partners of a partnership holding our common shares should consult their own tax advisors.

The discussion below is based upon the provisions of the U.S. Internal Revenue Code of 1986, as amended, or the Code, and regulations, including proposed regulations, Internal Revenue Service, or the IRS, rulings and judicial decisions thereunder as of the date of this prospectus supplement. These authorities may be replaced, revoked or modified so as to result in U.S. federal income tax consequences different from those discussed below. This discussion does not contain a detailed description of all U.S. federal income tax consequences applicable to a U.S. Holder in light of such U.S. Holder’s particular circumstances, including U.S. federal estate, gift and alternative minimum tax consequences, the special tax accounting rules under Section 451(b) of the Code, or any state, local or non-U.S. tax consequences.

If you are considering the purchase of our common shares, you should consult your own tax advisors concerning the U.S. federal income tax consequences to you in light of your particular situation as well as any consequences arising under the laws of any other taxing jurisdiction.

Taxation of Dividends

Subject to the discussion below under "Passive Foreign Investment Company Consequences," the gross amount of distributions on our common shares (including amounts withheld to pay Canadian withholding taxes) will be taxable as dividends to a U.S. Holder to the extent paid out of our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. Dividends paid on our common shares (including withheld taxes) will be includable in a U.S. Holder's gross income as dividend income when actually or constructively received. Such dividends will not be eligible for the dividends-received deduction generally allowed to corporations with respect to dividends received from U.S. corporations. Distributions treated as dividends that are received by non-corporate U.S. Holders may qualify for reduced tax rates applicable to long term capital gains on dividends received from a "qualified foreign corporation" provided certain holding period and other requirements are met. A non-U.S. corporation generally will be considered to be a qualified foreign corporation if (i) it is eligible for the benefits of a comprehensive tax treaty with the United States, which the Secretary of Treasury of the United States determines is satisfactory for purposes of this provision, and which includes an exchange of information provision; or (ii) with respect to any dividend, it pays on shares that are readily tradeable on an established securities market in the United States. However, if we are a Passive Foreign Investment Company, or PFIC, for the taxable year in which the dividends are paid or the preceding taxable year (see "Passive Foreign Investment Company Consequences" below), we will not be treated as a qualified foreign corporation, and therefore the reduced tax rate described above will not apply. Non-corporate U.S. Holders that do not meet a minimum holding period requirement during which they are not protected from the risk of loss or that elect to treat the dividend income as "investment income" under applicable Code provisions will not be eligible for the reduced rates of taxation regardless of our status as a qualified foreign corporation. Further, the rate reduction will not apply to dividends if the recipient of a dividend is obligated to make related payments with respect to positions in substantially similar or related property. This disallowance applies even if the minimum holding period has been met.

Subject to certain conditions and limitations, Canadian tax withheld from dividends paid on our common shares may be deducted by a U.S. Holder from adjusted gross income or claimed as a credit against the U.S. Holder's U.S. federal income tax liability. A U.S. Holder may claim a deduction for Canadian taxes withheld from dividends paid in a taxable year only if the U.S. Holder elects to deduct all foreign income taxes paid in that taxable year. A foreign tax credit may only be claimed against U.S. federal income tax liability on foreign source income subject to the foreign tax credit limitation. The credit is calculated separately with respect to different categories of income. Dividends paid on our common shares will generally constitute foreign source "passive category income" for foreign tax credit purposes. A special rule will apply if we are a "United States-owned foreign corporation." In that case, dividends paid in a taxable year will be treated as dividends from U.S. sources and foreign sources in proportion to our earnings and profits for the taxable year from U.S. sources and from foreign sources. A U.S. Holder who is eligible to claim benefits under the United States-Canada Income Tax Convention, September 26, 1980, as amended, however, may treat the entire dividend as one from foreign sources for the purpose of claiming a credit for any Canadian withholding tax deducted from the dividend if the U.S. Holder files the appropriate election on its U.S. federal tax return. We will be treated as a U.S.-owned foreign corporation as long as shares representing 50% or more of the voting power or value of our common shares is owned, directly or indirectly, by U.S. persons. The rules relating to the determination of foreign source income and the foreign tax credit are complex, and availability of a foreign tax credit depends on numerous factors. Each U.S. Holder should consult with its own tax advisor to determine whether its income with respect to our common shares would be foreign source income and whether and to what extent that U.S. Holder would be entitled to the foreign tax credit.

To the extent that the amount of any distribution exceeds our current and accumulated earnings and profits for a taxable year, as determined under U.S. federal income tax principles, the distribution will first be treated as a tax-free return of capital, causing a reduction (but not below zero) in the adjusted basis of the common shares (thereby increasing the amount of gain, or decreasing the amount of loss, to be recognized on a subsequent disposition of the common shares), and the balance in excess of adjusted basis will be taxed as capital gain recognized on a sale or exchange. However, we cannot provide any assurance that we will maintain or provide earnings and profits determinations in accordance with U.S. federal income tax principles. Therefore, U.S. Holders should expect that a distribution will generally be treated as a dividend (as discussed above) even if that distribution would otherwise be treated as a non-taxable return of capital or as capital gain under the rules described above.

If a distribution is paid in Canadian dollars, the U.S. dollar value of such distribution on the date of receipt is used to determine the amount of the distribution received by a U.S. Holders. A U.S. Holder who continues to hold such Canadian dollars after the date on which they are received may recognize gain or loss upon their disposition due to exchange rate fluctuations. Generally, such gains and losses will be ordinary income or loss from U.S. sources.

Taxation of Capital Gains

Subject to the discussion below under "Passive Foreign Investment Company Consequences," a U.S. Holder will recognize taxable gain or loss on the sale of our common shares equal to the difference between the amount realized for the common shares and the U.S. Holder's adjusted tax basis in the common shares. Such gain or loss will be capital gain or loss. Capital gains of non-corporate U.S. Holders, including individual U.S. Holders, derived with respect to capital assets held for more than one year are eligible for reduced rates of taxation. The deductibility of capital losses is subject to limitations. Any gain or loss recognized by a U.S. Holder will generally be U.S. source gain or loss for foreign tax credit limitation purposes.

Passive Foreign Investment Company Consequences

In general, a corporation organized outside the U.S. will be treated as a PFIC in any taxable year, after applying certain look-through rules with respect to the income and assets of its subsidiaries, in which either (i) at least 75% of its gross income is "passive income" or (ii) on average at least 50% of its assets is attributable to assets that produce passive income or are held for the production of passive income. Passive income for this purpose generally includes, among other things, dividends, interest, royalties, rents, and gains from commodities and currency transactions and from the sale or exchange of property that gives rise to passive income. Assets that produce or are held for the production of passive income include cash, even if held as working capital or raised in a public offering, marketable securities and other assets that may produce passive income. In the case of a publicly traded corporation, the average percentage of a corporation's assets that produce or are held for the production of passive income generally is determined on the basis of the fair market value of the corporation's assets at the end of each quarter (which may be determined in part by the market value of our common shares, which is subject to change). In determining whether a foreign corporation is a PFIC, a proportionate share of the income and assets of each corporation in which it owns, directly or indirectly, at least a 25% interest (by value) is taken into account.

Based on the price of our common shares and the composition of our gross income and gross assets, we do not believe we were a PFIC for the taxable years ended December 31, 2020 and 2019, but we could be a PFIC in subsequent years.

Our status as a PFIC is a fact-intensive determination made on an annual basis and we cannot provide any assurance regarding our PFIC status for the current taxable year or for future taxable years. Neither our U.S. counsel nor U.S. tax advisor expresses any opinion with respect to our PFIC status or with respect to our expectations regarding our PFIC status.

If we are a PFIC in any taxable year during which a U.S. Holder owns our common shares, such U.S. Holder would be subject to taxation under the rules related to "excess distributions." Under such rules, additional taxes and interest charges would apply to certain distributions by us or to gain upon dispositions of our common shares if a U.S. Holder has not elected to have his or her investment in our common shares treated as an investment in a "qualified electing fund" or has not made a "mark-to-market election." If we are a PFIC, all the gains recognized on disposition of our common shares would be treated as an excess distribution. In the case of an actual distribution, such distribution from us would be treated as an excess distribution only to the extent the total of actual distributions during a taxable year received by the U.S. Holder exceeds 125% of the average of actual distributions received in the three preceding taxable years, or, if shorter, the U.S. Holder's holding period for our common shares. In these circumstances, the tax and interest charges will be determined by allocating such distributions ratably over the U.S. Holder's holding period for the common shares. The amount allocated to the current taxable year (i.e. the year in which the gain is recognized or the distribution occurs) and any year prior to the first taxable year in which we are a PFIC would be taxed as ordinary income earned in the current taxable year, and the amount allocated to each of the other years in the holding period would be subject to a special tax and interest charge.

The amount allocated to prior taxable years in which we are a PFIC will be taxed at the highest marginal rates in effect for individuals or corporations as applicable to ordinary income for each such taxable year, and an interest charge, generally applicable to underpayments of tax, will be added to the tax. If we are a PFIC at any time when a U.S. Holder holds our common shares, we will generally continue to be treated as a PFIC with respect to the U.S. Holder for all succeeding years during which the U.S. Holder holds our common shares even if we cease to meet the PFIC gross income test or asset test. However, if we cease to meet these tests, a U.S. Holder can avoid the continuing impact of the PFIC rules by making a special election, a "Purging Election", to recognize gain in the manner described above as if our common shares had been sold on the last day of the last taxable year during which we were a PFIC. In addition, for a U.S. Holder making such an election, a new holding period would be deemed to begin for our common shares for purposes of the PFIC rules. After the Purging Election, the common shares with respect to which the Purging Election was made will not be treated as shares in a PFIC unless we subsequently become a PFIC.

The tax consequences that would apply if we were a PFIC would be different from those described above if a U.S. Holder were able to make a valid "qualified electing fund," or QEF, election. For each year that we meet the PFIC gross income test 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, as determined under U.S. federal income tax principles. The U.S. Holder's adjusted tax basis in our common shares would be increased by the amount of such inclusions. An actual distribution to the U.S. Holder out of such income generally would not be treated as a dividend and would decrease the U.S. Holder's adjusted tax basis in our common shares. A U.S. Holder that has made a timely and effective QEF election generally may receive a distribution tax-free to the extent that such distribution represents "earnings and profits" that were previously included in income by the U.S. Holder because of such election and will adjust such U.S. Holder's tax basis in our common shares to reflect the amount allowed as a tax-free distribution because of such QEF election. Gain realized from the sale of our common shares covered by a QEF election would be taxed as a capital gain.

Generally, a QEF election must be made by the U.S. Holder in a timely filed tax return for the first taxable year in which the U.S. Holder held our common shares that includes the close of our taxable year for which we met the PFIC gross income test or asset test. A QEF election is made on IRS Form 8621. U.S. Holders will be eligible to make QEF elections only if we agree to provide U.S. Holders with the information they will need to comply with the QEF rules. If we believe we are a PFIC in the current or a future tax year, we will provide, upon request, U.S. Holders with the information that is necessary in order for them to make a QEF election and to report their common shares of ordinary earnings and net capital gains for each year for which we are a PFIC.

The tax consequences that would apply if we were a PFIC would also be different from those described above if a timely and valid "mark-to-market" election is made by a U.S. Holder of our common shares. An electing U.S. Holder generally would take into account as ordinary income for each year that we meet the PFIC gross income test or asset test, the excess of the fair market value of our common shares held at the end of the taxable year over the adjusted tax basis of such common shares. The U.S. Holder would also take into account, as an ordinary loss for each year that we meet the PFIC gross income test or asset test, the excess of the adjusted tax basis of such common shares over their fair market value at the end of the taxable year, but only to the extent of the aggregate of the amounts previously included in income as a result of the mark-to-market election. The U.S. Holder's tax basis in our common shares would be adjusted to reflect any income or loss resulting from the mark-to-market election. Any gain from a sale, exchange or other disposition of the common shares in any taxable year in which we are a PFIC would be treated as ordinary income and any loss from such sale, exchange or other disposition would be treated first as ordinary loss to the extent of any net mark-to-market gains previously included in income and thereafter as capital loss. If, after having been a PFIC for one or more taxable years, we cease to be classified as a PFIC, the U.S. Holder would not be required to take into account any latent gain or loss in the manner described above and any realized gain or loss would be classified as a capital gain or loss. A mark-to-market election will not apply to our common shares for any taxable year during which we are not a PFIC, but it will remain in effect with respect to any subsequent taxable year in which we become a PFIC. Such election will not apply to any subsidiary that we own.

A mark-to-market election is available to a U.S. Holder only if the common shares are considered "marketable stock." Generally, stock will be considered marketable stock if it is "regularly traded" on a "qualified exchange" within the meaning of applicable U.S. Treasury regulations. A class of stock is regularly traded during any calendar year during which such class of stock is traded, other than in de minimis quantities, on at least 15 days during each calendar quarter. We expect that our common shares will be marketable stock as long as they remain listed on the Nasdaq Global Market and are regularly traded.

If we are a PFIC in any taxable year during which a U.S. Holder owns the common shares, such U.S. Holder may also suffer adverse tax consequences under the PFIC rules described above with respect to any lower-tier PFIC in which we have a direct or indirect equity interest.

Each U.S. Holder who is a shareholder of a PFIC must file an annual report containing certain information as the U.S. Treasury may require.

U.S. Holders should consult their own tax advisors with respect to their particular circumstances, making any of the elections described above and any related reporting requirements if we are a PFIC in any taxable year.

Net Investment Income Tax

Certain U.S. Holders who are individuals, estates or trusts will be subject to a 3.8% U.S. federal tax on all or a portion of their "net investment income," which includes all or a portion of their dividends (or deemed dividends) on our common shares and net gains from the disposition of our common shares. U.S. Holders that are individuals, estates or trusts should consult their tax advisors regarding the applicability of the U.S. federal tax on net investment income to any of their income or gains in respect of our common shares.

Information Reporting and Backup Withholding

In general, information reporting will apply to dividends in respect of our common shares and the proceeds from the sale or disposition of our common shares that are paid to a U.S. Holder within the U.S. (and in certain cases, outside the U.S.), unless the U.S. Holder is an exempt recipient. Backup withholding may apply to such payments if the U.S. Holder fails to provide a taxpayer identification number or certification of other exempt status or if the U.S. Holder has previously failed to report in full dividend or interest income. If backup withholding applies to a payment, we or our paying agent will deduct the amount of any required withholding directly from such payment and remit it directly to the U.S. Treasury on behalf of the U.S. Holder. Backup withholding is not an additional tax. Any amounts withheld by us or our paying agent under the backup withholding rules will be allowed as a refund or a credit against the U.S. Holder's U.S. federal income tax liability provided the required information is timely furnished to the IRS.

U.S. Holders are urged to consult with their tax advisors regarding the applicable U.S. disclosure and information reporting requirements. In certain circumstances, the failure to comply with disclosure and information reporting requirements will result in an extension of the statute of limitations on the assessment and collection of U.S. federal income taxes applicable to the U.S. Holder.

Disclosure Requirements for Specified Foreign Financial Assets

Certain U.S. Holders (and to the extent provided in IRS guidance, certain non-U.S. Holders) who hold interests in "specified foreign financial assets" (as defined in Section 6038D of the Code) are generally required to file an IRS Form 8938 as part of their U.S. federal income tax returns with information relating to such assets for each taxable year in which the aggregate value of all such assets exceeds $75,000 at any time during the taxable year or $50,000 on the last day of the taxable year (or such higher dollar amount as prescribed by applicable IRS guidance). "Specified foreign financial assets" generally include, among other assets, financial accounts maintained by foreign financial institutions, and our common shares, unless the common shares are held through an account maintained with a financial institution. Substantial penalties may apply to any failure to timely file IRS Form 8938. Additionally, in the event an applicable U.S. Holder (and to the extent provided in IRS guidance, a non-U.S. Holder) that is required to file IRS Form 8938 does not file such form, the statute of limitations on the assessment and collection of U.S. federal income taxes of such holder for the related tax year may not close until three years after the date that the required information is filed. Prospective investors are encouraged to consult with their own tax advisors regarding the possible reporting obligations under these disclosure requirements.

Canadian Federal Income Tax Information

The following summary describes, as of the date hereof, the principal Canadian federal income tax consequences under the Income Tax Act (Canada), or the Canadian Tax Act, generally applicable to a holder, or a Holder, who acquires our common shares and who, for the purposes of the Canadian Tax Act, and at all relevant times, beneficially owns the common shares as capital property, and deals at arm's length with, and is not affiliated with, us or the underwriters. The common shares will generally be considered to be capital property for this purpose unless either the Holder holds (or will hold) such common shares in the course of carrying on a business of trading or dealing in securities, or the Holder has acquired (or will acquire) such common shares in a transaction or transactions considered to be an adventure or concern in the nature of trade.

This summary is not applicable to: (a) a Holder that is a "financial institution," as defined in the Canadian Tax Act for purposes of the mark-to-market rules; (b) a Holder, an interest in which is or would be a "tax shelter investment" as defined in the Canadian Tax Act; (c) a Holder that is a "specified financial institution" as defined in the Canadian Tax Act; (d) a Holder that is a corporation that has elected in the prescribed form and manner and has otherwise met the requirements to use functional currency tax reporting as set out in the Canadian Tax Act; (e) a Holder that is a corporation resident in Canada, or a corporation that does not deal at arm's length (for purposes of the Canadian Tax Act) with a corporation resident in Canada, and is, or becomes, controlled by a non-resident person, or group of non-resident persons not dealing with each other at arm's length, for the purposes of the "foreign affiliate dumping" rules in section 212.3 of the Canadian Tax Act; or (f) a Holder that, with respect to the common shares, has or that has entered into a "synthetic disposition arrangement " or a "derivative forward agreement" as those terms are defined in the Canadian Tax Act. In addition, this summary does not address the deductibility of interest by a Holder of common shares that has borrowed money or otherwise incurred debt in connection with the acquisition of common shares. Any such Holder to which this summary does not apply should consult its own tax advisor.

This summary is based upon the current provisions of the Canadian Tax Act, the regulations adopted thereunder, or the Canadian Tax Regulations, and counsel's understanding of the current published administrative and assessing policies and practices of the Canada Revenue Agency. The summary also takes into account all specific proposals to amend the Canadian Tax Act and the Canadian Tax Regulations that have been publicly announced by or on behalf of the Minister of Finance (Canada) prior to the date hereof, or the Canadian Tax Proposals, and assumes that all such Canadian Tax Proposals will be enacted in the form proposed. No assurance can be given that the Canadian Tax Proposals will be enacted in the form proposed or at all. This summary does not otherwise take into account or anticipate any changes in law, administrative policy or assessing practice, whether by way of legislative, regulatory, judicial or administrative action or interpretation, nor does it address any provincial, territorial or foreign tax considerations.

This summary is not exhaustive of all possible Canadian federal income tax considerations of acquiring common shares. The summary is of a general nature only and is not intended to be, and should not be construed to be, legal, business, or tax advice to any prospective Holder. Prospective Holders should consult their own tax advisors as to the Canadian federal tax consequences, and the tax consequences of any other jurisdiction, applicable to them having regard to their own particular circumstances.

All amounts calculated in a currency other than the Canadian dollar relating to the acquisition, holding and disposition of the common shares must be converted into Canadian dollars based on the exchange rates determined in accordance with the Canadian Tax Act. The amount of dividends to be included in income, and capital gains and losses realized by a Holder, may be affected by fluctuations in the relevant exchange rates.

Residents of Canada

The following discussion applies to Holders who, for the purposes of the Canadian Tax Act, and at all relevant times, are (or are deemed to be) residents of Canada, or Canadian Resident Holders.

Certain Canadian Resident Holders whose common shares might not otherwise qualify as capital property may, in certain circumstances, treat such common shares and every Canadian security, as defined in the Canadian Tax Act, owned or subsequently acquired by such holder as capital property by making an irrevocable election pursuant to subsection 39(4) of the Canadian Tax Act. Canadian Resident Holders contemplating making a subsection 39(4) election should consult their advisor for advice as to whether the election is available or advisable in their particular circumstances.

Dividends on the Common Shares

Dividends received or deemed to be received on the common shares by a Canadian Resident Holder who is an individual (other than certain trusts) will be included in income and will be subject to the gross-up and dividend tax credit rules normally applicable under the Canadian Tax Act to taxable dividends received from "taxable Canadian corporations" (as defined in the Canadian Tax Act). We may designate all or a portion of such dividends as "eligible dividends" that are entitled to an enhanced gross-up and dividend tax credit regime. There may be limitations on our ability to designate dividends as "eligible dividends." We will notify our shareholders of any such designations at the appropriate times.

Dividends received or deemed to be received on the common shares by a Canadian Resident Holder that is a corporation will be included in its income and will generally be deductible in computing its taxable income. In certain circumstances, however, subsection 55(2) of the Canadian Tax Act may deem a dividend received (or deemed received) by a corporate Canadian Resident Holder to be proceeds of disposition or a capital gain. Corporate Canadian Resident Holders should consult their own tax advisers with respect to the application of these rules to their particular circumstances.

A Canadian Resident Holder that is a "private corporation" or a "subject corporation," each as defined in the Canadian Tax Act, may be liable under Part IV of the Canadian Tax Act to pay a refundable tax on dividends received or deemed to be received on the common shares to the extent such dividends are deductible in computing the Canadian Resident Holder's taxable income.

Dispositions of the Common Shares

A disposition, or a deemed disposition, of a common share (other than to us unless purchased by us in the open market in the manner in which shares are normally purchased by any member of the public in the open market) by a Canadian Resident Holder will generally give rise to a capital gain (or a capital loss) equal to the amount by which the proceeds of disposition of the common share, net of any reasonable costs of disposition, exceed (or are less than) the adjusted cost base of the common share to the Canadian Resident Holder. For this purpose, the adjusted cost base to a Canadian Resident Holder of the common shares will be determined at any time by averaging the cost of such common shares with the adjusted cost base of any other common shares owned by the Canadian Resident Holder as capital property at that time. Such capital gain (or capital loss) will be subject to the treatment described below under "Taxation of Capital Gains and Capital Losses."

Refundable Tax

A Canadian Resident Holder that is throughout the year a "Canadian-controlled private corporation," as defined in the Canadian Tax Act, may be liable to pay a refundable tax on certain investment income, including taxable capital gains (as defined below), but excluding dividends or deemed dividends deductible in computing taxable income.

Taxation of Capital Gains and Capital Losses

Generally, one-half of any capital gain (a taxable capital gain) realized by a Canadian Resident Holder for a taxation year must be included in the Canadian Resident Holder's income in the year. Subject to and in accordance with the provisions of the Canadian Tax Act, a Canadian Resident Holder is required to deduct one-half of any capital loss (an allowable capital loss) realized in the year from taxable capital gains realized in that year, and allowable capital losses in excess of taxable capital gains may be carried back and deducted in any of the three preceding taxation years, or carried forward and deducted in any subsequent year, from net taxable capital gains realized in such years (but not against other income) to the extent and under the circumstances described in the Canadian Tax Act. If the Canadian Resident Holder is a corporation, any such capital loss realized on the sale of a common share may in certain circumstances be reduced by the amount of any dividends which have been received or which are deemed to have been received on the common share. Similar rules may apply where a corporation is a member of a partnership or a beneficiary of a trust that owns shares, directly or indirectly through a partnership or a trust.

Minimum Tax

Individuals, including certain trusts, may be subject to a minimum tax. Generally, dividends received or deemed to be received on the common shares and capital gains realized on the disposition of common shares may result in a Canadian Resident Holder being liable for minimum tax. Canadian Resident Holders should consult with their own tax advisors with respect to the potential application of the minimum tax.

Non-Residents of Canada

The following discussion applies to a Holder who, for the purposes of the Canadian Tax Act, and at all relevant times, is not (and is not deemed to be) resident in Canada and will not use or hold (and will not be deemed to use or hold) the common shares in, or in the course of, carrying on a business or part of a business in Canada, or a Non-Resident of Canada Holder. In addition, this discussion does not apply to a Non-Resident of Canada Holder that carries on or is deemed to carry on, an insurance business in Canada and elsewhere or to an "authorized foreign bank," as defined in the Canadian Tax Act. Such Holders should consult their own tax advisors.

Dividends on the Common Shares

Canadian withholding tax at a rate of 25% (subject to reduction under the provisions of any applicable income tax treaty or convention) will be payable on the gross amount of dividends on the common shares paid or credited, or deemed to be paid or credited, to a Non-Resident of Canada Holder. For instance, the rate of withholding tax applicable to a dividend paid on the common shares to a Non-Resident of Canada Holder who is a resident of the U.S. for purposes of the Canada-United States Tax Convention (1990), or the Convention, beneficially owns the dividend and qualifies for the full benefits of the Convention will generally be reduced to 15% or, if such a Non-Resident of Canada Holder is a corporation that owns at least 10% of our voting shares, to 5%. The Canadian withholding taxes will be deducted directly by us or our paying agent from the amount of the dividend otherwise payable and remitted to the Receiver General of Canada. Not all persons who are residents of the U.S. for purposes of the Convention will qualify for the benefits of the Convention. A Non-Resident of Canada Holder that is a resident of the U.S. is advised to consult its tax advisor in this regard. The rate of withholding tax on dividends may also be reduced under other bilateral income tax treaties or conventions to which Canada is a signatory.

Dispositions of the Common Shares

A Non-Resident of Canada Holder will not be subject to tax under the Canadian Tax Act in respect of any capital gain realized by such Non-Resident of Canada Holder on a disposition, or deemed disposition, of the common shares unless the common shares constitute "taxable Canadian property," as defined in the Canadian Tax Act, of the Non-Resident of Canada Holder at the time of disposition and the holder is not entitled to an exemption under the applicable income tax treaty or convention. As long as the common shares are then listed on a "designated stock exchange" (which currently includes Nasdaq), the common shares generally will not constitute taxable Canadian property of a Non-Resident of Canada Holder, unless (a) at any time during the 60-month period preceding the disposition: (i) one or any combination of (A) the Non-Resident of Canada Holder, (B) persons not dealing at arm's length with such Non-Resident of Canada Holder, and (C) partnerships in which the Non-Resident of Canada Holder or a person described in (B) holds a membership interest directly or indirectly through one or more partnerships, owned 25% or more of our issued shares of any class or series; and (ii) more than 50% of the fair market value of the common shares was derived, directly or indirectly, from one or a combination of real or immoveable property situated in Canada, "Canadian resource properties" (as such term is defined in the Canadian Tax Act), "timber resource properties" (as such term is defined in the Canadian Tax Act), or options in respect of interests in, or for civil law rights in, any such properties whether or not the property exists, or (b) the common shares are otherwise deemed to be taxable Canadian property. If the common shares are considered taxable Canadian property to a Non-Resident of Canada Holder, an applicable income tax treaty or convention may in certain circumstances exempt that Non-Resident of Canada Holder from tax under the Canadian Tax Act in respect of the disposition or deemed disposition of the common shares. Non-Resident of Canada Holders whose common shares are, or may be, taxable Canadian property should consult their own tax advisors for advice having regard to their particular circumstances.

As long as the common shares are listed at the time of their disposition or deemed disposition on a "recognized stock exchange" (which currently includes Nasdaq), as defined in the Canadian Tax Act, a Non-Resident of Canada Holder who disposes of common shares that are taxable Canadian property will not be required to satisfy the obligations imposed under section 116 of the Canadian Tax Act and, as such, the purchaser of such shares will not be required to withhold any amount on the purchase price paid. An exemption from such requirements may also be available in respect of such disposition if the common shares are "treaty-exempt property," as defined in the Canadian Tax Act.

In the event that a common share constitutes taxable Canadian property of a Non-Resident of Canada Holder and any capital gain that would be realized on the disposition or deemed disposition thereof is not exempt from tax under the Canadian Tax Act pursuant to an applicable income tax convention or treaty, the income tax consequences discussed under "Residents of Canada - Dispositions of the Common Shares" and "Residents of Canada - Taxation of Capital Gains and Capital Losses" will generally apply to the Non-Resident of Canada Holder but any such Holder should consult its own tax advisor in this regard.

UNDERWRITING

Subject to the terms and conditions set forth in the underwriting agreement, dated October , 2021, among us and Jefferies, SVB Leerink LLC, or SVB Leerink, and Stifel, as the representatives of the underwriters named below and joint book-running managers of this offering, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us the respective number of common shares shown opposite its name below:

UNDERWRITERS	Number of Common Shares
Jefferies LLC	
SVB Leerink LLC	
Stifel, Nicolaus & Company, Incorporated	
RBC Capital Markets, LLC	
Total	

The underwriting agreement provides that the obligations of the several underwriters are subject to certain conditions precedent, such as the receipt by the underwriters of officers' certificates and legal opinions and approval of certain legal matters by their counsel and may be terminated at their discretion upon the occurrence of certain stated events. The underwriting agreement provides that the underwriters will purchase all of the common shares if any of them are purchased, other than those common shares covered by the option to purchase additional common shares described below. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the non-defaulting underwriters may be increased or the underwriting agreement may be terminated. We have agreed to indemnify the underwriters and certain of their controlling persons against certain liabilities, including liabilities under the Securities Act of 1933, as amended, or the Securities Act. We have also agreed to contribute to payments that the underwriters may be required to make in respect of those liabilities.

The underwriters have advised us that, following the completion of this offering, they currently intend to make a market in our common shares as permitted by applicable laws and regulations. However, the underwriters are not obligated to do so, and the underwriters may discontinue any market-making activities at any time without notice in their sole discretion. Accordingly, no assurance can be given as to the liquidity of the trading market for our common shares, that you will be able to sell any of the common shares held by you at a particular time or that the prices that you receive when you sell will be favorable.

The underwriters are offering the common shares subject to their acceptance of the common shares from us and subject to prior sale. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part. In addition, the underwriters have advised us that they do not intend to confirm sales to any account over which they exercise discretionary authority.

Commission and Expenses

The underwriters have advised us that they propose to offer the common shares to the public at the public offering price set forth on the cover page of this prospectus supplement and to certain dealers, which may include the underwriters, at that price less a concession not in excess of $ per common share. After the offering, the public offering price, concession and reallowance to dealers may be reduced by the representatives. No such reduction will change the amount of proceeds to be received by us as set forth on the cover page of this prospectus supplement.

The following table shows the public offering price, the underwriting discounts and commissions that we are to pay the underwriters and the proceeds, before expenses, to us in connection with this offering. Such amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional common shares.

	Per Share		Total	
	Without Option to Purchase Additional Common Shares	With Option to Purchase Additional Common Shares	Without Option to Purchase Additional Common Shares	With Option to Purchase Additional Common Shares
Public offering price	$	$	$	$
Underwriting discounts and commissions, paid by us	$	$	$	$
Proceeds to us, before expenses	$	$	$	$

We estimate expenses payable by us in connection with this offering, other than the underwriting discounts and commissions referred to above, will be approximately $325,000. We have also agreed to reimburse the underwriters for up to $20,000 of expenses related to the review of this offering by the Financial Industry Regulatory Authority, Inc.

Listing

Our common shares are listed on the Nasdaq Global Market, or Nasdaq, under the trading symbol "XENE". We have applied to have the common shares that we are issuing and selling in this offering listed on Nasdaq. Listing will be subject to us fulfilling all the listing requirements of Nasdaq.

Option to Purchase Additional Common Shares

We expect to grant the underwriters an option, exercisable for 30 days from the date of this prospectus supplement, to purchase, from time to time, in whole or in part, up to an aggregate of common shares from us at the public offering price set forth on the cover page of this prospectus supplement, less underwriting discounts and commissions. If the underwriters exercise this option, each underwriter will be obligated, subject to specified conditions, to purchase a number of additional common shares proportionate to that underwriter's initial purchase commitment as indicated in the table above. This option may be exercised only if the underwriters sell more common shares than the total number set forth on the cover page of this prospectus supplement.

No Sales of Similar Securities

We and our executive officers and directors have agreed, subject to specified exceptions, not to directly or indirectly:

- sell, offer, contract or grant any option to sell (including any short sale), lend, pledge, transfer, establish or increase an open "put equivalent position" or liquidate or decrease a "call equivalent position" within the meaning of Rule 16a-1(h) and Rule 16a-1(b) under the Exchange Act, or
- otherwise dispose of any common shares, options or warrants to acquire common shares, or securities exchangeable or exercisable for or convertible into common shares currently or hereafter owned either of record or beneficially, or
- enter into any swap, hedge or similar arrangement or agreement that transfers, in whole or in part, the economic risk of ownership of common shares, or of options or warrants to acquire common shares, or securities or rights exchangeable or exercisable for or convertible into common shares, or
- make any demand for, or exercise any right with respect to, the registration under the Securities Act of the offer and sale of any common shares, or of options or warrants to acquire common shares, or securities or rights exchangeable or exercisable for or convertible into common shares, or cause to be filed a registration statement, prospectus or prospectus supplement (or an amendment or supplement thereto) with respect to any such registration, or
- publicly announce an intention to do any of the foregoing for a period of 90 days, with respect to us, and 30 days, with respect to our executive officers and directors, after the date of this prospectus supplement without the prior written consent of Jefferies, SVB Leerink and Stifel.

The foregoing restriction terminates after the close of trading of our common shares on and including the 90th day, with respect to us, and the 30th day, with respect to our executive officers and directors, after the date of this prospectus supplement and shall not apply to our issuance during the 90-day restricted period of a number of common shares not greater than 5% of the total number of common shares outstanding to one or more counterparties in connection with the consummation of any strategic transaction.

Jefferies, SVB Leerink and Stifel may, in their sole discretion and at any time or from time to time before the termination of the 90-day and 30-day period, release all or any portion of the securities subject to lock-up agreements. There are no existing agreements between the underwriters and any of our shareholders who will execute a lock-up agreement, providing consent to the sale of common shares prior to the expiration of the lock-up period.

Stabilization

The underwriters have advised us that, pursuant to Regulation M under the Exchange Act, certain persons participating in the offering may engage in short sale transactions, stabilizing transactions, syndicate covering transactions or the imposition of penalty bids in connection with this offering. These activities may have the effect of stabilizing or maintaining the market price of our common shares at a level above that which might otherwise prevail in the open market. Establishing short sales positions may involve either “covered” short sales or “naked” short sales.

“Covered” short sales are sales made in an amount not greater than the underwriters’ option to purchase additional common shares in this offering. The underwriters may close out any covered short position by either exercising their option to purchase additional common shares or purchasing common shares in the open market. In determining the source of common shares to close out the covered short position, the underwriters will consider, among other things, the price of common shares available for purchase in the open market as compared to the price at which they may purchase common shares through the option to purchase additional common shares.

“Naked” short sales are sales in excess of the option to purchase additional common shares. The underwriters must close out any naked short position by purchasing common shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common shares in the open market after pricing that could adversely affect investors who purchase in this offering.

A stabilizing bid is a bid for the purchase of common shares on behalf of the underwriters for the purpose of fixing or maintaining the price of the common shares. A syndicate covering transaction is the bid for or the purchase of common shares on behalf of the underwriters to reduce a short position incurred by the underwriters in connection with the offering. Similar to other purchase transactions, an underwriter’s purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common shares or preventing or retarding a decline in the market price of our common shares. As a result, the price of our common shares may be higher than the price that might otherwise exist in the open market. A penalty bid is an arrangement permitting the underwriters to reclaim the selling concession otherwise accruing to a syndicate member in connection with the offering if the common shares originally sold by such syndicate member are purchased in a syndicate covering transaction and therefore have not been effectively placed by such syndicate member.

Neither we nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common shares. The underwriters are not obligated to engage in these activities and, if commenced, any of the activities may be discontinued at any time.

The underwriters may also engage in passive market making transactions in our common shares on the Nasdaq Global Market in accordance with Rule 103 of Regulation M during a period before the commencement of offers or sales of common shares in this offering and extending through the completion of distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker’s bid, that bid must then be lowered when specified purchase limits are exceeded.

Electronic Distribution

This prospectus supplement and the accompanying prospectus in electronic format may be made available by e-mail or on the websites or through online services maintained by one or more of the underwriters or their affiliates. In those cases, prospective investors may view offering terms online and may be allowed to place orders online. The underwriters may agree with us to allocate a specific number of common shares for sale to online brokerage account holders. Any such allocation for online distributions will be made by the underwriters on the same basis as other allocations. Other than this prospectus supplement and the accompanying prospectus in electronic format, the information on the underwriters’ websites and any information contained in any other website maintained by any of the underwriters is not part of this prospectus supplement or the accompanying prospectus, has not been approved and/or endorsed by us or the underwriters and should not be relied upon by investors.

Other Activities and Relationships

The underwriters and certain of their respective affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. The underwriters and certain of their respective affiliates have, from time to time, performed, and may in the future perform, various commercial and investment banking and financial advisory services for us and our affiliates, for which they received or will receive customary fees and expenses. For example, Jefferies and Stifel have acted as the sales agents under our "at-the-market" equity offering sales agreements, most recently as of August 2020, pursuant to which we may offer and sell from time to time up to $100.0 million of our common shares through them. As of June 30, 2021, we had sold an aggregate of 733,000 common shares for proceeds of $10.7 million, net of commissions paid, but excluding estimated transaction expenses. Jefferies and Stifel also acted as underwriters in our underwritten public offerings in January 2020 and March 2021.

In the ordinary course of their various business activities, the underwriters and certain of their respective affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers, and such investment and securities activities may involve securities and/or instruments issued by us and our affiliates. If the underwriters or their respective affiliates have a lending relationship with us, they routinely hedge their credit exposure to us consistent with their customary risk management policies. The underwriters and their respective affiliates may hedge such exposure by entering into transactions which consist of either the purchase of credit default swaps or the creation of short positions in our securities or the securities of our affiliates, including potentially the common shares offered hereby. Any such short positions could adversely affect future trading prices of the common shares offered hereby. The underwriters and certain of their respective affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Disclaimers About Non-U.S. Jurisdictions

Canada

The securities which are the subject of the offering contemplated by this prospectus supplement and the accompanying prospectus are not being offered or sold, directly or indirectly, in Canada or to any resident of Canada, and there has not been any advertisement or solicitation in furtherance of such offering of securities in Canada. Each underwriter has agreed that it will not, directly or indirectly, offer or sell any of the securities which are the subject of the offering contemplated by this prospectus supplement and the accompanying prospectus in Canada or to any resident of Canada, and that any selling agreement or similar agreement with respect to such securities will require each dealer or other party thereto to make an agreement to the same effect.

Australia

Neither this prospectus supplement nor the accompanying prospectus is a disclosure document for the purposes of Australia's Corporations Act 2001 (Cth) of Australia, or Corporations Act, or has been lodged with the Australian Securities & Investments Commission, and each is only directed to the categories of exempt persons set out below. Accordingly, if you receive this prospectus supplement and the accompanying prospectus in Australia, you confirm and warrant that you are either:

- a "sophisticated investor" under section 708(8)(a) or (b) of the Corporations Act;
- a "sophisticated investor" under section 708(8)(c) or (d) of the Corporations Act and that you have provided an accountant's certificate to the company which complies with the requirements of section 708(8)(c)(i) or (ii) of the Corporations Act and related regulations before the offer has been made;
- a person associated with the company under Section 708(12) of the Corporations Act; or
- a "professional investor" within the meaning of section 708(11)(a) or (b) of the Corporations Act.

To the extent that you are unable to confirm or warrant that you are an exempt sophisticated investor, associated person or professional investor under the Corporations Act, any offer made to you under this prospectus supplement and the accompanying prospectus is void and incapable of acceptance.

You warrant and agree that you will not offer any of the securities issued to you pursuant to this prospectus supplement and the accompanying prospectus for resale in Australia within 12 months of those securities being issued unless any such resale offer is exempt from the requirement to issue a disclosure document under section 708 of the Corporations Act.

European Economic Area

In relation to each Member State of the European Economic Area (each a Relevant State), no securities have been offered or will be offered pursuant to the offering to the public in that Relevant State prior to the publication of a prospectus in relation to the securities which has been approved by the competent authority in that Relevant State or, where appropriate, approved in another Relevant State and notified to the competent authority in that Relevant State, all in accordance with the Prospectus Regulation, except that the securities may be offered to the public in that Relevant State at any time:

(a) to any legal entity which is a qualified investor as defined under Article 2 of the Prospectus Regulation;

(b) to fewer than 150 natural or legal persons (other than qualified investors as defined under Article 2 of the Prospectus Regulation), subject to obtaining the prior consent of representatives for any such offer; or

(c) in any other circumstances falling within Article 1(4) of the Prospectus Regulation,

provided that no such offer of the securities shall require us or any of the representatives to publish a prospectus pursuant to Article 3 of the Prospectus Regulation or supplement a prospectus pursuant to Article 23 of the Prospectus Regulation.

For the purposes of this provision, the expression an “offer to the public” in relation to the securities in any Relevant State means the communication in any form and by any means of sufficient information on the terms of the offer and any securities to be offered so as to enable an investor to decide to purchase or subscribe for any common shares, and the expression “Prospectus Regulation” means Regulation (EU) 2017/1129.

France

Neither this prospectus supplement, the accompanying prospectus nor any other offering material relating to the securities described in this prospectus supplement or the accompanying prospectus has been submitted to the clearance procedures of the Autorité des Marchés Financiers or of the competent authority of another member state of the European Economic Area and notified to the Autorité des Marchés Financiers. The securities have not been offered or sold and will not be offered or sold, directly or indirectly, to the public in France. Neither this prospectus supplement nor any other offering material relating to the securities has been or will be:

- released, issued, distributed or caused to be released, issued or distributed to the public in France; or
- used in connection with any offer for subscription or sale of the securities to the public in France.
- Such offers, sales and distributions will be made in France only:
- to qualified investors (investisseurs qualifiés) and/or to a restricted circle of investors (cercle restreint d'investisseurs), in each case investing for their own account, all as defined in, and in accordance with articles L.411-2, D.411-1, D.411-2, D.734-1, D.744-1, D.754-1 and D.764-1 of the French Code monétaire et financier;
- to investment services providers authorized to engage in portfolio management on behalf of third parties; or
- in a transaction that, in accordance with article L.411-2-II-1°-or-2°-or 3° of the French Code monétaire et financier and article 211-2 of the General Regulations (Règlement Général) of the Autorité des Marchés Financiers, does not constitute a public offer (appel public à l'épargne).

The securities may be resold directly or indirectly, only in compliance with articles L.411-1, L.411-2, L.412-1 and L.621-8 through L.621-8-3 of the French Code monétaire et financier.

Hong Kong

No securities have been offered or sold, and no securities may be offered or sold, in Hong Kong, by means of any document, other than to persons whose ordinary business is to buy or sell shares or debentures, whether as principal or agent; or to “professional investors” as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong, or SFO, and any rules made under that Ordinance; or in other circumstances which do not result in the document being a “prospectus” as defined in the Companies Ordinance (Cap. 32) of Hong Kong, or CO, or which do not constitute an offer or invitation to the public for the purpose of the CO or the SFO. No document, invitation or advertisement relating to the securities has been issued or may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere),

which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted under the securities laws of Hong Kong) other than with respect to securities which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" as defined in the SFO and any rules made under that Ordinance.

Neither this prospectus supplement nor the accompanying prospectus have been registered with the Registrar of Companies in Hong Kong. Accordingly, this prospectus supplement and the accompanying prospectus may not be issued, circulated or distributed in Hong Kong, and the securities may not be offered for subscription to members of the public in Hong Kong. Each person acquiring the securities will be required, and is deemed by the acquisition of the securities, to confirm that he is aware of the restriction on offers of the securities described in this prospectus supplement and the accompanying prospectus and the relevant offering documents and that he is not acquiring, and has not been offered any securities in circumstances that contravene any such restrictions.

Israel

This document does not constitute a prospectus under the Israeli Securities Law, 5728-1968, or the Securities Law, and has not been filed with or approved by the Israel Securities Authority. In Israel, this prospectus supplement is being distributed only to, and is directed only at, and any offer of the securities is directed only at, (i) a limited number of persons in accordance with the Israeli Securities Law and (ii) investors listed in the first addendum, or the Addendum, to the Israeli Securities Law, consisting primarily of joint investment in trust funds, provident funds, insurance companies, banks, portfolio managers, investment advisors, members of the Tel Aviv Stock Exchange, underwriters, venture capital funds, entities with equity in excess of NIS 50 million and "qualified individuals," each as defined in the Addendum (as it may be amended from time to time), collectively referred to as qualified investors (in each case, purchasing for their own account or, where permitted under the Addendum, for the accounts of their clients who are investors listed in the Addendum). Qualified investors are required to submit written confirmation that they fall within the scope of the Addendum, are aware of the meaning of same and agree to it.

Japan

The offering has not been and will not be registered under the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948 of Japan, as amended), or FIEL, and the underwriters will not offer or sell any securities, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the FIEL and any other applicable laws, regulations and ministerial guidelines of Japan.

Singapore

Neither this prospectus supplement nor the accompanying prospectus has been and neither will be lodged or registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus supplement and the accompanying prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the securities may not be circulated or distributed, nor may the securities be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore, or the SFA, (ii) to a relevant person pursuant to Section 275(1), or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275, of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the securities are subscribed or purchased under Section 275 of the SFA by a relevant person, which is:

(a) a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or

(b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor,

securities (as defined in Section 239(1) of the SFA) of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the securities pursuant to an offer made under Section 275 of the SFA except:

(i) to an institutional investor or to a relevant person defined in Section 275(2) of the SFA, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;

(ii) where no consideration is or will be given for the transfer;

(iii) where the transfer is by operation of law;

(iv) as specified in Section 276(7) of the SFA; or

(v) as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore.

Solely for the purposes of its obligations pursuant to Section 309B of the SFA, we have determined, and hereby notify all relevant persons (as defined in the CMP Regulations 2018), that the securities are "prescribed capital markets products" (as defined in the CMP Regulations 2018) and Excluded Investment Products (as defined in MAS Notice SFA 04-N12: Notice on the Sale of Investment Products and MAS Notice FAA-N16: Notice on Recommendations on Investment Products).

Switzerland

The securities may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange, or SIX, or on any other stock exchange or regulated trading facility in Switzerland. This prospectus supplement and the accompanying prospectus has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this prospectus supplement, the accompanying prospectus nor any other offering or marketing material relating to the securities or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this prospectus supplement, the accompanying prospectus nor any other offering or marketing material relating to the offering, the company or the securities have been or will be filed with or approved by any Swiss regulatory authority. In particular, this prospectus supplement and the accompanying prospectus will not be filed with, and the offer of securities will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA, and the offer of securities has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes, or CISA. The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of securities.

United Arab Emirates

The securities have not been, and are not being, publicly offered, sold, promoted or advertised in the United Arab Emirates (including the Dubai International Financial Centre) other than in compliance with the laws of the United Arab Emirates (and the Dubai International Financial Centre) governing the issue, offering and sale of securities. Further, this prospectus supplement does not constitute a public offer of securities in the United Arab Emirates (including the Dubai International Financial Centre) and is not intended to be a public offer. Neither this prospectus supplement nor the accompanying prospectus has been approved by or filed with the Central Bank of the United Arab Emirates, the Securities and Commodities Authority or the Dubai Financial Services Authority.

United Kingdom

No securities have been offered or will be offered pursuant to the offering to the public in the United Kingdom prior to the publication of a prospectus in relation to the securities which has been approved by the Financial Conduct Authority, except that the securities may be offered to the public in the United Kingdom at any time:

(a) to any legal entity which is a qualified investor as defined under Article 2 of the UK Prospectus Regulation;

(b) to fewer than 150 natural or legal persons (other than qualified investors as defined under Article 2 of the UK Prospectus Regulation), subject to obtaining the prior consent of the representatives for any such offer; or

(c) in any other circumstances falling within Section 86 of the FSMA.

provided that no such offer of the securities shall require the Issuer or any Manager to publish a prospectus pursuant to Section 85 of the FSMA or supplement a prospectus pursuant to Article 23 of the UK Prospectus Regulation. For the purposes of this provision, the expression an "offer to the public" in relation to the securities in the United Kingdom means the communication in any form and by any means of sufficient information on the terms of the offer and any securities to be offered so as to enable an investor to decide to purchase or subscribe for any securities and the expression "UK Prospectus Regulation" means Regulation (EU) 2017/1129 as it forms part of domestic law by virtue of the European Union (Withdrawal) Act 2018.

We are being represented by Wilson Sonsini Goodrich & Rosati, Professional Corporation, Palo Alto, California. The validity of the common shares being offered by this prospectus supplement and legal matters relating to Canadian laws will be passed upon for us by Blake, Cassels & Graydon LLP, Vancouver, British Columbia. The underwriters are being represented by Cooley LLP, San Francisco, California. Stikeman Elliott LLP, Vancouver, British Columbia, is acting as Canadian counsel to the underwriters.

EXPERTS

The consolidated financial statements of Xenon Pharmaceuticals Inc. as of December 31, 2020 and 2019, and for each of the years in the two-year period ended December 31, 2020, have been incorporated by reference herein in reliance upon the report of KPMG LLP, independent registered public accounting firm, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and other reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at http://www.sec.gov. Our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K, including any amendments to those reports, and other information that we file with or furnish to the SEC pursuant to Section 13(a) or 15(d) of the Exchange Act can also be accessed free of charge through the Internet. These filings will be available as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. You may also access these filings through our website at www.xenon-pharma.com.

INFORMATION INCORPORATED BY REFERENCE

The SEC allows us to incorporate by reference into this prospectus supplement the information we file with it, which means that we can disclose important information by referring you to those documents. The information incorporated by reference is considered to be a part of this prospectus supplement, and information that we file later with the SEC will automatically update and supersede information contained in this prospectus supplement. We incorporate by reference the documents listed below that we have previously filed with the SEC (excluding any portions of any Form 8-K that are not deemed "filed" pursuant to the General Instructions of Form 8-K):

- our Annual Report on Form 10-K for the fiscal year ended December 31, 2020, filed with the SEC on March 1, 2021;
- the portions of our Definitive Proxy Statement on Schedule 14A (other than information furnished rather than filed) that are incorporated by reference into our Annual Report on Form 10-K, filed with the SEC on April 28, 2021;
- our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2021 and June 30, 2021, filed with the SEC on May 11, 2021, and August 11, 2021, respectively;
- our Current Reports on Form 8-K filed with the SEC on January 14, 2021, January 14, 2021 (amendment), March 1, 2021 (only as to Item 5.02), March 10, 2021, March 12, 2021, June 3, 2021, August 23, 2021, September 8, 2021 and October 4, 2021; and
- the description of our common shares contained in our Registration Statement on Form 8-A as filed with the SEC on October 10, 2014 pursuant to Section 12(b) of the Exchange Act, including any amendment or report filed for the purpose of updating such description.

We also incorporate by reference into this prospectus supplement additional documents (other than current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits on such form that are related to such items) that we may file with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act prior to the completion or termination of the offering of the securities described in this prospectus, including all such documents we may file with the SEC after the date of the initial registration statement and prior to the effectiveness of the registration statement, but excluding any information deemed furnished and not filed with the SEC. Any statements contained in a previously filed document incorporated by reference into this prospectus supplement is deemed to be modified or superseded for purposes of this prospectus supplement to the extent that a statement contained in this prospectus, or in a subsequently filed document also incorporated by reference herein, modifies or supersedes that statement.

You should rely only on the information incorporated by reference or provided in this prospectus supplement. We have not authorized anyone else to provide you with different information. You should not assume that the information in this prospectus supplement is accurate as of any date other than the date of this prospectus supplement or the date of the documents incorporated by reference in this prospectus supplement.

We will provide to each person, including any beneficial owner, to whom this prospectus supplement is delivered, upon written or oral request, at no cost to the requester, a copy of any and all of the information that is incorporated by reference in this prospectus supplement.

Requests for such documents should be directed to:

Xenon Pharmaceuticals Inc.
Attn: Investor Relations
200 - 3650 Gilmore Way
Burnaby, BC V5G 4W8
Canada
(604) 484-3353

You may also access the documents incorporated by reference in this prospectus supplement through our website at *www.xenon-pharma.com*. Except for the specific incorporated documents listed above, no information available on or through our website shall be deemed to be incorporated in this prospectus supplement or the registration statement of which it forms a part.

PROSPECTUS

Xenon Pharmaceuticals Inc.

Common Shares
Preferred Shares
Warrants
Units

We may offer and sell from time to time, in one or more series or issuances and on terms that we will determine at the time of the offering, any combination of the securities described in this prospectus, either individually or as units comprised of one or more of the other classes of securities.

This prospectus provides a general description of the securities we may offer. Each time we offer and sell securities, we will provide specific terms of the securities offered in a supplement to this prospectus. We may also authorize one or more free writing prospectuses to be provided to you in connection with these offerings. A prospectus supplement and any free writing prospectus may also add, update or change information contained in this prospectus. You should carefully read this prospectus, the applicable prospectus supplement, and any related free writing prospectus, as well as the documents incorporated or deemed to be incorporated by reference in this prospectus, before you invest in any of our securities offered hereby.

This prospectus may not be used to consummate a sale of any securities unless it is accompanied by a prospectus supplement.

We may offer and sell the securities described in this prospectus and any prospectus supplement to or through one or more underwriters, broker-dealers, agents, directly to purchasers, or through any other means described in this prospectus under "Plan of Distribution" and in supplements to this prospectus in connection with a particular offering of securities. If any underwriters, dealers or agents are involved in the sale of any of these securities, their names and any applicable purchase price, fee, commission or discount arrangement between or among them will be set forth, or will be calculable from the information set forth, in the applicable prospectus supplement. The price to the public of such securities and the net proceeds we expect to receive from such sale will also be set forth in a prospectus supplement.

Our common shares are listed on The Nasdaq Global Market, or Nasdaq, under the symbol "XENE." On October 1, 2021, the last reported sale price of our common shares on Nasdaq was $15.60. There is currently no market for the other securities we may offer; however, we will provide information in any applicable prospectus supplement regarding any listing of securities other than our common shares on any securities exchange.

INVESTING IN OUR SECURITIES INVOLVES SIGNIFICANT RISKS. PLEASE CAREFULLY READ THE INFORMATION UNDER THE HEADINGS "RISK FACTORS" BEGINNING ON PAGE 4 OF THIS PROSPECTUS AND "ITEM 1A – RISK FACTORS" OF OUR MOST RECENT REPORT ON FORM 10-K OR 10-Q THAT IS INCORPORATED BY REFERENCE IN THIS PROSPECTUS BEFORE YOU INVEST IN OUR SECURITIES.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus is October 4, 2021.

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ABOUT THIS PROSPECTUS

This prospectus is part of an automatic shelf registration statement that we filed with the Securities and Exchange Commission, or the SEC, as a "well-known seasoned issuer" as defined in Rule 405 under the Securities Act of 1933, as amended, or the Securities Act. Under this shelf registration process, we may, from time to time, sell any combination of the securities described in this prospectus in one or more offerings. There is no limit on the aggregate amount of the securities that we may offer pursuant to the registration statement of which this prospectus forms a part. This prospectus provides you with a general description of the securities we may offer.

Each time we sell securities, we will provide one or more prospectus supplements that will contain specific information about the terms of the offering. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to these offerings, hereinafter referred to as an issuer free writing prospectus. The prospectus supplement and any issuer free writing prospectus may also add to, update or change information contained in the prospectus and, accordingly, to the extent inconsistent, information in this prospectus is superseded by the information in the prospectus supplement or the issuer free writing prospectus, as applicable. You should carefully read this prospectus, any prospectus supplement, and any issuer free writing prospectus, together with the additional information described under the heading "Information Incorporated by Reference."

The prospectus supplement to be attached to the front of this prospectus may describe, as applicable, the terms of the securities offered; the initial price to the public; the price paid for the securities; net proceeds; and the other specific terms related to the offering of the securities.

THIS PROSPECTUS MAY NOT BE USED TO OFFER AND SELL SECURITIES UNLESS IT IS ACCOMPANIED BY A PROSPECTUS SUPPLEMENT.

You should only rely on the information contained or incorporated by reference in this prospectus and any prospectus supplement or issuer free writing prospectus relating to a particular offering. No person has been authorized to give any information or make any representations in connection with this offering other than those contained or incorporated by reference in this prospectus, any accompanying prospectus supplement and any related issuer free writing prospectus in connection with the offering described herein and therein, and, if given or made, such information or representations must not be relied upon as having been authorized by us. Neither this prospectus nor any prospectus supplement nor any related issuer free writing prospectus shall constitute an offer to sell or a solicitation of an offer to buy offered securities in any jurisdiction in which it is unlawful for such person to make such an offering or solicitation. This prospectus does not contain all of the information included in the registration statement. For a more complete understanding of the offering of the securities, you should refer to the registration statement, including its exhibits.

You should read the entire prospectus and any prospectus supplement and any related issuer free writing prospectus, as well as the documents incorporated by reference into this prospectus or any prospectus supplement or any related issuer free writing prospectus, before making an investment decision. Neither the delivery of this prospectus or any prospectus supplement or any issuer free writing prospectus nor any sale made hereunder shall under any circumstances imply that the information contained or incorporated by reference herein or in any prospectus supplement or issuer free writing prospectus is correct as of any date subsequent to the date hereof or of such prospectus supplement or issuer free writing prospectus, as applicable. You should assume that the information appearing in this prospectus, any prospectus supplement, any issuer free writing prospectus, or any document incorporated by reference is accurate only as of the date of the applicable documents, regardless of the time of delivery of this prospectus or any sale of securities. Our business, financial condition, results of operations and prospects may have changed since that date.

PROSPECTUS SUMMARY

This summary highlights selected information that is presented in greater detail elsewhere, or incorporated by reference, in this prospectus. It does not contain all of the information that may be important to you and your investment decision. Before investing in our securities, you should carefully read this entire prospectus, including the matters set forth under the section of this prospectus captioned "Risk Factors" and the financial statements and related notes and other information that we incorporate by reference herein, including our Annual Report on Form 10-K and our Quarterly Reports on Form 10-Q. Unless the context indicates otherwise, references in this prospectus to "Xenon Pharmaceuticals Inc.," "we," "our" and "us" refer, collectively, to Xenon Pharmaceuticals Inc. and its wholly-owned subsidiary.

Overview

We are a clinical stage biopharmaceutical company committed to developing innovative therapeutics to improve the lives of patients with neurological disorders. We are advancing a novel product pipeline of neurology-focused therapies to address areas of high unmet medical need, with a focus on epilepsy. In addition to our proprietary product candidates, we also have partnered programs with several pharmaceutical companies, including Neurocrine Biosciences, Inc., or Neurocrine Biosciences, and Flexion Therapeutics, Inc., or Flexion.

Our proprietary product candidates include:

- XEN1101, a differentiated Kv7 potassium channel modulator being developed for the treatment of epilepsy, major depressive disorder and potentially other neurological disorders.
- XEN496, a Kv7 potassium channel modulator, is a proprietary pediatric formulation of the active ingredient ezogabine being developed for the treatment of KCNQ2 developmental and epileptic encephalopathy.
- XEN007 (active ingredient flunarizine) is a CNS-acting Cav2.1 and T-type calcium channel modulator that is being studied in treatment-resistant absence seizures and potentially other neurological disorders.

Our clinical stage partnered programs include:

- Our ongoing collaboration 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 with potential in SCN8A developmental and epileptic encephalopathy and other forms of epilepsy.
- Flexion acquired the global rights to develop and commercialize XEN402, a Nav1.7 inhibitor also known as funapide. Flexion's FX301 consists of XEN402 formulated for extended release from a thermosensitive hydrogel. The initial development of FX301 is intended to support administration as a peripheral nerve block for control of post-operative pain.

In addition to current product candidates in development and our partnered programs, we intend to expand our pipeline from our internal research efforts and may expand our pipeline through the acquisition or in-licensing of other product candidates.

Corporate Information

We were incorporated in the Province of British Columbia on November 5, 1996 under the predecessor to the Business Corporations Act (British Columbia) under the name "Xenon Bioresearch Inc." We continued from British Columbia to the federal jurisdiction pursuant to Section 187 of the Canada Business Corporations Act, or the CBCA, on May 17, 2000 and concurrently changed our name to "Xenon Genetics Inc." We registered as an extra-provincial company in British Columbia on July 10, 2000 and changed our name to "Xenon Pharmaceuticals Inc." on August 24, 2004. We have one wholly-owned subsidiary as of December 31, 2020, Xenon Pharmaceuticals USA Inc., which was incorporated in Delaware on December 2, 2016. Our principal executive offices are located at 200 – 3650 Gilmore Way, Burnaby, British Columbia, Canada V5G 4W8, and our telephone number is (604) 484-3300. Our website address is http://www.xenon-pharma.com. The information on, or that can be accessed through, our website is not incorporated by reference into this prospectus and should not be considered to be a part of this prospectus.

"Xenon," the Xenon logo and other trademarks or service marks of Xenon appearing in this prospectus are trademarked and are the property of Xenon Pharmaceuticals Inc. This prospectus contains references to our trademarks and service marks and to those belonging to other entities. Solely for convenience, trademarks and trade names referred to in this prospectus, including logos, artwork and other visual displays, may appear without the ® or ™ symbols, but such references are not intended to indicate in any way that we will not assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensor to these trademarks and trade names. We do not intend our use or display of other entities' trade names, trademarks or service marks to imply a relationship with, or endorsement or sponsorship of us by, any other entity.

The Securities We May Offer

We may offer and sell common shares, preferred shares, warrants and/or units in one or more offerings and in any combination, either individually or as units comprised of one or more of the other classes of securities. This prospectus provides you with a general description of the securities we may offer. A prospectus supplement, which we will provide each time we offer securities, will describe the specific amounts, prices and terms of these securities.

We may sell the securities to or through underwriters, dealers or agents or directly to purchasers or as otherwise set forth in the section of this prospectus captioned "Plan of Distribution." We, as well as any agents acting on our behalf, reserve the sole right to accept and to reject in whole or in part any proposed purchase of securities. Each prospectus supplement will set forth the names of any underwriters, dealers, agents or other entities involved in the sale of securities described in that prospectus supplement and any applicable fee, commission or discount arrangements with them.

Common Shares

Each holder of one common share is entitled to one vote for each common share on all matters submitted to a vote of the shareholders, including the election of directors. There are no cumulative voting rights. Subject to preferences that may be applicable to any then outstanding preferred shares, holders of common shares are entitled to receive ratably those dividends, if any, as may be declared from time to time by our board of directors out of legally available funds. In the event of our liquidation, dissolution or winding up, holders of common shares will be entitled to share ratably in the net assets legally available for distribution to shareholders after the payment of all of our debts and other liabilities and the satisfaction of any liquidation preference granted to the holders of any then outstanding preferred shares.

Preferred Shares

Our board of directors has the authority, without further action by the shareholders, to issue an unlimited number of preferred shares in one or more series. Subject to the provisions of the CBCA and the provisions of our outstanding Series 1 preferred shares, our board of directors has the discretion to determine the rights, preferences, privileges, restrictions and conditions, including, among others, dividend rights, conversion rights, voting rights, redemption rights, and liquidation preference of each series of preferred shares. As of June 30, 2021, there were 1,016,000 Series 1 preferred shares outstanding. Any new series of preferred shares authorized by our board of directors will have rights, preferences and privileges that are substantially the same as our Series 1 preferred shares. For additional information regarding our Series 1 preferred shares, see the section of this prospectus titled "Description of Share Capital – Series 1 Preferred Shares."

Each series of preferred shares will be more fully described in the particular prospectus supplement that will accompany this prospectus, including redemption provisions, rights in the event of our liquidation, dissolution or winding up, dividend and voting rights and rights to convert into common shares. No rights, privileges, restrictions or conditions attached to a series of preferred shares shall confer on a series a priority in respect of dividends or return of capital over any other series of preferred shares that are then outstanding.

If any cumulative dividends or amounts payable on return of capital in respect of a series of preferred shares are not paid in full, all series of the preferred shares participate ratably in respect of accumulated dividends and return of capital.

Warrants

We may issue warrants for the purchase of common shares or preferred shares. We may issue warrants independently or together with other securities.

Units

We may issue units comprised of one or more of the other classes of securities issued by us as described in this prospectus in any combination. Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit.

RISK FACTORS

An investment in our securities involves a high degree of risk. The prospectus supplement applicable to each offering of our securities will contain a discussion of the risks applicable to an investment in our securities. Prior to making a decision about investing in our securities, you should carefully consider the specific factors discussed under the heading "Risk Factors" in the applicable prospectus supplement, together with all of the other information contained or incorporated by reference in the prospectus supplement or appearing or incorporated by reference in this prospectus. You should also consider the risks, uncertainties and assumptions discussed under "Part I—Item 1A—Risk Factors," of our most recent Annual Report on Form 10-K and in "Part II—Item 1A—Risk Factors" in our most recent Quarterly Report on Form 10-Q, filed subsequent to such Form 10-K that are incorporated herein by reference, as may be amended, supplemented or superseded from time to time by other reports we file with the SEC in the future and any prospectus supplement related to a particular offering. The risks and uncertainties we have described are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect our operations.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, each prospectus supplement and the information incorporated by reference in this prospectus and each prospectus supplement contain certain statements that constitute forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. The words "aim," "anticipate," "assume," "believe," "contemplate," "continue," "could," "due," "estimate," "expect," "goal," "intend," "may," "objective," "plan," "predict," "positioned," "potential," "seek," "should," "target," "will," "would" and similar expressions and variations thereof are intended to identify forward-looking statements, but are not the exclusive means of identifying such statements. Those statements appear in this prospectus, any accompanying prospectus supplement and the documents incorporated herein and therein by reference, particularly in the sections captioned "Prospectus Summary," "Risk Factors," "Management's Discussion and Analysis of Financial Condition and Results of Operations" and "Business" and include statements regarding the intent, belief or current expectations of our management that are subject to known and unknown risks, uncertainties and assumptions. You are cautioned that any such forward-looking statements are not guarantees of future performance and involve risks and uncertainties, and that actual results may differ materially from those projected in the forward-looking statements as a result of various factors.

Forward-looking statements are subject to certain risks and uncertainties that could cause actual results to differ materially from those anticipated in the forward-looking statements. Factors that might cause such a difference include, but are not limited to, those described in "Risk Factors", elsewhere in this prospectus or any applicable prospectus supplement and the documents incorporated by reference in this prospectus. Forward-looking statements are based on our management's beliefs and assumptions and on information currently available to our management. These statements, like all statements in this prospectus, speak only as of their date, and we undertake no obligation to update or revise these statements in light of future developments, except as required by law.

This prospectus, any accompanying prospectus supplement and the documents incorporated herein and therein by reference may also contain estimates and other information concerning our industry that are based on government and industry publications. This information involves a number of assumptions and limitations, and you are cautioned not to give undue weight to these estimates. These government and industry publications generally indicate that their information has been obtained from sources believed to be reliable.

In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this prospectus, and although we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted a thorough inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and investors are cautioned not to unduly rely upon these statements.

USE OF PROCEEDS

Specific information about the use of proceeds from the specific issuance of any securities will be set forth in the applicable prospectus supplement.

DIVIDEND POLICY

We have never declared or paid any cash dividends on our common shares or any other securities. We currently anticipate that we will retain all available funds and any future earnings, if any, in the foreseeable future for use in the operation of our business and do not currently anticipate paying cash dividends in the foreseeable future. Payment of future cash dividends, if any, will be at the discretion of the board of directors, subject to applicable law and will depend on various factors, including our financial condition, operating results, current and anticipated cash needs, the requirements of current or then-existing debt instruments and other factors the board of directors deems relevant.

DESCRIPTION OF SHARE CAPITAL

The description of our share capital is incorporated by reference to Exhibit 4.4 to our Annual Report on Form 10-K for the fiscal year ended December 31, 2019, filed with the SEC on March 9, 2020.

DESCRIPTION OF THE WARRANTS

We may issue warrants to purchase preferred shares or common shares. We may offer warrants separately or together with one or more additional warrants, preferred shares or common shares, or any combination of those securities in the form of units, as described in the applicable prospectus supplement. If we issue warrants as part of a unit, the applicable prospectus supplement will specify whether those warrants may be separated from the other securities in the unit prior to the expiration date of the warrants. The applicable prospectus supplement will also describe the following terms of any warrants:

- the specific designation and aggregate number of, and the offering price at which we will issue, the warrants;
- the date on which the right to exercise the warrants will begin and the date on which that right will expire or, if you may not continuously exercise the warrants throughout that period, the specific date or dates on which you may exercise the warrants;
- whether the warrants are to be sold separately or with other securities as parts of units;
- whether the warrants will be issued in definitive or global form or in any combination of these forms, although, in any case, the form of a warrant included in a unit will correspond to the form of the unit and of any security included in that unit;
- the identity of the warrant agent for the warrants and of any other depositaries, execution or paying agents, transfer agents, registrars or other agents;
- the proposed listing, if any, of the warrants or any securities purchasable upon exercise of the warrants on any securities exchange;
- the designation and terms of any equity securities purchasable upon exercise of the warrants;
- if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each security;
- if applicable, the date from and after which the warrants and any securities issued with the warrants will be separately transferable;
- the number of common shares or preferred shares that may be purchased upon exercise of a warrant and the exercise price for the warrants;
- if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;
- information with respect to book entry procedures, if any;
- the currency or currency units in which the offering price, if any, and the exercise price are payable;
- if applicable, a discussion of material U.S. and Canadian federal income tax considerations;

- the anti-dilution provisions, and other provisions for changes to or adjustments in the exercise price, of the warrants, if any;
- the redemption or call provisions, if any, applicable to the warrants;
- any adjustments to the terms of the warrants resulting from the occurrence of certain events or from the entry into or consummation by us of certain transactions;
- any provisions with respect to the holder's right to require us to repurchase the warrants upon a change in control or similar event; and
- any additional terms of the warrants, including procedures and limitations relating to the exchange, exercise and settlement of the warrants.

Holders of warrants will not be entitled:

- to vote or receive dividends;
- receive notice with respect to any meeting of shareholders for the election of our directors or any other matter; or
- exercise any rights as shareholders of us.

This summary of certain provisions of the warrants is not complete. For the terms of a particular series of warrants, you should refer to the prospectus supplement for that series of warrants and the warrant agreement for that particular series.

DESCRIPTION OF THE UNITS

We may issue units comprising two or more securities described in this prospectus in any combination. The following description sets forth certain general terms and provisions of the units that we may offer pursuant to this prospectus. The particular terms of the units and the extent, if any, to which the general terms and provisions may apply to the units so offered will be described in the applicable prospectus supplement.

Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the unit will have the rights and obligations of a holder of each included security. Units will be issued pursuant to the terms of a unit agreement, which may provide that the securities included in the unit may not be held or transferred separately at any time or at any time before a specified date. A copy of the forms of the unit agreement and the unit certificate relating to any particular issue of units will be filed with the SEC each time we issue units, and you should read those documents for provisions that may be important to you. For more information on how you can obtain copies of the forms of the unit agreement and the related unit certificate, see the section of this prospectus captioned "Where You Can Find More Information."

The prospectus supplement relating to any particular issuance of units will describe the terms of those units, including, to the extent applicable, the following:

- the designation and terms of the units and the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately;
- any provision for the issuance, payment, settlement, transfer or exchange of the units or the securities comprising the units;
- a discussion of material U.S. and Canadian federal income tax considerations, if applicable; and
- whether the units will be issued in fully registered or global form.

PLAN OF DISTRIBUTION

We may sell the securities offered through this prospectus (1) to or through underwriters or dealers, (2) directly to purchasers, including our affiliates, (3) through agents, or (4) through a combination of any these methods. The securities may be distributed at a fixed price or prices, which may be changed, market prices prevailing at the time of sale, prices related to the prevailing market prices, or negotiated prices.

The prospectus supplement relating to any offering will include the following information:

- the terms of the offering;
- the names of any underwriters or agents;
- the name or names of any managing underwriter or underwriters;
- the purchase price of the securities;
- the net proceeds from the sale of the securities;
- any delayed delivery arrangements
- any underwriting discounts, commissions or agency fees and other items constituting underwriters' or agents' compensation;
- any initial price to public;
- any exchanges on which the securities will be listed;
- any discounts or concessions allowed or reallowed or paid to dealers; and
- any commissions paid to agents.

In addition, the manner in which we may sell some or all of the securities covered by this prospectus includes, without limitation, through:

- a block trade in which a broker-dealer will attempt to sell as agent, but may position or resell a portion of the block, as principal, in order to facilitate the transaction;
- purchases by a broker-dealer, as principal, and resale by the broker-dealer for its account;
- ordinary brokerage transactions and transactions in which a broker solicits purchasers; or
- privately negotiated transactions.

We may engage in at-the-market offerings into an existing trading market in accordance with Rule 415(a)(4) in the manner described below under "—At-the-Market Offerings."

Sales through Underwriters or Dealers

If underwriters are used in the sale, the underwriters will acquire the securities for their own account, including through underwriting, purchase, security lending or repurchase agreements with us. The underwriters may resell the securities from time to time in one or more transactions, including negotiated transactions. Underwriters may sell the securities in order to facilitate transactions in any of our other securities (described in this prospectus or otherwise), including other public or private transactions and short sales. Underwriters may offer securities to the public either through underwriting syndicates represented by one or more managing underwriters or directly by one or more firms acting as underwriters. Unless otherwise indicated in the prospectus supplement, the obligations of the underwriters to purchase the securities will be subject to certain conditions, and the underwriters will be obligated to purchase all the offered securities if they purchase any of them (other than any securities purchased upon exercise of any option to purchase additional securities). In connection with any offering of securities pursuant to this prospectus, underwriters may have an option to purchase additional securities from us. We will provide information regarding any such option to purchase additional securities from us in the applicable prospectus supplement. The underwriters may change from time to time any initial public offering price and any discounts or concessions allowed or reallowed or paid to dealers. The prospectus supplement will include the names of the principal underwriters the respective amount of securities underwritten, the nature of the obligation of the underwriters to take the securities and the nature of any material relationship between an underwriter and us.

Some or all of the securities that we offer through this prospectus may be new issues of securities with no established trading market. Any underwriters to whom we sell securities for public offering and sale may make a market in those securities, but they will not be obligated to do so and they may discontinue any market making at any time without notice. Accordingly, we cannot assure you of the liquidity of, or continued trading markets for, any securities offered pursuant to this prospectus.

If dealers are used in the sale of securities offered through this prospectus, we will sell the securities to them as principals. They may then resell those securities to the public at varying prices determined by the dealers at the time of resale. The prospectus supplement will include the names of the dealers and the terms of the transaction.

Direct Sales and Sales through Agents

We may sell the securities offered through this prospectus directly. In this case, no underwriters or agents would be involved. Such securities may also be sold through agents designated from time to time. The applicable prospectus supplement will name any agent involved in the offer or sale of the offered securities and will describe any commissions payable to the agent by us. Unless otherwise indicated in the prospectus supplement, any agent will agree to use its reasonable best efforts to solicit purchases for the period of its appointment.

We may sell the securities directly to institutional investors or others who may be deemed to be underwriters within the meaning of the Securities Act with respect to any sale of those securities. The terms of any such sales will be described in the prospectus supplement.

Delayed Delivery Contracts

If so indicated in the applicable prospectus supplement, we will authorize underwriters or other persons acting as our agents to solicit offers by certain institutions to purchase securities from us pursuant to delayed delivery contracts providing for payment and delivery on the date stated in the prospectus supplement. Each contract will be for an amount not less than, and the aggregate amount of securities sold pursuant to such contracts shall not be less nor more than, the respective amounts stated in the prospectus supplement. Institutions with whom the contracts, when authorized, may be made include commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable institutions and other institutions, but shall in all cases be subject to our approval. Delayed delivery contracts will not be subject to any conditions except that:

- the purchase by an institution of the securities covered under that contract shall not at the time of delivery be prohibited under the laws of the jurisdiction to which that institution is subject; and
- if the securities are also being sold to underwriters acting as principals for their own account, the underwriters shall have purchased such securities not sold for delayed delivery.

The underwriters and other persons acting as agents will not have any responsibility in respect of the validity or performance of delayed delivery contracts.

Certain agents, underwriters and dealers, and their associates and affiliates may be customers of, have borrowing relationships with, engage in other transactions with, and/or perform services, including investment banking services, for us or one or more of our respective affiliates in the ordinary course of business.

At-the-Market Offerings

To the extent that we make sales through one or more underwriters or agents in at-the-market offerings, we will do so pursuant to the terms of a sales agency financing agreement or other at-the-market offering arrangement between us, on one hand, and the underwriters or agents, on the other. If we engage in at-the-market sales pursuant to any such agreement, we will issue and sell our securities through one or more underwriters or agents, which may act on an agency basis or a principal basis. During the term of any such agreement, we may sell securities on a daily basis in exchange transactions or otherwise as we agree with the underwriters or agents. Any such agreement will provide that any securities sold will be sold at prices related to the then prevailing market prices for our securities. Therefore, exact figures regarding proceeds that will be raised or commissions to be paid cannot be determined as of the date of this prospectus. Pursuant to the terms of the agreement, we may agree to sell, and the relevant underwriters or agents may agree to solicit offers to purchase, blocks of our common shares or other securities. The terms of any such agreement will be set forth in more detail in the applicable prospectus or prospectus supplement.

Market Making, Stabilization, Other Transactions and Settlement

In order to facilitate the offering of the securities, any underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the securities or any other securities the prices of which may be used to determine payments on such securities. Specifically, any underwriters may over-allot in connection with the offering, creating a short position for their own accounts. In addition, to cover over-allotments or to stabilize the price of the securities or of any such other securities, the underwriters may bid for, and purchase, the securities or any such other securities in the open market. Finally, in any offering of the securities through a syndicate of underwriters, the underwriting syndicate may reclaim selling concessions allowed to an underwriter or a dealer for distributing the securities in the offering if the syndicate repurchases previously distributed securities in transactions to cover syndicate short positions, in stabilization transactions or otherwise. Any of these activities may stabilize or maintain the market price of the securities above independent market levels. Any such underwriters are not required to engage in these activities and may end any of these activities at any time.

Under Rule 15c6-1 of the Exchange Act, trades in the secondary market generally are required to settle in two business days, unless the parties to any such trade expressly agree otherwise. The applicable prospectus supplement may provide that the original issue date for your securities may be more than two scheduled business days after the trade date for your securities. Accordingly, in such a case, if you wish to trade securities on any date prior to the third business day before the original issue date for your securities, you will be required, by virtue of the fact that your securities initially are expected to settle in more than three scheduled business days after the trade date for your securities, to make alternative settlement arrangements to prevent a failed settlement.

Unless the applicable prospectus supplement states otherwise, each offered security will be a new issue and will have no established trading market, with the exception of our common shares. We may elect to list any offered securities on an exchange. Any underwriters that we use in the sale of offered securities may make a market in such securities, but may discontinue such market making at any time without notice. Accordingly, we cannot assure you of the liquidity of, or continued trading markets for, any securities offered pursuant to this prospectus.

Derivative Transactions and Hedging

We, the underwriters or other agents may engage in derivative transactions involving the securities. These derivatives may consist of short sale transactions and other hedging activities. The underwriters or agents may acquire a long or short position in the securities, hold or resell securities acquired and purchase options or futures on the securities and other derivative instruments with returns linked to or related to changes in the price of the securities. In order to facilitate these derivative transactions, we may enter into security lending or repurchase agreements with the underwriters or agents. The underwriters or agents may effect the derivative transactions through sales of the securities to the public, including short sales, or by lending the securities in order to facilitate short sale transactions by others. The underwriters or agents may also use the securities purchased or borrowed from us or others (or, in the case of derivatives, securities received from us in settlement of those derivatives) to directly or indirectly settle sales of the securities or close out any related open borrowings of the securities.

Electronic Auctions

We may also make sales through the Internet or through other electronic means. Since we may from time to time elect to offer securities directly to the public, with or without the involvement of agents, underwriters or dealers, utilizing the Internet or other forms of electronic bidding or ordering systems for the pricing and allocation of such securities, you should pay particular attention to the description of that system we will provide in a prospectus supplement.

Such electronic system may allow bidders to directly participate, through electronic access to an auction site, by submitting conditional offers to buy that are subject to acceptance by us, and which may directly affect the price or other terms and conditions at which such securities are sold. These bidding or ordering systems may present to each bidder, on a so-called "real-time" basis, relevant information to assist in making a bid, such as the clearing spread at which the offering would be sold, based on the bids submitted, and whether a bidder's individual bids would be accepted, prorated or rejected.

Upon completion of such an electronic auction process, securities will be allocated based on prices bid, terms of bid or other factors. The final offering price at which securities would be sold and the allocation of securities among bidders would be based in whole or in part on the results of the Internet or other electronic bidding process or auction.

General Information

Agents, underwriters, and dealers may be entitled, under agreements entered into with us, to indemnification by us against certain liabilities, including liabilities under the Securities Act. Our agents, underwriters, and dealers, or their affiliates, may be customers of, engage in transactions with or perform services for us, in the ordinary course of business.

MATERIAL INCOME TAX CONSIDERATIONS

The applicable prospectus supplement may describe material U.S. federal income tax consequences of the acquisition, ownership and disposition of any of the securities offered by such prospectus supplement by an investor who is subject to U.S. federal taxation.

The applicable prospectus supplement may also describe material Canadian federal income tax considerations generally applicable to investors described therein of purchasing, holding and disposing of securities offered by such prospectus supplement, including, in the case of an investor who is not a resident of Canada, Canadian non-resident withholding tax considerations.

You should read the tax discussion in any prospectus supplement with respect to a particular offering and consult your own tax advisors with respect to the specific tax consequences of the acquisition, ownership and disposition of the securities offered by such prospectus supplement, including the applicability and effect of state, local and non-U.S. or Canadian tax laws, as well as U.S. and Canadian federal tax laws.

LEGAL MATTERS

We are being represented by Wilson Sonsini Goodrich & Rosati, Professional Corporation, Palo Alto, California. Certain legal matters relating to the securities offered by this prospectus under Canadian laws will be passed upon for us by Blake, Cassels & Graydon LLP, Vancouver, British Columbia. Additional legal matters may be passed on for us, or any underwriters, dealers or agents, by counsel that we will name in the applicable prospectus supplement.

EXPERTS

The consolidated financial statements of Xenon Pharmaceuticals Inc. as of December 31, 2020 and 2019, and for each of the years in the two-year period ended December 31, 2020 have been incorporated by reference herein in reliance upon the report of KPMG LLP, independent registered public accounting firm, also incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and other reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at http://www.sec.gov. Our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, and Current Reports on Form 8-K, including any amendments to those reports, and other information that we file with or furnish to the SEC pursuant to Section 13(a) or 15(d) of the Exchange Act can also be accessed free of charge through the Internet. These filings will be available as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. You may also access these filings through our website at www.xenon-pharma.com.

We have filed with the SEC a registration statement under the Securities Act relating to the offering of these securities. The registration statement, including the attached exhibits, contains additional relevant information about us and the securities. This prospectus does not contain all of the information set forth in the registration statement. You can obtain a copy of the registration statement, at prescribed rates, from the SEC as discussed above. The registration statement and the documents referred to below under "Incorporation by Reference" are also available on our Internet website, www.xenon-pharma.com. We have not incorporated by reference into this prospectus the information on our website, and you should not consider it to be a part of this prospectus.

Forms of any documents establishing the terms of the offered securities are filed as exhibits to the registration statement of which this prospectus forms a part or under cover of a Current Report on Form 8-K and incorporated in this prospectus by reference. Statements in this prospectus or any prospectus supplement about these documents are summaries and each statement is qualified in all respects by reference to the document to which it refers. You should read the actual documents for a more complete description of the relevant matters.

INFORMATION INCORPORATED BY REFERENCE

The SEC allows us to incorporate by reference much of the information that we file with the SEC, which means that we can disclose important information to you by referring you to those publicly available documents. The information that we incorporate by reference in this prospectus is considered to be part of this prospectus. Because we are incorporating by reference future filings with the SEC, this prospectus is continually updated and those future filings may modify or supersede some of the information included or incorporated by reference in this prospectus. This means that you must look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus or in any document previously incorporated by reference have been modified or superseded. This prospectus incorporates by reference the documents listed below and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (in each case, other than those documents or the portions of those documents furnished pursuant to Items 2.02 or 7.01 of any Current Report on Form 8-K and, except as may be noted in any such Form 8-K, exhibits filed on such form that are related to such information), until the offering of the securities under the registration statement of which this prospectus forms a part is terminated or completed:

- our Annual Report on Form 10-K for the fiscal year ended December 31, 2020, filed with the SEC on March 1, 2021;
- the portions of our Definitive Proxy Statement on Schedule 14A (other than information furnished rather than filed) that are incorporated by reference into our Annual Report on Form 10-K, filed with the SEC on April 28, 2021;
- our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2021 and June 30, 2021, filed with the SEC on May 11, 2021, and August 11, 2021, respectively;
- our Current Reports on Form 8-K filed with the SEC on January 14, 2021, January 14, 2021 (amendment), March 1, 2021(only as to Item 5.02), March 10, 2021, March 12, 2021, June 3, 2021, August 23, 2021, September 8, 2021 and October 4, 2021; and
- the description of our common shares contained in our Registration Statement on Form 8-A as filed with the SEC on October 10, 2014 pursuant to Section 12(b) of the Exchange Act, including any amendment or report filed for the purpose of updating such description.

We will provide to each person, including any beneficial owner, to whom this prospectus is delivered, upon written or oral request, at no cost to the requester, a copy of any and all of the information that is incorporated by reference in this prospectus.

Requests for such documents should be directed to:

Xenon Pharmaceuticals Inc.
Attn: Investor Relations
200 – 3650 Gilmore Way
Burnaby, BC V5G 4W8
Canada
(604) 484-3353

You may also access the documents incorporated by reference in this prospectus through our website at www.xenon-pharma.com. Except for the specific incorporated documents listed above, no information available on or through our website shall be deemed to be incorporated in this prospectus or the registration statement of which it forms a part.

$250,000,000

Common Shares

PROSPECTUS SUPPLEMENT

Joint Book-Running Managers

Jefferies
SVB Leerink
Stifel
RBC Capital Markets

October , 2021