

Xenon Pharmaceuticals Inc.
Form 424B5
September 07, 2016
Filed Pursuant to Rule 424(b)(5)

Registration No. 333-208376

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 SEPTEMBER 7, 2016

PRELIMINARY PROSPECTUS SUPPLEMENT

(To Prospectus Dated January 5, 2016)

Shares

Common Shares

We are offering _____ of our common shares. The selling securityholders identified in this prospectus supplement are offering an additional _____ common shares. We will not receive any of the proceeds from the sale of the common shares sold by the selling securityholders. Our common shares are listed on The NASDAQ Global Market under the symbol “XENE.” The last reported sale price of our common shares on The NASDAQ Global Market on September 6, 2016 was \$8.06 per share.

Investing in our common shares involves a high degree of risk. See “Risk Factors” beginning on page S-6 of this prospectus supplement and under similar headings in the documents incorporated by reference into this prospectus supplement and the accompanying prospectus.

We are an “emerging growth company” under applicable Securities and Exchange Commission rules and are eligible for reduced public company disclosure requirements. See “Prospectus Supplement Summary—Implications of Being an Emerging Growth Company.”

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	\$	\$
Proceeds to the selling securityholders, before expenses	\$	\$

(1) We have agreed to reimburse the underwriters for certain expenses. See “Underwriting” beginning on page S-53 of this prospectus supplement for additional information regarding underwriters’ compensation.

Delivery of the common shares is expected to be made on or about September , 2016. We and the selling securityholders named in this prospectus expect to grant the underwriters an option for a period of 30 days to purchase up to an additional common shares and common shares, respectively. If the underwriters exercise the option in full, the total underwriting discounts and commissions will be \$, the total proceeds to us, before expenses, will be \$, and the total proceeds to the selling securityholders, before expenses, will be \$.

Joint Book-Running Managers

Jefferies StifelGuggenheim Securities

Prospectus Supplement dated September , 2016

Table of Contents

Prospectus Supplement

	Page
<u>About this Prospectus Supplement</u>	S-1
<u>Prospectus Supplement Summary</u>	S-2
<u>The Offering</u>	S-5
<u>Risk Factors</u>	S-6
<u>Forward-Looking Statements</u>	S-38
<u>Use of Proceeds</u>	S-40
<u>Price Range of Common Shares</u>	S-41
<u>Dividend Policy</u>	S-42
<u>Capitalization</u>	S-43
<u>Dilution</u>	S-44
<u>Material Income Tax Considerations</u>	S-45
<u>Selling Securityholders</u>	S-52
<u>Underwriting</u>	S-53
<u>Legal Matters</u>	S-60
<u>Experts</u>	S-60
<u>Where You Can Find More Information</u>	S-60
<u>Information Incorporated by Reference</u>	S-61

Prospectus

	Page
<u>About this Prospectus</u>	1
<u>Prospectus Summary</u>	2
<u>Risk Factors</u>	4
<u>Special Note Regarding Forward-Looking Statements</u>	4
<u>Ratio of Earnings to Fixed Charges and Preference Dividends</u>	4
<u>Use of Proceeds</u>	4
<u>Description of Share Capital</u>	5
<u>Description of the Warrants</u>	9
<u>Description of the Units</u>	10
<u>Selling Securityholders</u>	11
<u>Plan of Distribution</u>	11
<u>Material Income Tax Considerations</u>	13
<u>Legal Matters</u>	13
<u>Experts</u>	13
<u>Where You Can Find More Information</u>	13
<u>Information Incorporated by Reference</u>	14

ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus dated January 5, 2016 form part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission (SEC), utilizing a “shelf” registration process. This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of this common share 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.

We, the selling securityholders and the underwriters have not 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, the selling securityholders 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 and the selling securityholders are offering to sell, and seeking offers to buy, common shares 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 common shares 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 common shares 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.

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 common shares. 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-6 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 discovering and developing a pipeline of differentiated therapeutics for orphan indications that we intend to commercialize on our own, and for larger market indications that we intend to partner with global pharmaceutical companies. We have built a core enabling discovery platform for the discovery of validated drug targets by studying rare human diseases with extreme traits, including diseases caused by mutations in ion channels, known as channelopathies. We have an integrated platform that includes in-house capabilities for human genetics, small molecule drug discovery, as well as preclinical and clinical development.

Our pharmaceutical partners include Teva Pharmaceutical Industries, Ltd., or Teva (through its subsidiary, Ivax International GmbH), Genentech, Inc., or Genentech, and Merck & Co., Inc., or Merck (through its affiliate, Essex Chemie AG). Our pharmaceutical collaborations have generated in aggregate over \$155.0 million in non-equity funding to date with the potential to provide us with over \$1.0 billion in future milestone payments, as well as royalties and co-promotion income on product sales.

Our business was founded on our proprietary discovery platform, which we refer to as Extreme Genetics. Extreme Genetics involves the study of families where individuals exhibit inherited severe traits, or phenotypes. By identifying and characterizing single-gene defects responsible for these phenotypes, we gain insights into human disease biology to better select targets for therapeutic intervention. We believe that our Extreme Genetics discovery platform enhances the likelihood of discovering a drug target that has a major effect in humans. From these discoveries, we can gain an improved understanding of how a drug that modulates the target might act when given to a human. Our Extreme Genetics discovery platform has yielded the first approved gene therapy product in the European Union, or the EU, and we are advancing a broad proprietary development pipeline and multiple pharmaceutical partnerships.

Glybera

Glybera, developed by our licensee uniQure Biopharma B.V., or uniQure, is the first gene therapy product approved in the EU for the treatment of the orphan disorder lipoprotein lipase deficiency, or LPLD. The first patient treated with Glybera as a commercially-available gene therapy was announced by uniQure in November 2015 and enabled by its commercialization partner in the EU, Chiesi Farmaceutici S.p.A., or Chiesi, which has sole control over commercialization in the EU.

TV-45070: A Small Molecule for the Treatment of Pain

TV-45070 (formerly XEN402), is a product candidate being developed in collaboration with Teva for the treatment of pain. Teva is currently conducting a randomized, double-blind, placebo-controlled Phase 2b clinical trial in patients with post-herpetic neuralgia, or PHN, with results expected in the first half of 2017. TV-45070 is a topically applied

small-molecule inhibitor of the sodium channel Nav1.7 and other sodium channels, including those that are expressed in the pain-sensing peripheral nervous system.

GDC-0276, GDC-0310, and Other Selective Inhibitors of Nav1.7 for the Treatment of Pain

GDC-0276 and GDC-0310 – which are both oral, selective and potent Nav1.7 small-molecule inhibitors – are being developed in collaboration with Genentech for the potential treatment of pain. GDC-0276 has sub nanomolar IC₅₀ potency and has greater than 25-fold selectivity over other sodium channels, including greater than 100-fold selectivity over Nav1.5. To study the effects of targeting Nav1.7 for the treatment of pain, we developed an animal model of inherited erythromelalgia, or IEM, by expressing human Nav1.7 carrying a known IEM mutation in mice. Using this IEM model, with a single dose of GDC-0276, these mice had fewer pain events demonstrating the ability of GDC-0276 to inhibit Nav1.7 in vivo. Phase 1 clinical trials for both GDC-0276 and GDC-0310 are currently ongoing. The single-ascending dose portion of the GDC-0276 Phase 1 trial is now complete, with the multiple ascending dose portion anticipated to be completed this year. Pending a full assessment of the Phase 1 results, Genentech intends to initiate a Phase 2 clinical trial in late 2016 or early 2017. Xenon and Genentech also have an active research collaboration focused on other orally selective small molecule inhibitors of Nav1.7.

S-2

XEN801 for the Treatment of Acne

XEN801 is a topical stearoyl Co-A desaturase-1, or SCD1 inhibitor, being developed for the treatment of moderate to severe acne. By targeting a reduction in the size and number of sebaceous glands, thereby reducing sebum production, Xenon believes XEN801 is a promising, novel treatment for acne, which could be better tolerated and without the serious side effects that often limit the use of currently approved retinoid treatments. XEN801 demonstrated efficacy in multiple preclinical models, showing a reduction in the size and number of sebaceous glands, as well as induced apoptosis in a human sebocyte cell line.

Xenon disclosed data from the XEN801 Phase 1 clinical trial where 48 healthy volunteers were dosed for either a 14-day or 21-day treatment period. A number of different dose volumes of the 1% XEN801 drug product were evaluated in the Phase 1 clinical trial with dosing on the back and face of healthy volunteers to determine the maximum tolerated dose. As expected, the most common side effects were localized, generally mild skin reactions. No serious adverse events were observed. Maximal plasma concentrations of XEN801 were low, whereas skin biopsies from the back of subjects showed a concentration of approximately two orders of magnitude higher than the IC₅₀ and expected to be higher than that required for 100% block of SCD1.

It is expected that XEN801 could achieve even better penetration in the facial skin, as currently applied in the ongoing Phase 2 clinical trial, which was initiated in February 2016 in patients with moderate to severe facial acne. A Phase 2 dose was selected based on favorable tolerability and skin drug concentrations. We anticipate topline results from the ongoing Phase 2 clinical trial in the first quarter of 2017.

As of June 30, 2016, we owned or co-owned four issued U.S. patents related to XEN801, and methods of making and using this and certain related compounds. These issued patents are expected to expire between 2024 and 2025 (absent any extensions of term). In addition, we have 30 foreign issued patents (exclusive of European patent national validations) and have filed seven corresponding applications in various foreign jurisdictions relating to XEN801 and certain related compounds. We have also filed a further U.S. provisional application directed to pharmaceutical compositions containing XEN801 and their associated methods of use. We intend to convert this U.S. provisional application into a corresponding U.S. non-provisional application in 2017, any patents issuing from which would be expected to expire in 2037 (absent any extensions of term).

Selective Small-Molecule Sodium Channel Inhibitors for the Treatment of Severe Childhood Epilepsy Disorders

Xenon is developing a Nav1.6 sodium channel inhibitor for the treatment of rare infantile epileptic encephalopathies – such as Dravet Syndrome and SCN8A (Nav1.6 gain-of-function) epilepsy. Xenon has identified potent, selective Nav1.6 inhibitors, and encouraging results from in vivo animal studies indicate that selective Nav1.6 inhibitors have demonstrated efficacy for seizures in a model of Nav1.6 gain-of-function SCN8A epilepsy, supporting the hypothesis that SCN8A epilepsies can be treated with potent, selective Nav1.6 inhibitors. Xenon expects to file an investigational new drug (IND) application in mid-2017.

Financial Information

As of June 30, 2016, we had \$50.7 million of cash and cash equivalents and marketable securities and an accumulated deficit of \$129.0 million.

Implications of Being an Emerging Growth Company

As a company with less than \$1.0 billion in revenue during our last fiscal year, we qualify as an “emerging growth company” as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. An emerging growth company may take advantage of specified reduced reporting requirements that are otherwise applicable generally to public companies. These provisions include:

an exemption from compliance with the auditor attestation requirement on the effectiveness of our internal controls over financial reporting;

an exemption from compliance with any requirement that the Public Company Accounting Oversight Board may adopt regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;

reduced disclosure about our executive compensation arrangements; and

exemptions from the requirements to obtain a non-binding advisory vote on executive compensation or a shareholder approval of any golden parachute arrangements.

Under the JOBS Act, we will remain an "emerging growth company" until the earliest of:

the last day of the fiscal year during which we have total annual gross revenue of \$1.0 billion or more;

December 31, 2019;

the date on which we have, during the previous three-year period, issued more than \$1.0 billion in non-convertible debt; or

S-3

n the date on which we are deemed to be a “large accelerated filer” under the Securities Exchange Act of 1934, as amended, or the Exchange Act (we will qualify as a large accelerated filer as of the first day of the first fiscal year after we have (i) more than \$700.0 million in outstanding common equity held by our non-affiliates and (ii) been public for at least 12 months; the value of our outstanding common equity will be measured each year on the last day of our second fiscal quarter).

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This provision allows an emerging growth company to delay the adoption of some accounting standards until those standards would otherwise apply to private companies. However, we have irrevocably elected not to avail ourselves of this exemption, and as a result, we will comply with new or revised accounting standards on the relevant dates on which adoption of such standards is required for non-emerging growth companies.

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, 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 no subsidiaries. We are a reporting issuer in British Columbia, Alberta and Ontario, but our shares are not listed on any recognized Canadian securities exchange. Our common shares trade on The NASDAQ Global Market under the symbol “XENE.”

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 www.xenon-pharma.com. The information contained in, or that can be accessed through, our website is not part of this prospectus supplement.

THE OFFERING

Common shares offered by us shares (shares if the underwriters' option to purchase additional shares is exercised in full).

Common shares offered by the selling securityholders shares (shares if the underwriters' option to purchase additional shares is exercised in full).

Option to purchase additional shares We and the selling securityholders expect to grant the underwriters an option to purchase up to additional common shares and additional common shares, respectively. 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 shares (shares if the underwriters elect to exercise in full their option to purchase additional shares from us).

Selling securityholders The selling securityholders are August Troendle and entities affiliated with InterWest Management Partners VII, LLC. See "Selling Securityholders."

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, will be approximately \$ million, or approximately \$ million if the underwriters exercise their option to purchase additional 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 ongoing development of our XEN801 product candidate, which is currently in a Phase 2 clinical trial; for external and personnel-related research and development expenses associated with the ongoing preclinical and potential future clinical development of our Nav1.6 program; to fund genetic research using our Extreme Genetics discovery platform and ion channel drug discovery activities; and for working capital, capital expenditures and other general corporate purposes. We will not receive any of the proceeds from the sale of common shares by the selling securityholders. See "Use of Proceeds" on page S-40 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-6 of this prospectus supplement and the similarly titled sections in the documents incorporated by reference into this prospectus supplement.

Nasdaq Global Market symbol XENE

Outstanding Shares

The number of common shares to be outstanding after this offering is based on 14,415,347 common shares outstanding as of June 30, 2016, and excludes:

- n 1,983,674 common shares issuable upon the exercise of outstanding options to purchase common shares as of June 30, 2016, at a weighted average exercise price of \$7.19 per common share; and
- n 86,055 common shares reserved for future issuance under our 2014 Equity Incentive Plan, as amended, as of June 30, 2016.

Except as otherwise indicated herein, all information in this prospectus supplement, including the number of shares that will be outstanding after this offering, assumes no exercise by the underwriters of their option to purchase additional 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 are a clinical-stage biotechnology company and, other than the years ended December 31, 2014 and 2013, we have recorded net losses in each annual reporting period since inception in 1996, and we do not expect to have sustained profitability for the foreseeable future. We had net losses of \$9.3 million for the six months ended June 30, 2016 and an accumulated deficit of \$129.0 million as of June 30, 2016, which were driven by expenses incurred in connection with our research 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 preclinical development activities. To date, we have financed our operations through the sale of equity securities, funding received from our licensees and collaborators and, to a lesser extent, government funding. Other than royalties we are eligible to receive from sales of Glybera under our license to uniQure Biopharma B.V., or uniQure, which we do not expect to be significant in the near-term, we have not generated any royalty revenue from product sales and our product candidates will require substantial additional investment before they will provide us with any product royalty revenue.

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

- continue our research and preclinical and clinical development of our product candidates;
 - expand the scope of our clinical studies for our current and prospective product candidates;
- initiate additional preclinical, clinical or other studies for our product candidates, including under our collaboration agreements;
 - change or add additional manufacturers or suppliers;
- 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 agreements including, without limitation, our agreements with the University of British Columbia, or UBC, and the Memorial University of Newfoundland;
- maintain, protect and expand our intellectual property portfolio;
- establish a sales, marketing and distribution infrastructure to commercialize any products for which we or one of our collaborators may obtain marketing approval, and for which we have maintained commercial rights;
 - create additional infrastructure to support our operations as a public company 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 U.S. Food and Drug Administration, or FDA, the European Medicines Agency, or EMA, or other regulatory agencies, domestic or foreign, to perform clinical and other studies 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.

S-6

Other than royalties we are eligible to receive from sales of Glybera, we have not generated any royalty 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. Other than royalties we are eligible to receive from sales of Glybera under our license to uniQure, we have not generated any royalty revenue from product sales, and do not otherwise anticipate generating revenue from product sales for the foreseeable future, if ever. Commercial sales of Glybera commenced in November 2015, but we do not expect to receive significant revenue in the near-term from these sales. If any of our product candidates fail in clinical trials or do not gain regulatory approval, or if Glybera or any of our future products, if any, once approved, fail to achieve market acceptance or adequate market share, we may never become profitable. Although we were profitable for the years ended December 31, 2014 and 2013, we may not be able to sustain profitability in subsequent periods. Our ability to generate future revenue from product sales depends heavily on our success, and the success of our collaborators, in:

- n completing research, preclinical and clinical development of our product candidates;
- n seeking and obtaining regulatory and marketing approvals for product candidates for which we complete clinical studies;
- n 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;
- n negotiating favorable terms in any collaboration, licensing or other arrangements into which we may enter;
- n obtaining market acceptance of products for which we obtain regulatory and marketing approval as therapies;
- n addressing any competing technological and market developments;
- n 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;
- n developing sustainable, scalable, reproducible, and transferable manufacturing processes for any of our products approved in the future;
- n maintaining, protecting, expanding and enforcing our portfolio of intellectual property rights, including patents, trade secrets and know-how;
- n implementing additional internal systems and infrastructure, as needed; and
- n 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 Glybera and 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 our trading price might be harmed.

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 proprietary preclinical 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, manufacturing of product candidates and products approved for sale, conducting preclinical 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, 2016, we incurred approximately \$9.5 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:

- nthe number and characteristics of the future product candidates we pursue;
- nthe scope, progress, results and costs of independently researching and developing any of our future product candidates, including conducting preclinical research and clinical trials;
- nwhether our existing collaborations continue to generate substantial milestone payments and, ultimately, royalties on future approved products for us;

S-7

nthe timing of, and the costs involved in, obtaining regulatory approvals for any future product candidates we develop independently;

nthe cost of future commercialization activities, including activities required pursuant to our option to co-promote TV-45070, if exercised by us, and the cost of commercializing any future products we develop independently that are approved for sale;

nthe cost of manufacturing our future product candidates and products, if any;

nour ability to maintain existing collaborations and to establish new collaborations, licensing or other arrangements and the financial terms of such agreements;

nthe costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing patents, including litigation costs and the outcome of such litigation; and

nthe timing, receipt and amount of sales of, or royalties on, Glybera, and 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 this report and research funding that we expect to receive under our existing collaborations, will enable us to fund our operating expenses and capital expenditure requirements for at least the next 12 to 24 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.

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 would dilute all of our shareholders. The incurrence of indebtedness would result in increased fixed payment obligations and, potentially, the imposition of restrictive covenants. Those covenants may 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.

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

Global credit and financial markets experienced extreme disruptions at various points over the last decade, characterized by diminished liquidity and credit availability, 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 debt or equity 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 common share price and could require us to delay or abandon development or commercialization plans. In addition, there is a risk that one or more of our current collaborators, service providers, manufacturers and other partners would not survive or be able to meet their commitments to us under such circumstances, which could directly affect our ability to attain our operating goals on schedule and on budget.

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

As of June 30, 2016, approximately 71% of our cash and cash equivalents and marketable securities were denominated in Canadian dollars. Historically, the majority of our operating expenses have been denominated in Canadian dollars and the majority of our revenue has been denominated in U.S. dollars and we expect this trend to continue.

S-8

Prior to December 31, 2014, our functional currency was the Canadian dollar. On January 1, 2015, our functional currency changed from the Canadian dollar to the U.S. dollar based on our analysis of the changes in the primary economic environment in which we operate. As a result, changes in the exchange rate between the Canadian dollar and the U.S. dollar could materially impact our reported results of operations and distort period to period comparisons. In particular, to the extent that foreign currency-denominated (i.e., non-U.S. dollar) monetary assets do not equal the amount of our foreign currency denominated monetary liabilities, foreign currency gains or losses could arise and materially impact our financial statements. As a result of such foreign currency fluctuations, it could be more difficult to detect underlying trends in our business and results of operations. In addition, to the extent that fluctuations in currency exchange rates cause our results of operations to differ from our expectations or the expectations of our investors, the trading price of our common shares could be adversely affected.

From time to time, we may engage in exchange rate hedging activities in an effort to mitigate the impact of exchange rate fluctuations. For example, we maintain a natural currency hedge against fluctuations in the U.S./Canadian foreign exchange rate by matching the amount of U.S. dollar and Canadian dollar investments to the expected amount of future U.S. dollar and Canadian dollar obligations, respectively. 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 trading price of our common shares.

Risks Related to Our Business

We, or our collaborators, may fail to successfully develop our product candidates.

Our product candidates, including TV-45070, GDC-0276, GDC-0310 and XEN801, and compounds in our preclinical and discovery pipeline, are in varying stages of development and will require substantial clinical development, testing and regulatory approval prior to commercialization. It may be several more years before these product candidates or any of our other product candidates receive marketing approval, if ever. If any of our product candidates fail to become approved products, our business, growth prospects, operating results and financial condition may be adversely affected and a decline of our common share price could result. For example, in July 2015, we and our partner Teva Pharmaceutical Industries Ltd., or Teva, announced top line results from a Phase 2b study designed to evaluate the safety and efficacy of topically applied TV-45070 in patients with chronic pain due to osteoarthritis, or OA, of the knee. Results from this trial showed that TV-45070 did not demonstrate statistically significant difference from placebo in efficacy endpoints of reductions in pain due to OA and neither we nor Teva have plans for further development of TV-45070 in OA, although clinical development of TV-45070 in post-herpetic neuralgia, or PHN, continues.

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 target discovery and product development from many different approaches and sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies and 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, convenience and price; the effectiveness and safety of alternative products; the level of generic competition; and the availability of coverage and adequate reimbursement from government and other third-party payers.

With respect to target discovery activities, competitors and other third parties, including academic and clinical researchers, may access rare families and identify novel targets for drug development before we do.

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, preclinical 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 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 common share price may suffer.

S-9

There are no approved gene therapies currently on the market for lipoprotein lipase deficiency, or LPLD, in the U.S. The current management of LPLD consists of strict adherence to an extremely low-fat diet, but compliance with such a diet is challenging. Lipid-lowering drugs are generally not effective for treating LPLD. We are not aware of any other drugs or therapies currently in development that treat LPLD by using the lipoprotein lipase, or LPL, sequence containing the LPL^{S447X} genetic variant or otherwise.

Drug discovery and development for various pain applications is intensely competitive. There are a large number of approved products for neuropathic pain, inflammatory pain and other pain indications. These approved products include capsaicin, celecoxib, lidocaine, narcotic analgesics and pregabalin. We are also aware of clinical-stage development programs at several pharmaceutical and biotechnology companies that are developing Nav1.7 inhibitors or other sodium channel inhibitors for the treatment of pain, including Amgen Inc., Biogen Inc., Dainippon Sumitomo Co., Ltd., Eli Lilly and Company, Merck & Co., Inc., or Merck, NeuroQuest Inc., and Vertex Pharmaceuticals Inc. Moreover, we are aware of various other product candidates in development that target other mechanisms of action to treat various pain indications, including calcium channel inhibitors, nerve growth factor inhibitors and P2X purinoceptor 3 inhibitors.

If XEN801 were approved for the treatment of acne, we anticipate it would compete with other approved prescription acne products including topical retinoids, oral hormonal therapies, topical and oral antimicrobials, and oral isotretinoin. In addition to approved prescription therapies, there are a wide range of over-the-counter, or OTC, treatments targeted at treating acne. Additionally, there are a number of prescription products that are used “off-label” for the treatment of acne. We are also aware of several products in clinical development that could potentially compete with XEN801, including products in development from Allergan PLC, AOBiome LLC, Braintree Laboratories Inc., Cassiopea SpA, Dermira Inc., Foamix Pharmaceuticals Ltd., Galderma SA, Mimetica Pty Ltd, Novan Therapeutics, Phosphagenics Ltd, Thesan Pharmaceuticals, Inc., Valeant Pharmaceuticals, and XBiotech Inc.

The novelty of gene therapy products and their lack of a commercial track record may hinder market acceptance of Glybera among physicians, patients, healthcare payers and the medical community.

Glybera is the first gene therapy product approved in the EU, and to date only one other gene therapy product has been approved in the EU, and no gene therapy product has been approved in the U.S. Because Glybera is the first gene therapy to be marketed in the EU, gaining market acceptance and overcoming any safety or efficacy concerns may be more challenging than for a more traditional therapy. Glybera’s commercial success will depend, in part, on the success of efforts to educate the market regarding gene therapy products. In particular, the success of Glybera will depend upon physicians who treat patients with LPLD, prescribing Glybera. With respect to Glybera and any other gene therapy products we or a collaborator may develop, public perception may be influenced by claims that gene therapy is unsafe, and, if so, gene therapy may not gain the acceptance of the public or the medical community.

We have no marketed products and have not yet advanced a product candidate 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.

We have no experience in Phase 3 and later stage clinical development, and related regulatory requirements or the commercialization of products. uniQure controls and has been responsible for the development and commercialization of Glybera; Teva is responsible for the on-going clinical development of TV-45070; and Genentech Inc., or Genentech, is responsible for the on-going clinical development of GDC-0276 and GDC-0310. Accordingly, we have not yet demonstrated our ability to independently and repeatedly conduct clinical development after Phase 2, obtain regulatory approval and commercialize therapeutic products. We will need to develop such abilities if we are to execute on our business strategy to selectively develop and independently commercialize product candidates for orphan and niche indications. To execute on our business plan for the development of independent programs, we will need to successfully:

nexecute our clinical development plans for later-stage product candidates;
nobtain required regulatory approvals in each jurisdiction in which we will seek to commercialize products;
nbuild and maintain appropriate sales, distribution and marketing capabilities;
ngain market acceptance for our future products, if any; and
nmanage 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 would not be able to develop and commercialize any future orphan and niche disease product candidates independently, and could fail to realize the potential advantages of doing so.

S-10

If we are not successful in leveraging our Extreme Genetics discovery platform to discover product candidates in addition to TV-45070, GDC-0276, GDC-0310 and XEN801, our ability to expand our business and achieve our strategic objectives may be impaired.

We rely on our Extreme Genetics discovery platform to identify validated drug targets and develop new product candidates. To date, our Extreme Genetics discovery platform has yielded one approved product, Glybera, and four clinical development candidates TV-45070, GDC-0276, GDC-0310 and XEN801. Use of our discovery platform requires substantial technical, financial and human resources, regardless of whether we identify any novel drug targets. Our Extreme Genetics discovery platform 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 we are unable to identify additional product candidates suitable for clinical development and commercialization, 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 our trading price.

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 Extreme Genetics discovery platform 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.

There are various challenges in utilizing our Extreme Genetics discovery platform to successfully identify novel drug targets, including locating families suffering from rare disorders and severe phenotypes, entering into agreements with foreign collaborators, complying with various domestic and foreign privacy laws, accessing required technologies in a timely manner and transporting DNA across national borders.

To date, only Glybera has been both developed using our Extreme Genetics discovery platform and approved for commercial sale. If the use of our Extreme Genetics discovery platform fails to identify novel targets for drug discovery, or such targets prove to be unsuitable for treating human disease, or 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.

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 successfully developed product candidates for orphan and niche indications independently. In order to execute on this strategy, we will need to build out a regulatory, sales, manufacturing, distribution 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. We anticipate that we may need to hire additional accounting, legal and financial staff with appropriate public company experience and technical accounting and other knowledge to address the added burdens of operating as a public company. There are likely to be additional infrastructure costs associated with public company compliance as well.

As our operations expand, we expect that we will need to manage additional relationships with various strategic collaborators, suppliers and other third parties.

Drs. Simon Pimstone and Y. Paul Goldberg each devote a small amount of their time to clinical work outside of their duties at our company, conducting, generally, two to three outpatient clinics per month. Future growth will impose significant added responsibilities on members of management, and 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.

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.

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.

S-11

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 Dr. Pimstone, our Chief Executive Officer and President; Mr. Ian Mortimer, our Chief Financial Officer and Chief Operating Officer; and Dr. Goldberg, our Vice President, Clinical Development, as well as other employees. In the near future, the loss of services of any of these individuals or one or more of our other 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 and other non-U.S. regulators, provide accurate information to the FDA, EMA and other non-U.S. 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, as well as comparable laws in non-U.S. 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 obtain through our direct-to-patient web-based recruitment approach for identifying patients with rare or extreme phenotypes.

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, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity 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 or 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.

Our business and operations could suffer in the event of system failures.

Computer system, network or telecommunications failures due to events such as damage from malware, unauthorized access, terrorism, war, or natural disasters could interrupt our internal or partner operations. For example, the loss of preclinical trial data or data from completed or ongoing clinical trials for our product candidates could result in delays in our regulatory filings and development efforts and significantly increase our costs. To the extent that any disruption or security breach were to result in a loss of or damage to our data, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the development of our product candidates could be delayed. While we have implemented security measures and, to date, have not detected a cyber security breach nor experienced

a material system failure, our internal computer systems and those of our contractors and consultants remain potentially vulnerable to damage from these events.

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

Glybera has been approved for commercial sale in the EU by the EMA, subject to uniQure's compliance with certain post-approval reporting and monitoring obligations. Our collaborator for TV-45070, Teva, is based in Israel and a significant portion of the research and development activities under our collaboration with Teva are performed outside of North America. If we continue to engage in significant cross-border activities, we will be subject to risks related to international operations, including:

- n different regulatory requirements for maintaining approval of drugs and biologics in foreign countries;
- n reduced protection for intellectual property rights in certain countries;
- n unexpected changes in tariffs, trade barriers and regulatory requirements;
- n economic weakness, including inflation, political instability or open conflict in particular foreign economies and markets;
- n compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- n foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations of doing business in another country;
- n workforce uncertainty in countries where labor unrest is more common than in North America;

S-12

n 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 export control and sanctions regulations, which likelihood may increase with an increase of operations in foreign jurisdictions;
n tighter restrictions on privacy and the collection and use of data, including genetic material, may apply in jurisdictions outside of North America, where we find some of the families with individuals that exhibit the severe phenotypes that we study; and
n business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters including earthquakes, typhoons, floods and fires.
If any of these issues were to occur, our business could be materially harmed.

Our near-term operating revenue is partially dependent upon the regulatory and marketing efforts of uniQure, or its sublicensee, for the development and commercialization of Glybera.

Under the terms of our license agreement with uniQure, we rely on uniQure, or its sublicensees, to market Glybera and to obtain and maintain regulatory approval of Glybera. In July 2013, uniQure announced that it had granted to Chiesi Farmaceutici, S.p.A., or Chiesi, an Italian pharmaceutical firm, an exclusive license to commercialize Glybera in the European Union, or the EU, and certain other countries outside of North America and Japan. Commercial sales of Glybera commenced in November 2015. Despite the efforts of uniQure and Chiesi, Glybera may not gain market acceptance among physicians, patients, healthcare payers and the medical community.

Glybera is approved in the EU under exceptional circumstances and full approval may never be granted or the existing approval under exceptional circumstances could be revoked. As a condition to approval of Glybera, uniQure is required to complete a post-approval clinical trial and is required to implement a disease registry as well as implement risk management procedures, distribute educational materials to healthcare professionals and patients, implement an additional manufacturing process step, comply with certain notification obligations and undergo annual reassessment, any negative outcome of which could potentially lead to a withdrawal of marketing approval for Glybera.

Any failure of uniQure or its sublicensee to successfully commercialize Glybera or revocation of Glybera's marketing approval in the EU could have an adverse effect on our near-term operating revenue and financial condition and could result in a decline in the price of our common shares.

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 composition of our gross income and gross assets and the nature of our business, we do not believe that we were a PFIC for the taxable years ended December 31, 2015 and 2014, although we could be a PFIC for the calendar year ending December 31, 2016 or 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 taxable year ending December 31, 2016 or for future taxable years.

If we are a PFIC for any subsequent 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.

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. If we are a PFIC in the current or a future tax year, we will provide 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 for which we are a PFIC.

A U.S. Holder may also mitigate the adverse tax consequences if we are a PFIC by timely making a mark-to-market election. Generally, for each year that we would 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.

S-13

We may become subject to income tax in jurisdictions in which we are organized or operate, including the United States, which would reduce our future earnings.

There is a risk that we may become subject to income tax in jurisdictions outside of Canada, including 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 or joint ventures could disrupt our business, cause dilution to our shareholders and otherwise harm our business.

We actively evaluate various strategic transactions on an ongoing basis and may acquire other businesses, products or technologies as well as pursue strategic alliances, joint ventures 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 management of strategic alliances or joint ventures or acquisition integration challenges;
- 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.

Risks Related to Development, Clinical Testing and Regulatory Approval of Our Product Candidates

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

The regulatory approval process is expensive and the time required to obtain approval from the FDA, EMA 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 preclinical and clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. Other than for Glybera in the EU, neither we nor our collaborators have obtained regulatory approval for any of our product candidates. It is 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:

- nthe FDA, EMA or other regulatory authorities may disagree with the design or implementation of our or our collaborators' clinical trials;
- nwe or our collaborators may be unable to demonstrate to the satisfaction of the FDA, EMA or other regulatory authorities that a product candidate is safe and effective for its proposed indication;
- nthe results of clinical trials may not meet the level of statistical significance required by the FDA, EMA or other regulatory authorities for approval;
- nwe, or our collaborators, may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- nthe FDA, EMA or other regulatory authorities may disagree with our or our collaborators' interpretation of data from preclinical studies or clinical trials;

S-14

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 or other regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we or our collaborators contract for clinical and commercial supplies; and the approval policies or regulations of the FDA, EMA or other regulatory authorities outside of the U.S. 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 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.

Clinical drug development involves a lengthy and expensive process with uncertain timelines and uncertain outcomes. If clinical trials are prolonged or delayed, we, or our collaborators, may be unable to commercialize our product candidates on a timely basis.

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.

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 contract research organizations, or 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;
- 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 preclinical studies to generate data required to support the submission of an NDA;
- inability to enroll sufficient patients to complete a protocol, particularly in orphan diseases;
- difficulty in having patients complete a trial or return for post-treatment follow-up;
 - clinical sites deviating from trial protocol or dropping out of a trial;
- problems with drug product or drug substance storage and distribution;
- adding new clinical trial sites;
- our inability to manufacture, or obtain from third parties, adequate supply of drug substance or drug product sufficient to complete our preclinical studies and clinical trials; and
- governmental or regulatory delays and changes in regulatory requirements, policy and guidelines.

The results of any Phase 3 or other pivotal clinical 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. In addition, if the FDA, EMA or another applicable regulator disagrees with our or our collaborator's choice of the key testing criterion, or primary endpoint, or the results for the primary endpoint are not robust or significant relative to the control group of patients not receiving the experimental therapy, such regulator may refuse to approve our product candidate in the region in which it has jurisdiction. The FDA, EMA or other applicable non-U.S. regulators also may require additional clinical trials as a condition for approving any of these product candidates.

We could also encounter delays if a clinical trial is suspended or terminated by us, by our collaborators, by the IRBs of the institutions in which such trial is being conducted, by any Data Safety Monitoring Board for such trial, or by the FDA, EMA or other regulatory authorities. Such authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA, EMA or other 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.

S-15

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 will be harmed, could shorten the patent protection period during which we may have the exclusive right to commercialize our products 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 product candidates.

Our TV-45070, GDC-0276 and GDC-0310 product candidates for treatment of pain and XEN801 product candidate for the treatment of acne target novel molecular mechanisms. Regulatory authorities may require more extensive studies of the long-term effects of such product candidates for regulatory approval, which could delay development of our product candidates or our future product candidates based on novel mechanisms.

Our clinical trials may fail to demonstrate adequately the safety and efficacy of our product candidates, which could prevent or delay regulatory approval and commercialization.

Before obtaining regulatory approvals for the commercial sale of our products, we must demonstrate through lengthy, complex and expensive preclinical testing and clinical trials that the product candidate is both safe and effective for use in each target indication. 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. For example, in July 2015, we and our partner Teva announced top line results from a Phase 2b study designed to evaluate the safety and efficacy of topically applied TV-45070 in patients with chronic pain due to OA of the knee. Results from this trial showed that TV-45070 did not demonstrate statistically significant difference from placebo in efficacy endpoints of reductions in pain due to OA and neither we nor Teva have plans for further development of TV-45070 in OA, although clinical development of TV-45070 in PHN continues.

In the case of some of our product candidates, we are seeking to develop treatments for diseases for which there is relatively limited clinical experience, and, in some cases our clinical trials use novel end points and measurement methodologies or subjective patient feedback, which adds a layer of complexity to our clinical trials and may delay regulatory approval. In addition, our focus on orphan and niche markets may cause us to select target indications that are in more challenging therapeutic areas. For example, clinical trials for pain, the indication for which TV-45070, GDC-0276 and GDC-0310 are being developed, are inherently difficult to conduct. The primary measure of pain is subjective patient feedback, which can be influenced by factors outside of our control, and can vary widely from day to day for a particular patient, and from patient to patient and site to site within a clinical study. The placebo effect also tends to have a more significant impact on pain trials.

If our product candidates are not shown to be both safe and effective in clinical trials, we will not be able to obtain regulatory approval or commercialize these product candidates and products. In such case, we would need to develop other compounds and conduct associated preclinical 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 may find it difficult to enroll patients in our clinical studies, including for orphan or niche indications, which could delay or prevent clinical studies of our product candidates.

We 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 our clinical studies in a timely manner. Patient enrollment for clinical trials for orphan and niche indications and for more prevalent conditions is affected by factors including:

nseverity of the disease under investigation;

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

S-16

The limited patient populations in orphan and niche indications present significant recruitment challenges for clinical trials. As an example of a rare childhood epilepsy disorder, the prevalence of Dravet Syndrome, or DS, is estimated to be 7,500-15,000 patients in the U.S. Many of these patients may not be suitable or available for clinical trials. This means that we or our collaborators generally will have to run multi-site and potentially multi-national trials, which can be expensive and require close coordination and supervision. If we 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 technology or termination of the clinical studies altogether.

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.

A product candidate that receives orphan drug designation can benefit from a streamlined regulatory process as well as potential commercial benefits following approval. 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. This 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. TV-45070 has received both fast track and orphan drug designations for the treatment of erythromelalgia, or EM, by the FDA. If we seek orphan drug designations for other indications or in other jurisdictions, such as for TV-45070 in the EU, 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.

Results of earlier clinical trials may not be predictive of the results of later-stage clinical trials.

The results of preclinical studies and early clinical trials 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 candidates. 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 under study lack established clinical endpoints and validated measures of efficacy, as is often the case with orphan diseases for which no drugs have been developed previously. For example, our results for two small exploratory clinical trials for primary EM pain, one using a topical formulation and the other an oral formulation of TV-45070, used novel measures of efficacy assessment. While these studies provided promising results, further larger clinical trials will be necessary to confirm and extend these observations.

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

As product candidates are developed through preclinical to late stage clinical trials towards approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods and formulation, are altered along the way in an effort to optimize processes and results. Such changes carry the risk that they will not achieve these intended objectives. Any of these changes could cause our product candidates to

perform differently and 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 bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidates and/or jeopardize our or our collaborators' ability to commence product sales and generate revenue.

S-17

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 are, and will be, subject to U.S. and foreign regulatory requirements governing clinical trials and marketing approval, and we plan to seek 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 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 greater than, those in the U.S., including additional preclinical 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 or the EMA, 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 clinical trials or reporting as conditions of approval. 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. and the EMA 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 and could delay or prevent the introduction of our current and any future products, in certain countries.

If we 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.

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

We work with scientific advisors and collaborators at academic research institutions in connection with our Extreme Genetics discovery platform. These scientific advisors serve as our link to the various families with extreme phenotypes in that these advisors may:

- n identify families as potential candidates for study;
- n obtain their consent to participate in our research;
- n perform medical examinations and gather medical histories;
- n conduct the initial analysis of suitability of the families to participate in our research based on the foregoing; and
- n collect data and biological samples from the family members periodically in accordance with our study protocols.

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 Commercialization

If, in the future, we are unable to establish our own sales, marketing and distribution capabilities or enter into licensing or collaboration 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, in part, building our own commercial infrastructure to selectively commercialize future products in niche or orphan indications. Where we believe such involvement would advance our business, we seek to retain the right to participate in the future development and commercialization of such products. For example, we have a co-promotion option for TV-45070 with Teva in the U.S.

S-18

To develop internal sales, distribution and marketing capabilities, 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 proprietary product candidates will be approved. 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:

- nour inability to recruit and retain adequate numbers of effective sales and marketing personnel or develop alternative sales channels;
- nthe inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future products;
- nthe 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; and
- nunforeseen costs and expenses associated with creating and maintaining an independent sales and marketing organization.

Where and when appropriate, we may elect to utilize contract sales forces or distribution partners to assist in the commercialization of 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 the product candidates that we develop independently, 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 our product candidates we commercialize 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.

For any approved product, we 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 conduct post-approval. Later 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:

- nrestrictions on the marketing or manufacturing of the product, withdrawal of the product from the market or voluntary or mandatory product recalls;
- n fines, warning letters or holds on any post-approval clinical trials;
- nrefusal by the FDA, EMA 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;
- n product seizure or detention, or refusal to permit the import or export of products;
- and
- ninjunctive orders 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.

If the market opportunities for any product that we or our collaborators develop are smaller than we believe they are, our revenue may be adversely affected and our business may suffer.

We intend to focus our independent product development on treatments for rare diseases. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are based on estimates. Currently, most reported estimates of the prevalence of these diseases are based on studies of small subsets of the population in specific geographic areas, which are then extrapolated to estimate the prevalence of the diseases in the U.S. or elsewhere. As an example of a rare childhood epilepsy disorder, the prevalence of DS is estimated to be 7,500-15,000 patients in the U.S. These estimates may prove to be incorrect. If the prevalence of such diseases is smaller than we have projected, then, even if our products are approved, we may not be able to successfully commercialize them.

S-19

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 any 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 any collaborator 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 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 any collaborator's 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 any collaborator's 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.

Our target patient populations in orphan and niche indications, where we intend to selectively develop and commercialize products independently, are relatively small. In order for therapies that are designed to treat smaller patient populations to be commercially viable, the 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 a coverage and reimbursement strategy 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.

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, collectively, PPACA, was enacted in 2010 and includes measures that have significantly changed, or will significantly change, the way healthcare is financed by both governmental and private insurers. Among the provisions of PPACA of importance to the pharmaceutical industry are the following:

- n an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs, that began in 2011;
- n an increase in the rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23% and 13% of the average manufacturer price for branded and generic drugs, respectively;
- n a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts to negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- n extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;

S-20

nexpansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for certain individuals with income at or below 133% of the Federal Poverty Level beginning in 2014, thereby potentially increasing manufacturers' Medicaid rebate liability;

nexpansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;

nnew requirements under the federal Open Payments program, created under Section 6002 of the PPACA and its implementing regulations that manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) report annually to the U.S. Department of Health and Human Services, or HHS, information related to "payments or other transfers of value" made or distributed to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals and that applicable manufacturers and applicable group purchasing organizations report annually to the HHS ownership and investment interests held by physicians (as defined above) and their immediate family members, with data collection required beginning August 1, 2013 and reporting to the Centers for Medicare & Medicaid Services, or CMS, required by the 90th day of each subsequent calendar year, and disclosure of such information made on a publicly available website starting September 2014;

na requirement to annually report drug samples that manufacturers and distributors provide to physicians, effective in 2012;

nexpansion of healthcare fraud and abuse laws, including the False Claims Act and the Anti-Kickback Statute, new government investigative powers, and enhanced penalties for noncompliance;

na licensure framework for follow-on biologic products;

na new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;

ncreation of the Independent Payment Advisory Board which, beginning in 2014, has authority to recommend certain changes to the Medicare program that could result in reduced payments for prescription drugs and those recommendations could have the effect of law even if Congress does not act on the recommendations; and

nestablishment of a Center for Medicare Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending, that began, in 2011.

In the EU, similar political, economic and regulatory developments may affect our 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. Glybera and 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 Glybera and 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 abroad. 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, 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.

S-21

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 are 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

We depend on our collaborative relationship with Teva to further develop and commercialize TV-45070, and if our relationship is not successful or is terminated, we may not be able to effectively develop and/or commercialize TV-45070, which would have a material adverse effect on our business.

We depend on Teva to collaborate with us to develop and globally commercialize TV-45070. Under the agreement, Teva controls all decision-making with respect to the clinical development and commercialization for TV-45070.

As a result of our dependence on Teva, the eventual success or commercial viability of TV-45070 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 large part on Teva's performance under the agreement. We are subject to a number of additional specific risks associated with our dependence on our collaborative relationship with Teva, including:

- nadverse decisions by Teva or the Joint Development Committee regarding the development and commercialization of TV-45070;
- npossible disagreements as to the timing, nature and extent of our development plans, including clinical trials or regulatory approval strategy;
- nloss of significant rights if we fail to meet our obligations under the agreement;
- nour limited control over clinical trials of TV-45070;
- nchanges in key management personnel at Teva, including in members of the Joint Development Committee; and
- npossible disagreements with Teva regarding the agreement, for example, with regard to ownership of intellectual property rights.

If either we or Teva 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 Teva 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.

In addition, Teva's executive offices and a substantial percentage of their manufacturing capabilities are located in Israel. Teva's Israeli operations are dependent upon materials imported from outside Israel, and Teva also exports significant amounts of products from Israel. Accordingly, our collaboration with Teva could be materially and adversely affected by acts of terrorism or if major hostilities were to occur in the Middle East or trade between Israel and its present trading partners were curtailed, including as a result of acts of terrorism in the U.S. or elsewhere.

Any of the above discussed scenarios could adversely affect the timing and extent of our development and commercialization activities, which could cause significant delays and funding shortfalls for those activities and seriously harm our business.

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 uniQure, and its licensee Chiesi to successfully commercialize Glybera and on Teva, Genentech, and Merck to fund and conduct the research and any clinical development of product candidates under our collaboration 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:

- na 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;
- na collaborator may cease development in therapeutic areas which are the subject of our strategic alliances;

S-22

- na collaborator may change the success criteria for a particular program or product candidate thereby delaying or ceasing development of such program or candidate;
- na 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;
- na collaborator could develop a product that competes, either directly or indirectly, with our current or future products, if any;
- na collaborator with commercialization obligations may not commit sufficient financial or human resources to the marketing, distribution or sale of a product;
- na collaborator with manufacturing responsibilities may encounter regulatory, resource or quality issues and be unable to meet demand requirements;
- na collaborator may exercise its rights under the agreement to terminate our collaboration;
- na 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;
- na collaborator may not adequately protect the intellectual property rights associated with a product or product candidate; and
- na collaborator may use our proprietary information or intellectual property in such a way as to invite litigation from a third party.

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 would likely 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 would be materially and adversely affected.

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

We may seek to enter into additional product collaborations in the future, including alliances with other biotechnology or pharmaceutical companies, to enhance and accelerate the development of our 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 future product candidates because our research and development pipeline may be insufficient, our 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 is 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:

- nthe development of certain of our current or future product candidates may be terminated or delayed;
- nour cash expenditures related to development of our product candidates would increase significantly and we may need to seek additional financing sooner than expected;

n

we may be required to hire additional employees or otherwise develop expertise, such as clinical, regulatory, sales and marketing expertise, which we do not currently have;
n we will bear all of the risk related to the development of any such product candidates; and
n the competitiveness of any product that is commercialized could be reduced.

S-23

We intend to rely on third-party manufacturers to produce our clinical product candidate 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 or commercialize approved products.

We do not currently own or operate any manufacturing facilities nor do we have any in-house manufacturing experience or personnel. We rely on our collaborators to manufacture product candidates licensed to them or work with multiple third party contract manufacturers to produce sufficient quantities of materials required for the manufacture of our product candidates for preclinical testing and clinical trials and intend to do so for the commercial manufacture of our products. If we are unable to arrange for such third-party manufacturing sources, or fail to do so on commercially reasonable terms, we may not be able to successfully produce sufficient supply of product candidate or we 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 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 and certain state and foreign agencies. They are also subject to periodic unannounced inspections by the FDA, state and other foreign authorities. 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 marketed product recall, suspension of manufacturing, product seizure, or a voluntary withdrawal of the drug from the market. Any failure by our third-party manufacturers to comply with cGMP or failure to scale up manufacturing processes, including 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 monitor, support, conduct and/or oversee clinical trials of the product candidates that we are developing independently and, in some cases, to maintain regulatory files for those product candidates. We may not be able to obtain regulatory approval for our product candidates or commercialize any products that may result from our development efforts, if we are not able to maintain or secure agreements with such third parties on acceptable terms, if these third parties do not perform their services as required, or if these third parties fail to timely transfer any regulatory information held by them to us.

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 preclinical and clinical studies of our current and future product candidates. We also rely on third parties to perform clinical trials on our current and future product candidates when they reach that stage. 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.

If we are unable to maintain or enter into agreements with these third parties on acceptable terms, or if any such engagement is terminated prematurely, we may be unable to enroll patients on a timely basis or otherwise conduct our trials in the manner we anticipate. In addition, there is no guarantee that these third parties will devote adequate time and resources to our studies or perform as required by our contract or in accordance with regulatory requirements, including maintenance of clinical trial information regarding our product candidates. If these third parties fail to meet expected deadlines, fail to transfer to us any regulatory information in a timely manner, fail to adhere to protocols or fail to act in accordance with regulatory requirements or our agreements with them, or if they otherwise perform in a substandard manner or in a way that compromises the quality or accuracy of their activities or the data they obtain, then clinical trials of our future product candidates may be extended or delayed with additional costs incurred, or our

data may be rejected by the FDA, EMA or other 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 and our CROs are required to comply with cGCP regulations and guidelines enforced by the FDA, the competent authorities of the member states of the European Economic Area and comparable foreign regulatory authorities for products in clinical development. Regulatory authorities enforce these cGCP regulations through periodic inspections of clinical trial sponsors, principal investigators and clinical trial sites. If we or any of our CROs fail to comply with applicable cGCP regulations, the clinical data generated in our clinical trials may be deemed unreliable and our submission of marketing applications may be delayed or the FDA may require us to perform additional clinical trials before approving our marketing applications. Upon inspection, the FDA 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, and our clinical trials may require a large number of test subjects. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process and increase our costs. Moreover, our business may be implicated if any of our CROs violates federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws.

S-24

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 is terminated, we may be unable to enter into arrangements with alternative CROs on commercially reasonable terms, or at all.

Switching or adding CROs 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 or supplier commences work. As a result, delays may occur, which can materially impact our ability to meet our desired clinical development timelines. If we are required to seek alternative supply arrangements, the resulting delays and potential inability to find a suitable replacement could materially and adversely impact our business.

Risks Related to Intellectual Property

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

Our commercial success will depend, in large part, on our ability to obtain and maintain patent and other intellectual property protection with respect to our product candidates. 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. 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 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 many 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 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 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

S-25

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 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 selling 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 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 or licensors. Although we may, under such arrangements, have rights to consult with our collaborators on actions taken as well as back-up rights of prosecution and enforcement, we have in the past and may in the future relinquish rights to prosecute and maintain patents and patent applications within our portfolio as well as the ability to assert such patents against infringers. Currently, some of these rights relating to the patent portfolios for Glybera, TV-45070, GDC-0276 and GDC-0310, and some of our earlier stage product candidates are held by our collaborators.

S-26

If any current or future licensee or licensor 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 and 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 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 price of our common shares.

Claims that our product candidates or the sale 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, 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 are 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, 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 sale or use of our future products infringe, misappropriate or otherwise violate third-party intellectual property rights could therefore have a material adverse impact on our business.

S-27

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. For example, we have received, and may in the future 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 Teva, uniQure, Genentech or Merck 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.

The patent portfolio for Glybera is in-licensed from UBC. Under our existing license agreements, we are subject to various obligations, including diligence obligations such as development and commercialization obligations, as well as potential royalty 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. Generally, the loss of any one of our current licenses, or any other license we may acquire in the future, could materially harm our business, prospects, financial condition and results of operations.

S-28

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 Extreme Genetics 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 or clinical development 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.

Patent reform legislation and 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.

On September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law, including provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. The USPTO has and continues to develop and implement regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act. The full effect of these changes are currently unclear as the USPTO has not yet adopted all pertinent final rules and regulations, the courts have yet to address these provisions and the applicability of the Leahy-Smith Act and new regulations on specific patents, including our patents discussed herein, have not been determined and would need to be reviewed. Accordingly, it is not yet clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. As a result, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents, all of which could have a material adverse effect on our business and financial condition. On June 13, 2013, the U.S. Supreme Court decision in *Association for Molecular Pathology v. Myriad Genetics, Inc.*, held that isolated DNA sequences are not patentable. In December 2014, the USPTO issued its Interim Guidance on Patent Subject Matter Eligibility, in which it extended Myriad's "marked difference" standard for patent subject matter eligibility to all potential natural products. This standard applies to patent claims that recite not only nucleic acids (such as DNA in Myriad), but also other subject matter that could be considered a natural product, such as peptides, proteins, extracts, organisms, antibodies, chemicals, and minerals. As a consequence of the Myriad decision and the USPTO's Interim Guidance, if any of our future product candidates utilize isolated DNA, peptides, proteins or the like, we will not be able to obtain patents in the U.S. claiming such novel gene targets that we discover, which could limit our ability to prevent third parties from developing drugs directed against such targets.

If we do not obtain protection under the Hatch-Waxman Act 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 we request.

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 will be shortened and our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced, possibly materially.

S-29

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 Our Industry

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 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 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:

- n decreased demand for our product candidates or any resulting products;
- n injury to our reputation;
- n withdrawal of clinical trial participants;
- n costs to defend the related litigation;
- n a diversion of management's time and our resources;
- n substantial monetary awards to trial participants or patients;
- n product recalls, withdrawals or labeling, marketing or promotional restrictions;
- n loss of revenue;
- n the inability to commercialize our product candidates; and
- n a decline in our common share price.

We currently carry product liability insurance of \$5,000,000 per occurrence and \$10,000,000 aggregate limit. We believe our product liability insurance coverage is appropriate in light of 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 our common share price to decline and, if judgments exceed our insurance coverage, could adversely affect our future results of operations and business.

S-30

Patients with the diseases 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 relationships with customers and third-party payers 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 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, 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:

- nthe 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;
- n federal civil and criminal false claims laws and civil monetary penalty laws, including the federal False Claims Act, which impose criminal and civil penalties, including civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, including the Medicare and Medicaid programs, or other third party payers claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- nHIPAA, which imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters;
- nHIPAA, as amended by HITECH, and their respective implementing regulations, which impose obligations on covered healthcare providers, health plans, and healthcare clearinghouses, as well as their business associates that create, receive, maintain, or transmit individually identifiable health information for or on their behalf, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- nthe federal Open Payments program; and
- nanalogous 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; 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, imprisonment, exclusion from participation in government healthcare programs, such as Medicare and Medicaid, 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.

S-31

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 U.S. and Canadian federal, provincial, and local 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 third-party contract manufacturers, 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 insurance to compensate us for all losses that may occur. The disaster recovery and business continuity plans we have in place currently are limited and 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 this Offering, the Securities Markets and Ownership of Our Common Shares

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

Our common share price 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:

- actions by any of our collaborators regarding our product candidates they are developing, including announcements regarding clinical or regulatory decisions or developments or our collaboration;
- 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;
- unanticipated serious safety concerns related to the use of any of our products and product candidates;
- results from or 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, joint ventures or capital commitments;
- the results of our efforts to discover or develop additional product candidates;

nour dependence on third parties, including our collaborators, CROs, clinical trial sponsors and clinical investigators;
nregulatory or legal developments in Canada, the U.S. or other countries;
ndevelopments or disputes concerning patent applications, issued patents or other proprietary rights;
nthe recruitment or departure of key scientific or management personnel;
nour ability to successfully commercialize our future product candidates we develop independently, if approved;
nthe level of expenses related to any of our product candidates or clinical development programs;
nactual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
nactual or anticipated quarterly variations in our financial results or those of our competitors;

S-32

any change to the composition of the 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;
changes in the structure of healthcare payment systems;
commencement of, or our involvement in, litigation;
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. 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 our common share price to fall.

Our common share price 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.

Certain holders of our common shares are party to our amended and restated investor rights agreement, as amended, and have rights, subject to some conditions, to require us to file registration statements covering the sale of their common shares or to include their common shares in registration statements that we may file for ourselves or other shareholders. We also register the offer and sale of all common shares that we may issue under our equity compensation plans.

In addition, in the future, we may issue additional common shares or other equity or debt securities convertible into common shares in connection with a financing, acquisition, litigation settlement, employee arrangements or otherwise. Any such issuance could result in substantial dilution to our existing shareholders and could cause our common share price 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 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;

n

our board of directors may, without shareholder approval, issue preferred shares having any terms, conditions, rights, preferences and privileges as the board of directors may determine; and
nshareholders must give advance notice to nominate directors or to submit proposals for consideration at
shareholders' meetings.

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.

S-33

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 such 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 laws of Canada which in some cases have a different effect on shareholders than the corporate laws of Delaware, U.S.

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 a holder of 5% or more of our common shares can requisition a special meeting of shareholders, whereas such right does not exist under the DGCL.

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.

Complying with the laws and regulations affecting public companies will increase our costs and the demands on management and could harm our operating results and our ability to accurately report our financial condition, results of operations or cash flows, which may adversely affect investor confidence in us and, as a result, the value of our common shares.

As a public company, and particularly after we cease to be an “emerging growth company,” we will incur significant legal, accounting and other expenses. In addition, the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, and the related rules and regulations subsequently implemented by the Securities and Exchange Commission, or SEC, the applicable Canadian securities regulators and NASDAQ impose numerous requirements on public companies, including requiring changes in corporate governance practices. Also, the Securities Exchange Act of 1934, as amended, or the Exchange Act, requires, among other things, that we file annual, quarterly and current reports with respect to our business and operating results. We anticipate that we may need to hire additional accounting and financial staff with appropriate public company experience and technical accounting knowledge to address the added burdens of operating as a public company. Our management and other personnel have and will continue to devote a substantial amount of time to compliance with these laws and regulations. These requirements have increased and will continue to increase our legal, accounting, and financial compliance costs and have made and will continue to make some activities more time-consuming and costly. For example, these rules and regulations make it difficult and

expensive for us to maintain director and officer liability insurance and we may be required to accept reduced policy limits and coverage or to incur substantial costs to maintain the same or similar coverage. These rules and regulations could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors or our board committees or as executive officers.

S-34

The Sarbanes-Oxley Act requires, among other things, that we assess the effectiveness of our internal control over financial reporting annually and the effectiveness of our disclosure controls and procedures quarterly. In particular, Section 404 of the Sarbanes-Oxley Act, or Section 404, requires us to perform system and process evaluation and testing of our internal control over financial reporting to allow management to report on, and our independent registered public accounting firm potentially to attest to, the effectiveness of our internal control over financial reporting. As an “emerging growth company” we expect to avail 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 cease to be an “emerging growth company.” 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. Our compliance with applicable provisions of Section 404 will require that we incur substantial accounting expense and expend significant management time on compliance-related issues as we implement additional corporate governance practices and comply with reporting requirements. Moreover, if we are not able to comply with the requirements of Section 404 applicable to us in a timely manner, or 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, the market price of our common shares could 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.

Furthermore, investor perceptions of our company may suffer if deficiencies are found, and this could cause a decline in the market price of our common shares. 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. If we are unable to implement these requirements effectively or efficiently, it could harm our operations, financial reporting, or financial results and could result in an adverse opinion on our internal controls from our independent registered public accounting firm.

We are an “emerging growth company,” and any decision on our part to comply only with certain reduced reporting and disclosure requirements applicable to emerging growth companies could make our common shares less attractive to investors.

We are an “emerging growth company,” as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. For as long as we continue to be an “emerging growth company,” we may choose to take advantage of exemptions from various reporting requirements applicable to other public companies that are not “emerging growth companies,” including, but not limited to, not being required to have our independent registered public accounting firm audit our internal control over financial reporting under Section 404, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved. We could be an “emerging growth company” for up to five years following the completion of our initial public offering, although, if we have more than \$1.0 billion in annual revenue, if the market value of our common shares held by non-affiliates exceeds \$700 million as of June 30 of any year, or we issue more than \$1.0 billion of non-convertible debt over a three-year period before the end of that five-year period, we would cease to be an “emerging growth company” as of the following December 31. Investors could find our common shares less attractive if we choose to rely on these 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 our common share price may be more volatile.

As an “emerging growth company,” the JOBS Act allows us to delay adoption of new or revised accounting pronouncements applicable to public companies until such pronouncements are made applicable to private companies. However, we previously decided to “opt out” of such extended transition period, and as a result, we will comply with new or revised accounting standards on the relevant dates on which adoption of such standards is required for non-emerging growth companies. Section 107 of the JOBS Act provides that our decision to opt out of the extended

transition period for complying with new or revised accounting standards is irrevocable.

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 trading price of our common shares.

Effective internal controls over financial reporting are 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. In addition, any testing by us conducted in connection with Section 404 or any subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our common shares.

S-35

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. However, for as long as we are an “emerging growth company” under the JOBS Act, our independent registered public accounting firm will not be required to attest to the effectiveness of our internal controls over financial reporting pursuant to Section 404. An independent assessment of the effectiveness of our internal controls could detect problems that our management’s assessment might not. In addition, our management did not perform an evaluation of our internal control over financial reporting as of December 31, 2014 or December 31, 2013 and our independent registered public accounting firm did not perform an evaluation of our internal control over financial reporting during any period in accordance with the provisions of the Sarbanes-Oxley Act. Had we and our independent registered public accounting firm performed such an evaluation, control deficiencies may have been identified by management or our independent registered public accounting firm, and those control deficiencies could have also represented one or more material weaknesses. Undetected material weaknesses in our internal controls could lead to financial statement restatements and require us to incur the expense of remediation.

Future sales and issuances of our common shares or rights to purchase common shares, including pursuant to our equity incentive plans, could cause you to incur dilution and could cause our common share price to fall.

As of June 30, 2016, options to purchase 1,983,674 of our common shares with a weighted-average exercise price of \$7.19 per common share were outstanding. The exercise of any of these options would result in dilution to current shareholders. Further, because we will need to raise additional capital to fund our clinical development programs, we may in the future sell substantial amounts of common shares or securities convertible into or exchangeable for common shares. Pursuant to our equity incentive plans, our compensation committee (or a subset thereof) is authorized to grant equity-based incentive awards to our employees, directors and consultants. Future 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.

These future issuances of common shares or common share-related securities, together with the exercise of outstanding options and any additional common shares issued in connection with acquisitions, if any, may result in further dilution to our existing shareholders, and new investors could gain rights, preferences and privileges senior to those of holders of our common shares.

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 stock 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.

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.

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:

- n significant impairment of the liquidity for our common shares, which may substantially decrease the trading price of our common shares;
- na limited availability of market quotations for our securities;
- na 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;
- na limited amount of news and analyst coverage for our company; and
- na decreased ability to issue additional securities or obtain additional financing in the future.

If securities or industry analysts do not publish research reports about our business, or if they issue an adverse opinion about our business, our common share price and trading volume 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 trading price for 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, our common share price would likely decline. If one or more of these analysts cease coverage of our company or fail to publish reports on us regularly, demand for our common shares could decrease, which might cause our common share price and trading volume 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 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.

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 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 operation or enhance the value of our common shares. Our management will have broad discretion with respect to the use of proceeds of this offering, including for any of the purposes described in the section of this prospectus supplement entitled “Use of Proceeds.” 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.

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 of 1933, as amended (Securities Act), and Section 21E of the Securities Exchange Act of 1934, as amended (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 using our Extreme Genetics discovery platform;
- the initiation, timing, cost, progress and success of our research and development programs, preclinical 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 future clinical trials for orphan or more common indications;
- our ability to achieve profitability;
- our ability to obtain funding for our operations, including research funding;
- our ability to receive milestones, royalties and sublicensing fees under our collaborations, and the timing of such payments;
- the implementation of our business model and strategic plans;
- our ability to develop and commercialize product candidates for orphan and niche indications independently;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our ability to find families to support our Extreme Genetics discovery platform;
- our ability to discover genes and 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;
- the rate and degree of market acceptance and clinical utility of Glybera and future products, if any;
- 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 and cash equivalents, marketable securities and the net proceeds to us from this offering to meet our needs for at least the next 12 to 24 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,” 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-6 of this supplement and on page 4 of the accompanying prospectus), 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.

USE OF PROCEEDS

We estimate that the net proceeds to us from the issuance and sale of our common shares in this offering will be approximately \$ million, or approximately \$ million if the underwriters exercise in full their option to purchase up to additional common shares, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

As of June 30, 2016 we had cash and cash equivalents and marketable securities of \$50.7 million. We currently expect to use the net proceeds to us from this offering, together with our existing cash and cash equivalents and marketable securities, as follows:

- n for external and personnel-related expenses associated with the ongoing development of our XEN801 product candidate, which is currently in a Phase 2 clinical trial;
- n for external and personnel-related research and development expenses associated with the ongoing preclinical development and potential future clinical development of our Nav1.6 program;
- nto fund genetic research using our Extreme Genetics discovery platform and to fund ion channel drug discovery activities; and
- n 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; whether any co-funding or co-promotion rights under our strategic alliances are exercised; competitive and technological developments; and the anticipated growth of our business. Pending these uses, we plan to invest these net proceeds in Canadian guaranteed investment certificates, savings accounts, 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 to 24 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.

We will not receive any proceeds from the sale of common shares by the selling securityholders.

S-40

PRICE RANGE OF COMMON SHARES

Our common shares have been traded on The NASDAQ Global Market under the symbol “XENE” since our initial public offering in November 2014. The following table sets forth, for the periods indicated, the reported high and low sales prices per common share as reported by The NASDAQ Global Market.

	High	Low
Year Ended December 31, 2016		
Third Quarter (through September 6, 2016)	\$8.56	\$5.88
Second Quarter	\$7.72	\$5.65
First Quarter	\$8.42	\$6.31
Year Ended December 31, 2015		
Fourth Quarter	\$10.07	\$7.25
Third Quarter	\$11.75	\$7.94
Second Quarter	\$17.50	\$11.43
First Quarter	\$23.50	\$14.03
Year Ended December 31, 2014		
Fourth Quarter (commencing November 5, 2014)	\$21.95	\$9.21

S-41

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.

S-42

CAPITALIZATION

The following table sets forth our cash and cash equivalents and marketable securities and our capitalization as of June 30, 2016:

non an actual basis; and
 non an as adjusted basis to reflect our issuance and sale of common shares in this offering at the public offering price of \$ per common share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

You should read this table together with our financial statements and the related notes incorporated by reference in this prospectus supplement and the sections entitled “Management’s Discussion and Analysis of Financial Condition and Results of Operations” included in our most recent Annual Report on Form 10-K and Quarterly Report on Form 10-Q, each as incorporated by reference herein.

	AS OF JUNE 30, 2016	
	ACTUAL	AS ADJUSTED
	(unaudited)	
	(in thousands)	
Cash and cash equivalents and marketable securities	\$50,738	\$
Shareholder’s equity:		
Preferred shares, without par value, unlimited shares authorized; no shares issued or		
outstanding, actual; no shares issued or outstanding, as adjusted	—	
Common shares, without par value; unlimited shares authorized; 14,415,347 issued		
and outstanding, actual; shares issued and outstanding, as adjusted	148,867	
Additional paid-in capital	33,752	
Accumulated deficit	(128,972)	
Accumulated other comprehensive loss	(990))
Total shareholder’s equity	\$52,657	\$
Total capitalization	\$52,657	\$

The outstanding share information in the table above excludes, as of June 30, 2016:

n 1,983,674 common shares issuable upon the exercise of outstanding options to purchase common shares as of June 30, 2016, at a weighted average exercise price of \$7.19 per common share; and
 n 86,055 common shares reserved for future issuance under our 2014 Equity Incentive Plan, as amended, as of June 30, 2016.

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 of June 30, 2016, our net tangible book value was \$52.7 million, or \$3.65 per common share. After giving effect to our issuance and sale of common shares in this offering at the public offering price of \$ per common share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us, the as adjusted net tangible book value as of June 30, 2016 would have been \$ million, or \$ per common share. This represents an immediate increase in as adjusted net tangible book value to existing shareholders of \$ per common share and an immediate dilution to new investors purchasing common shares in this offering of \$ per common share.

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

Public offering price per common share	\$
Net tangible book value per common share at June 30, 2016	\$3.65
Increase in net tangible book value per common share attributable to new investors purchasing common shares in this offering	
As adjusted net tangible book value per common share after this offering	
Dilution per common share to new investors in this offering	\$

If the underwriters exercise their option to purchase additional common shares in full, at the public offering price of \$ per common share, the as adjusted net tangible book value will increase to \$ per common share, representing an immediate increase in net tangible book value to existing shareholders of \$ per common share and immediate dilution in net tangible book value of \$ per common share to new investors.

The foregoing table and calculations are based on 14,415,347 common shares outstanding as of June 30, 2016, and excludes:

- n 1,983,674 common shares issuable upon the exercise of outstanding options to purchase common shares as of June 30, 2016, at a weighted average exercise price of \$7.19 per common share; and
- n 86,055 common shares reserved for future issuance under our 2014 Equity Incentive Plan, as amended, as of June 30, 2016.

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 liable for alternative minimum tax;
- a person who owns, directly, indirectly or constructively, or is deemed to own 10% or more of our voting common shares;
- a partnership or other pass-through entity for U.S. federal income tax purposes; or
- a person whose “functional currency” is not the U.S. dollar.

If a partnership 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 hereof. 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 and does not address the effects of any state, local or non-U.S. tax laws.

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 are expected to qualify for the 20% reduced maximum tax rate available for dividends received from a “qualified foreign corporation” provided certain holding period and other requirements are met. 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 maximum 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 (see “Canadian Federal Income Tax Information—Non-Residents of Canada—Dividends on the 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. 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 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 Treaty 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 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. Holder. 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 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.

S-46

Passive Foreign Investment Company Consequences

In general, a corporation organized outside the U.S. will be treated as a PFIC in any taxable year 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. 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 nature of our business, the projected composition of our income and estimated fair market value of our assets, we do not believe that we were characterized as a PFIC in 2015 or 2014, although we could be a PFIC for the calendar year ending December 31, 2016 or 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 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. 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 are a PFIC in the current or a future tax year, we will provide 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.

S-47

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 NASDAQ 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.

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.

S-48

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, and is, or becomes, controlled by a non-resident corporation 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 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.

S-49

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. 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. 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 at a rate of 38 1/3 % 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. Such refundable tax will generally be refunded to a corporate Canadian Resident Holder at the rate of 38 1/3% of taxable dividends paid while it is a private corporation. 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.

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 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 at a rate of 10 2/3% on certain investment income, including taxable capital gains (as defined below), but excluding dividends or deemed dividends deductible in computing taxable income. Such refundable tax will generally be refunded to a corporate Canadian Resident Holder at the rate of 38 1/3% of taxable dividends paid while it is a private corporation.

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.

S-50

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. 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. 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-U.S. Tax Convention, 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%. 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 is also 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 immovable 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.

S-51

SELLING SECURITYHOLDERS

The following table sets forth:

the names of the selling securityholders;
 the number and percent of common shares that the selling securityholders beneficially owned prior to the offering for resale of the common shares under this prospectus supplement;
 the number of common shares that are being offered for resale for the account of the selling securityholders under this prospectus supplement; and
 the number and percentage of our common shares to be beneficially owned by the selling securityholders after the offering if all of the common shares offered by the selling securityholders and by us under this prospectus are sold. We will not receive any of the proceeds from the sale of common shares sold by the selling securityholders in this offering. We have determined beneficial ownership in accordance with SEC rules. The percent of common shares beneficially owned prior to the offering is based on 14,415,347 of our common shares issued and outstanding as of June 30, 2016. The number of common shares being offered by the selling securityholders, and the number and percent of common shares beneficially owned by the selling securityholders after the offering, assume no exercise by the underwriters of their option to purchase additional shares. The option to purchase additional shares includes up to an additional common shares that may be sold by the selling securityholders on a pro rata basis.

Name of Selling Securityholder ⁽¹⁾	Common Shares		Number of		
	Beneficially Owned Prior to the Offering	Percentage	Shares Being Offered	Common Shares Beneficially Owned After the Offering	
	Number			Number	Percentage
August J. Troendle ⁽²⁾	1,077,241	7.5	% 1,074,568		
Entities affiliated with InterWest Management					
Partners VII, LLC ⁽³⁾	806,061	5.6	% 803,925		

*Represents less than 1% of the total aggregate amount of our common shares

- (1) The selling securityholders set forth in the table are parties to our amended and restated investor rights agreement, as amended, and are participating in this offering pursuant to the exercise of certain registration rights provided by the terms of such agreement. For additional information regarding the terms of our amended and restated investor rights agreement, as amended, please see the section in the accompanying prospectus titled “Description of Share Capital—Registration Rights—Piggyback Registration Rights.”
- (2) August J. Troendle is the beneficial owner of 1,077,241 common shares, 1,074,568 of which are registrable securities under our amended and restated investor rights agreement, as amended. Dr. Troendle is an officer, director and stockholder of Medpace Holdings, Inc., or Medpace, a clinical contract research organization. If the underwriters exercise their option to purchase additional common shares, Dr. Troendle would beneficially own common shares after this offering. For more information regarding our existing contractual arrangement with Medpace, see the section titled “Management’s Discussion and Analysis of Financial Condition and Results of Operations—Contractual Obligations and Commitments” and Notes 10 and 12 to the financial statements in our Annual Report on Form 10-K filed with the SEC on March 8, 2016. The address for Dr. Troendle is 5375 Medpace Way, Cincinnati, Ohio 45227, USA.

(3) InterWest Management Partners VII, LLC, or IMP7, the general partner of InterWest Partners VII, LP, or IW7, and InterWest Investors VII, LP, or II7, has sole voting and investment power with respect to (i) 767,187 common shares held by IW7 and (ii) 36,738 common shares held by II7. Harvey B. Cash, Philip T. Gianos, W. Stephen Holmes, Gilbert H. Kliman and Arnold L. Oronsky as the managing directors of IMP7 share voting and investment power with respect to the common shares held by IW7 and II7. Gilbert H. Kliman and Arnold L. Oronsky each serve as an officer and director of InterWest Venture Management Company (“IVMC”) and share voting and dispositive power over the common shares owned by IVMC and may be deemed beneficially to own the 2,136 common shares held by IVMC. If the underwriters exercise their option to purchase additional common shares, IW7, II7, and IVMC would beneficially own common shares, common shares, and common shares after this offering, respectively. The address for these entities is c/o InterWest Partners, 2710 Sand Hill Road, Suite 200, Menlo Park, California 94025, USA.

S-52

UNDERWRITING

Subject to the terms and conditions set forth in the underwriting agreement, dated September , 2016, among us, the selling securityholders and Jefferies LLC, as the representative of the underwriters named below and a joint book-running manager of this offering, we and the selling securityholders have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us and the selling securityholders, the respective number of common shares shown opposite its name below, at a price of \$, payable to us and the selling securityholders against delivery of such common shares:

UNDERWRITERS	NUMBER OF COMMON SHARES
Jefferies LLC	
Stifel, Nicolaus & Company, Incorporated	
Guggenheim Securities, LLC	
Total	

We will not receive any of the proceeds from the sale of the common shares sold by the selling securityholders in this offering. The selling securityholders may be deemed underwriters with respect to the common shares they are offering.

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 and the selling securityholders have agreed to indemnify the underwriters and certain of their controlling persons, and we have agreed to indemnify the selling securityholders, 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 or selling securityholders, as applicable, 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 the selling securityholders 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. The underwriters may allow, and certain dealers may reallow, a discount from the concession not in excess of \$ per common share to certain brokers and dealers. After the offering, the public offering price, concession and reallowance to dealers may be reduced by the representative. 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 and the selling securityholders are to pay the underwriters and the proceeds, before expenses, to us and the selling securityholders 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 WITHOUT	WITH	TOTAL WITHOUT	WITH
	OPTION TO PURCHASE	OPTION TO PURCHASE	OPTION TO PURCHASE	OPTION TO PURCHASE
	ADDITIONAL COMMON	ADDITIONAL COMMON	ADDITIONAL COMMON	ADDITIONAL COMMON
	SHARES	SHARES	SHARES	SHARES
Public offering price	\$	\$	\$	\$
Underwriting discounts and commissions, paid by us	\$	\$	\$	\$
Proceeds to us, before expenses	\$	\$	\$	\$
Underwriting discounts and commissions, paid by the selling securityholders	\$	\$	\$	\$
Proceeds to the selling securityholders, before expenses	\$	\$	\$	\$

We estimate expenses payable by us in connection with this offering, other than the underwriting discounts and commissions referred to above, and including payments by us of up to \$25,000 to counsel for the selling securityholders, will be approximately \$. The selling securityholders will pay other expenses of this offering that they incur, including fees in excess of \$25,000 incurred by counsel for the selling securityholders, and underwriting discounts and commissions in connection with the common shares sold by the selling securityholders and. 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 Shares

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

nsell, 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 Securities Exchange Act of 1934, as amended, or the Exchange Act, or notherwise 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 nenter 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 nmake 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 npublicly announce an intention to do any of the foregoing for a period of 90 days after the date of this prospectus supplement without the prior written consent of Jefferies LLC.

S-54

The foregoing restriction terminates after the close of trading of our common shares on and including the 90th day 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 LLC may, in its sole discretion and at any time or from time to time before the termination of the 90-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.

None of us, the selling securityholders or 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.

S-55

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.

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 common shares 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 common shares in Canada. Each underwriter has agreed that it will not, directly or indirectly, offer or sell any of the common shares 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 common shares 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:

- na "sophisticated investor" under section 708(8)(a) or (b) of the Corporations Act;
- na "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;
- n a person associated with the company under Section 708(12) of the Corporations Act; or
- n 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 common shares issued to you pursuant to this prospectus supplement and the accompanying prospectus for resale in Australia within 12 months of those common shares 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 which has implemented the Prospectus Directive, each referred to herein as a Relevant Member State, an offer to the public of any common shares which are the subject of the offering contemplated by this prospectus supplement and the accompanying prospectus may not be made in that Relevant Member State except that an offer to the public in that Relevant Member State of any common shares may be made at any time under the following exemptions under the Prospectus Directive, if they have been implemented in that Relevant Member State:

(a) to any legal entity which is a “qualified investor” as defined in the Prospectus Directive;

S-56

(b) to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the underwriters or the underwriters nominated by us for any such offer; or

(c) in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of securities shall require us or any of the underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

For the purposes of this provision, the expression an “offer of securities to the public” in relation to any securities in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the securities to be offered so as to enable an investor to decide to purchase or subscribe the securities, as the same may be varied in that Relevant Member State by any measure implementing the Prospectus Directive in that Relevant Member State and the expression “Prospectus Directive” means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State), and includes any relevant implementing measure in the Relevant Member State and the expression “2010 PD Amending Directive” means Directive 2010/73/EU.

France

Neither this prospectus supplement, the accompanying prospectus nor any other offering material relating to the shares 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 common shares 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 common shares has been or will be:

n released, issued, distributed or caused to be released, issued or distributed to the public in France; or
n used in connection with any offer for subscription or sale of the common shares to the public in France.
Such offers, sales and distributions will be made in France only:

n 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;

n to investment services providers authorized to engage in portfolio management on behalf of third parties; or

n 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 common shares 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.

S-57

Israel

In the State of Israel this prospectus supplement and the accompanying prospectus shall not be regarded as an offer to the public to purchase securities under the Israeli Securities Law, 5728 - 1968, which requires a prospectus to be published and authorized by the Israel Securities Authority, if it complies with certain provisions of Section 15 of the Israeli Securities Law, 5728 - 1968, including, inter alia, if: (i) the offer is made, distributed or directed to not more than 35 investors, subject to certain conditions, or the Addressed Investors; or (ii) the offer is made, distributed or directed to certain qualified investors defined in the First Addendum of the Israeli Securities Law, 5728 - 1968, subject to certain conditions, or the Qualified Investors. The Qualified Investors shall not be taken into account in the count of the Addressed Investors and may be offered to purchase securities in addition to the 35 Addressed Investors. Our company has not and will not take any action that would require it to publish a prospectus in accordance with and subject to the Israeli Securities Law, 5728 - 1968. We have not and will not distribute this prospectus supplement or make, distribute or direct an offer to subscribe for our securities to any person within the State of Israel, other than to Qualified Investors and up to 35 Addressed Investors.

Qualified Investors may have to submit written evidence that they meet the definitions set out in of the First Addendum to the Israeli Securities Law, 5728 - 1968. In particular, we may request, as a condition to be offered securities, that Qualified Investors will each represent, warrant and certify to us or to anyone acting on our behalf: (i) that it is an investor falling within one of the categories listed in the First Addendum to the Israeli Securities Law, 5728 - 1968; (ii) which of the categories listed in the First Addendum to the Israeli Securities Law, 5728 - 1968 regarding Qualified Investors is applicable to it; (iii) that it will abide by all provisions set forth in the Israeli Securities Law, 5728 - 1968 and the regulations promulgated thereunder in connection with the offer to be issued securities; (iv) that the securities that it will be issued are, subject to exemptions available under the Israeli Securities Law, 5728 - 1968: (a) for its own account; (b) for investment purposes only; and (c) not issued with a view to resale within the State of Israel, other than in accordance with the provisions of the Israeli Securities Law, 5728 - 1968; and (v) that it is willing to provide further evidence of its Qualified Investor status. Addressed Investors may have to submit written evidence in respect of their identity and may have to sign and submit a declaration containing, inter alia, the Addressed Investor's name, address and passport number or Israeli identification number.

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 common shares 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

S-58

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

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 common shares 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

This prospectus supplement and the accompanying prospectus is only being distributed to, and is only directed at, persons in the United Kingdom that are qualified investors within the meaning of Article 2(1)(e) of the Prospectus Directive that are also (i) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended, or the Order, and/or (ii) high net worth entities falling within Article 49(2)(a) to (d) of the Order and other persons to whom it may lawfully be communicated, each such person being referred to as a relevant person.

This prospectus supplement, the accompanying prospectus and their contents are confidential and should not be distributed, published or reproduced (in whole or in part) or disclosed by recipients to any other persons in the United Kingdom. Any person in the United Kingdom that is not a relevant person should not act or rely on this document or any of its contents.

LEGAL MATTERS

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 McCarthy Tétrault LLP, Vancouver, British Columbia. The underwriters are being represented by Cooley LLP, San Diego and San Francisco, California. Blake, Cassels & Graydon LLP, Vancouver, British Columbia, is acting as Canadian counsel to the underwriters. The selling securityholders are being represented by Whalen LLP, Irvine, California, and McCullough O'Connor Irwin LLP, Vancouver, British Columbia, is acting as Canadian counsel to the selling securityholders. As of the date of this prospectus, the members and associates of Wilson Sonsini Goodrich & Rosati, Professional Corporation, as a group, own less than 1% of our outstanding securities, the partners and associates of McCarthy Tétrault LLP, as a group, own less than 1% of our outstanding securities, the partners and associates of Cooley LLP, as a group, own less than 1% of our outstanding securities, the partners and associates of Blake, Cassels & Graydon LLP, as a group, own less than 1% of our outstanding securities, the partners and associates of Whalen LLP, as a group, own less than 1% of our outstanding securities, and the partners and associates of McCullough O'Connor Irwin LLP, as a group, own less than 1% of our outstanding securities.

EXPERTS

KPMG LLP, independent registered public accounting firm, has audited our financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2015, as set forth in their report, which is incorporated by reference in this prospectus supplement and elsewhere in the registration statement. Our financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2015 are incorporated by reference in reliance upon the report of KPMG LLP, 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>. You may also read and copy any document we file at the SEC's Public Reference Room at 100 F Street, NE, Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the Public Reference Room. We also maintain a website at <http://www.xenon-pharma.com>. The information contained in, or that can be accessed through, our website is not part of this prospectus supplement.

We have filed with the SEC a registration statement under the Securities Act of 1933 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 at the address listed above. The registration statement and the documents referred to below under "Information Incorporated by Reference" are also available on our website, www.xenon-pharma.com. We have not incorporated by reference into this prospectus supplement the information on our website, and you should not consider it to be a part of this prospectus supplement.

INFORMATION INCORPORATED BY REFERENCE

The SEC allows us to incorporate by reference into this prospectus supplement certain 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, 2015, filed with the SEC on March 8, 2016;

the information specifically incorporated by reference into the Annual Report from our definitive proxy statement on Schedule 14A, filed with the SEC on April 27, 2016;

our Quarterly Reports on Form 10-Q for the fiscal quarters ended March 31, 2016 (filed with the SEC on May 10, 2016) and June 30, 2016 (filed with the SEC on August 3, 2016);

our Current Reports on Form 8-K filed with the SEC on March 9, 2016, March 11, 2016, March 31, 2016, and June 3, 2016, respectively; 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. Neither we nor the selling securityholders have 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) 484-3300

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.

S-61

PROSPECTUS

\$150,000,000

Xenon Pharmaceuticals Inc.

Common Shares

Preferred Shares

Warrants

Units

4,394,175 Common Shares

Offered by Selling Securityholders

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, up to an aggregate amount of \$150,000,000.

In addition, selling securityholders to be named in a prospectus supplement may from time to time offer and sell up to 4,394,175 of our common shares. We will not receive any of the proceeds from the sale of our common shares by the selling securityholders.

This prospectus provides a general description of the securities we may offer. Each time we or any of the selling securityholders offer and sell securities, we or such selling securityholders will provide specific terms of the securities offered and, if applicable, the selling securityholders, 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 or the selling securityholders 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 December 4, 2015, the last reported sale price of our common shares on NASDAQ was \$9.05 per share. 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.

We are an “emerging growth company” as defined under the federal securities laws and, as such, have elected to comply with certain reduced public company reporting requirements.

INVESTING IN OUR SECURITIES INVOLVES SIGNIFICANT RISKS. YOU SHOULD REVIEW CAREFULLY THE “RISK FACTORS” ON PAGE 4 OF THIS PROSPECTUS AND IN THE APPLICABLE PROSPECTUS SUPPLEMENT BEFORE INVESTING 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 January 5, 2016.

Table of Contents

	Page
<u>About this Prospectus</u>	1
<u>Prospectus Summary</u>	2
<u>Risk Factors</u>	4
<u>Special Note Regarding Forward-Looking Statements</u>	4
<u>Ratio of Earnings to Fixed Charges and Preference Dividends</u>	4
<u>Use of Proceeds</u>	4
<u>Description of Share Capital</u>	5
<u>Description of the Warrants</u>	9
<u>Description of the Units</u>	10
<u>Selling Securityholders</u>	11
<u>Plan of Distribution</u>	11
<u>Material Income Tax Considerations</u>	13
<u>Legal Matters</u>	13
<u>Experts</u>	13
<u>Where You Can Find More Information</u>	13
<u>Information Incorporated by Reference</u>	14

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the United States Securities and Exchange Commission, or the SEC, using a “shelf” registration process. Under this shelf process, we may, from time to time, sell any combination of the securities described in this prospectus in one or more offerings up to an aggregate dollar amount of \$150,000,000. In addition, the selling securityholders may from time to time sell up to an aggregate amount of 4,394,175 of our common shares in one or more offerings. This prospectus provides you with a general description of the securities we or the selling securityholders may offer.

Each time we or the selling securityholders sell securities, we will provide a prospectus supplement that will contain specific information about the terms of that 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 public offering price; 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.

References in this prospectus to the “company,” “we,” “us” and “our” and similar terms or “Xenon” refer to Xenon Pharmaceuticals Inc.

PROSPECTUS SUMMARY

This summary description about us and our business highlights selected information contained elsewhere in this prospectus or incorporated in this prospectus by reference. This summary does not contain all of the information you should consider before deciding to invest in our securities. You should carefully read this entire prospectus and any applicable prospectus supplement, 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” on page 4 and incorporated by reference to our annual report on Form 10-K and our quarterly reports on Form 10-Q, and any amendments thereto.

Overview

We are a clinical-stage biopharmaceutical company discovering and developing a pipeline of differentiated therapeutics for orphan indications that we intend to commercialize on our own, and for larger market indications that we intend to partner with global pharmaceutical companies. We have built a core enabling discovery platform for the discovery of validated drug targets by studying rare human diseases with extreme traits, including diseases caused by mutations in ion channels, known as channelopathies. We have an integrated platform that includes in-house capabilities for human genetics, small molecule drug discovery, as well as preclinical and clinical development.

Our business was founded on our proprietary discovery platform, which we refer to as Extreme Genetics. Extreme Genetics involves the study of families where individuals exhibit inherited severe traits, or phenotypes. By identifying and characterizing single-gene defects responsible for these phenotypes, we gain insights into human disease biology to better select targets for therapeutic intervention. Our Extreme Genetics discovery platform has yielded the first approved gene therapy product in the European Union, or the EU, and a broad development pipeline and multiple pharmaceutical partnerships. We believe that our Extreme Genetics discovery platform enhances the likelihood of discovering a drug target that has a major effect in humans. From these discoveries, we can gain an improved understanding of how a drug that modulates the target might act when given to a human.

Our pharmaceutical partners include Teva Pharmaceutical Industries, Ltd., or Teva (through its subsidiary, Ivax International GmbH), Genentech, Inc., or Genentech, and Merck & Co., Inc., or Merck (through its affiliate, Essex Chemie AG). Our pharmaceutical collaborations have generated in aggregate over \$155.0 million in non-equity funding to date with the potential to provide us with over \$1.0 billion in future milestone payments, as well as royalties and co-promotion income on product sales.

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 no subsidiaries. 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. We have included our website address as an inactive textual reference only.

“Xenon,” the Xenon logo, “Extreme Genetics” 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, including “Glybera®,” which is the property of uniQure. 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.

Implications of Being an Emerging Growth Company

We qualify as an “emerging growth company” as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. An emerging growth company may take advantage of relief from certain reporting requirements and other burdens that are otherwise applicable generally to public companies. As an emerging growth company:

- we have availed ourselves of the exemption from the requirement to obtain an attestation and report from our auditors on the assessment of our internal control over financial reporting pursuant to the Sarbanes-Oxley Act of 2002;
- we have provided and will continue to provide less extensive disclosure about our executive compensation arrangements; and
- we have not required and will not require shareholder non-binding advisory votes on executive compensation or golden parachute arrangements.

We may use these provisions until the last day of our fiscal year following the fifth anniversary of our initial public offering. However, if certain events occur prior to the end of such five-year period, including if we become a “large accelerated filer,” our annual gross revenues exceed \$1.0 billion or we issue more than \$1.0 billion of non-convertible debt in any three-year period, we will cease to be an emerging growth company prior to the end of such five-year period. We may choose to take advantage of some but not all of these reduced burdens. To the extent that we take advantage of these reduced burdens, the information that we provide securityholders may be different than you might obtain from other public companies in which you hold equity interests.

The Securities We May Offer

We may offer up to \$150,000,000 of common shares, preferred shares, warrants and/or units in one or more offerings and in any combination. In addition, the selling securityholders may sell up to 4,394,175 common shares from time to time in one or more offerings. This prospectus provides you with a general description of the securities we and the selling securityholders may offer. A prospectus supplement, which we will provide each time we or the selling securityholders offer securities, will describe the specific amounts, prices and terms of these securities.

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, 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 preferences of each series of 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. There are currently no preferred

shares outstanding.

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.

-3-

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,” in our Annual Report on Form 10-K for the fiscal year ended December 31, 2014 and “Part II—Item 1A—Risk Factors” in our Quarterly Reports on Form 10-Q, and any amendments thereto, all of which are incorporated herein by reference, and 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 may constitute forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. The words “aim,” “anticipate,” “assume,” “believe,” “contemplate,” “continue,” “could,” “due,” “estimate,” “goal,” “intend,” “may,” “objective,” “plan,” “predict,” “positioned,” “potential,” “seek,” “should,” “target,” “will,” “would” and expressions and variations thereof are intended to identify forward-looking statements, but are not the exclusive means of identifying such statements. Those statements may appear in this prospectus, any accompanying prospectus supplement and the documents incorporated herein and therein by reference, particularly in the sections entitled “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 Xenon and 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.

RATIO OF EARNINGS TO FIXED CHARGES AND PREFERENCE DIVIDENDS

Any time preferred shares are offered pursuant to this prospectus, we will provide a table setting forth our ratio of earnings to fixed charges and preference dividends on a historical basis in the applicable prospectus supplement, if required.

USE OF PROCEEDS

Unless otherwise indicated in the prospectus supplement, we will use the net proceeds from the sale of securities offered by us pursuant to this prospectus (i) to fund preclinical and clinical development of our product candidates; (ii) to fund genetic research using our Extreme Genetics discovery platform and to fund ion channel drug discovery activities; and (iii) for general corporate purposes, which may include working capital, capital expenditures, and other corporate expenses.

We may also use a portion of the net proceeds in connection with any exercise of co-development or co-promotion rights under our collaborations; however, no such rights are currently exercisable. In addition, we may also use a portion of the net proceeds to acquire, license and invest in complementary products, technologies or businesses; however, we currently have no agreements or commitments to complete any such transactions.

The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including cash flows from operations, the anticipated growth of our business, the progress of our development and commercialization efforts and the status and results of our clinical trials, as well as results from any ongoing collaborations and additional collaborations that we may enter into with third parties and any unforeseen cash needs. As a result, unless otherwise indicated in the prospectus supplement, our management will have broad discretion to allocate the net proceeds of the offerings. More detailed information regarding use of proceeds will be described in the applicable prospectus supplement.

We will not receive any proceeds from the sale of our common shares by the selling securityholders.

DESCRIPTION OF SHARE CAPITAL

General

The following is a summary of the material rights of our common shares and preferred shares, as contained in our articles and by-laws. This summary is not a complete description of the share rights associated with our common shares and preferred shares. For more detailed information, please see our articles and by-laws, which are filed as exhibits to our quarterly report on Form 10-Q for the period ended September 30, 2014, as filed on December 15, 2014.

Our authorized share capital consists of an unlimited number of common shares, each without par value, and an unlimited number of preferred shares, issuable in series, each without par value. Our board of directors is authorized, without shareholder approval except as required by the listing standards of The NASDAQ Global Market, to issue additional shares of our common shares or preferred shares.

Common Shares

Outstanding Shares

As of September 30, 2015, we had 14,344,267 common shares outstanding, held by approximately 196 holders of record.

As of September 30, 2015, we had outstanding options to purchase an aggregate of 1,637,174 common shares pursuant to our equity plans, at a weighted average exercise price of \$6.83 per common share. As of September 30, 2015, 149,492 common shares remain available for future grant or issuance under our 2014 Equity Incentive Plan.

Voting Rights

The holders of our common shares are entitled to one vote for each common share held on all matters submitted to a vote of the shareholders, including the election of directors. Our articles and by-laws do not provide for cumulative voting rights. Because of this, the holders of a plurality of the common shares entitled to vote in any election of directors can elect all of the directors standing for election, if they should so choose.

Dividends

Subject to priority rights that may be applicable to any then outstanding preferred shares, holders of our common shares are entitled to receive dividends, as and when declared by our board of directors in their absolute discretion out of legally available funds.

Liquidation

In the event of our liquidation, dissolution or winding up, holders of our 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.

Rights and Preferences

Holders of common shares have no pre-emptive or conversion rights and our common shares have no provisions for redemption or repurchase for cancellation, surrender or sinking or purchase funds. There are no provisions in our articles or by-laws requiring holders of common shares to contribute additional capital. The rights, preferences and privileges of the holders of common shares are subject to and may be adversely affected by, the rights of the holders of any series of preferred shares that we may designate and issue in the future.

-5-

Fully Paid and Nonassessable

All of our outstanding common shares are fully paid and nonassessable. Our board of directors has the authority to issue, without further action by our shareholders, additional common shares.

Preferred Shares

As of September 30, 2015, we had no preferred shares outstanding. Our board of directors has the authority to issue, without further action by our shareholders, an unlimited number of preferred shares, issuable in one or more series, and subject to the provisions of the CBCA, to fix such rights, preferences, privileges, restrictions and conditions thereon, including dividend and voting rights, as our board of directors may determine, and such rights, preferences and privileges, including dividend rights, voting rights and rights relating to the distribution of our assets in the event of liquidation, dissolution or winding up of our affairs, whether, voluntary or involuntary, or any other distribution of our assets among our shareholders for the purpose of winding up our affairs, may be superior to those of our common shares. The issuance of preferred shares, while providing flexibility in connection with possible acquisitions and other corporate purposes, could adversely affect the voting power of holders of common shares and the likelihood that such holders will receive dividend payments and payments upon liquidation. In addition, the issuance of preferred shares could, among other things, have the effect of delaying, deferring or preventing a change in control of our company or other corporate action and could adversely affect the market price of our common shares and the voting and other rights of the holders of our common shares.

Registration Rights

Under our amended and restated investor rights agreement, as amended, the holders of approximately 4,394,175 common shares or their transferees have the right to require us to register the offer and sale of their common shares, or to include their common shares in any registration statement we file, in each case as described below.

Demand Registration Rights

The holders of a majority of our common shares having registration rights have the right to demand that we file a registration statement for the offer and sale of at least such number of common shares, or a lesser amount if the anticipated offering proceeds would exceed CAD\$5,000,000, subject to specified limitations. We are only obligated to effect two registrations in connection with the exercise of demand registration rights. These registration rights are subject to specified conditions and limitations, including the right of the underwriters to limit the number of common shares included in any such registration under certain circumstances and our ability to defer the filing of a registration statement with respect to an exercise of such demand registration rights for up to 90 days under certain circumstances.

Form S-3 Registration Rights

Each holder of common shares having registration rights has the right to demand that we file a registration statement on Form S-3 so long as the aggregate amount of common shares to be offered and sold under such registration statement on Form S-3 is at least CAD\$500,000. We are not obligated to file any registration statements within 180 days following the effective date of a registration pertaining to a public offering or to effect more than two registrations on Form S-3 in any 12-month period. These registration rights are subject to specified conditions and limitations, including our ability to defer the filing of a registration statement with respect to an exercise of such Form S-3 registration rights for up to 90 days under certain circumstances.

Piggyback Registration Rights

If we propose to register the offer and sale of any of our securities under the Securities Act either for our own account or for the account of other shareholders, a shareholder with registration rights will have the right, subject to certain exceptions, to include their common shares in the registration statement. These registration rights are subject to specified conditions and limitations, including the right of the underwriters to limit the number of common shares included in any such registration statement under certain circumstances, but not below 25% of the total number of common shares covered by the registration statement.

Expenses of Registration

We will pay all expenses relating to any demand registrations, Form S-3 registrations and piggyback registrations, other than underwriting discounts and selling commissions.

-6-

Termination

The registration rights terminate upon the earliest of (1) the date that is four years after the closing of our initial public offering and (2) as to a given holder of registration rights, if (a) we are subject to the public company reporting requirements of the Securities Exchange Act of 1934, (b) such holder holds less than 1% of our outstanding common shares and (c) such holder can sell all of such holder's registrable securities in a three month-period pursuant to Rule 144 promulgated under the Securities Act.

Corporate Governance

Under the CBCA, we are required to hold a general meeting of our shareholders at least once every year at a time and place determined by our board of directors, provided that the meeting must not be held later than 15 months after the preceding annual general meeting and no later than six months after the end of the preceding financial year. The CBCA requires that meetings of shareholders shall be held at any place within Canada as our board of directors may from time to time determine. A notice to convene a meeting, specifying the date, time and location of the meeting must be sent to shareholders, to each director and the auditor not less than 21 days prior to the meeting or such other minimum period as required by the applicable securities laws. Under the CBCA, shareholders entitled to notice of a meeting may waive or reduce the period of notice for that meeting, provided applicable securities laws requirements are met.

Under the CBCA, all business transacted at a special meeting of shareholders and all business transacted at an annual meeting of shareholders, except consideration of the financial statements, auditor's report, election of directors and re-appointment of the incumbent auditor, is deemed to be special business. Notice of a meeting of shareholders at which special business is to be transacted shall state (a) the nature of that business in sufficient detail to permit the shareholder to form a reasoned judgment thereon; and (b) the text of any special resolution to be submitted to the meeting.

Under the CBCA, our board of directors has the power at any time to call a special meeting of our shareholders. In addition, the holders of not less than 5% of our shares that carry the right to vote at a meeting sought to be held can also requisition our board of directors to call a meeting of our shareholders for the purposes stated in the requisition. If our board of directors does not call the meeting within 21 days after receiving the requisition, our shareholders can call the meeting and the expenses reasonably incurred by such shareholders in requisitioning, calling and holding the meeting must be reimbursed by us.

Those entitled to vote at a meeting are entitled to attend meetings of our shareholders. Every shareholder entitled to vote may appoint a proxyholder to attend the meeting in the manner and to the extent authorized and with the authority conferred by the proxy. Directors, auditors, legal counsels, secretary (if any), and any other persons invited by the chair of the meeting or with the consent of those at the meeting are entitled to attend any meeting of our shareholders but will not be counted in quorum or be entitled to vote at the meeting unless he or she or it is a shareholder or proxyholder entitled to vote at the meeting.

Certain Takeover Bid Requirements

Unless such offer constitutes an exempt transaction, an offer made by a person, an "offeror", to acquire outstanding shares of a Canadian entity that, when aggregated with the offeror's holdings (and those of persons or companies acting jointly with the offeror), would constitute 20% or more of the outstanding shares in a class, would be subject to the take-over provisions of Canadian securities laws. The foregoing is a limited and general summary of certain aspects of applicable securities law in the provinces and territories of Canada, all in effect as of the date hereof.

In addition to those takeover bid requirements noted above, the acquisition of our shares may trigger the application of statutory regimes including among others, the Investment Canada Act (Canada) and the Competition Act (Canada).

Limitations on the ability to acquire and hold our common shares may be imposed by the Competition Act (Canada). This legislation permits the Commissioner of Competition, or the Commissioner, to review any acquisition of control over or of a significant interest in us. This legislation grants the Commissioner jurisdiction, for up to one year, to challenge this type of acquisition before the Canadian Competition Tribunal on the basis that it would, or would be likely to, substantially prevent or lessen competition in any market in Canada.

This legislation also requires any person who intends to acquire our common shares to file a notification with the Canadian Competition Bureau if certain financial thresholds are exceeded and if that person (and their affiliates) would hold more than 20% of our common shares. If a person already owns 20% or more of our common shares, a notification must be filed when the acquisition of additional shares would bring that person's holdings to over 50%. Where a notification is required, the legislation prohibits completion of the acquisition until the expiration of a statutory waiting period, unless the Commissioner provides written notice that the acquisition will not be challenged.

-7-

There is no limitation imposed by Canadian law or our articles on the right of non-residents to hold or vote our common shares, other than those imposed by the Investment Canada Act.

The Investment Canada Act requires any person that is a “non-Canadian” (as defined in the Investment Canada Act) who acquires control of an existing Canadian business, where the acquisition of control is not a reviewable transaction, to file a notification with Industry Canada. The Investment Canada Act generally prohibits the implementation of a reviewable transaction unless, after review, the relevant minister is satisfied that the investment is likely to be of net benefit to Canada. Under the Investment Canada Act, the acquisition of control of us (either through the acquisition of our common shares or all or substantially all our assets) by a non-Canadian investor who is a World Trade Organization member country investor, including a U.S. investor, but not a state-owned enterprise, would be reviewable only if our enterprise value (as determined pursuant to the Investment Canada Act) exceeds CAD\$600.0 million (which threshold will rise to CAD\$800.0 million starting on April 24, 2017 and CAD\$1.0 billion starting on April 24, 2019, and thereafter this threshold will increase on the basis of a prescribed formula in the Investment Canada Act to reflect changes in the Canadian gross domestic product). If the acquisition of control of us is by a state-owned enterprise that is a non-Canadian who is a World Trade Organization member country investor, including a U.S. investor, the acquisition of control would be reviewable only if the value of our assets was equal to or greater than a specified amount which is CAD\$369.0 million for 2015. The threshold amount is subject to an annual adjustment on the basis of a prescribed formula in the Investment Canada Act to reflect changes in Canadian gross domestic product.

The acquisition of a majority of the voting interests of an entity is deemed to be acquisition of control of that entity. The acquisition of less than a majority but one-third or more of the voting shares of a corporation or an equivalent undivided ownership interest in the voting shares of a corporation is presumed to be an acquisition of control of that corporation unless it can be established that, on the acquisition, the corporation is not controlled in fact by the acquirer through the ownership of voting shares. The acquisition of less than one-third of the voting shares of a corporation is deemed not to be an acquisition of control of that corporation. Certain transactions in relation to our common shares would be exempt from review by the Investment Canada Act including:

- the acquisition of our common shares by a person in the ordinary course of that person’s business as a trader or dealer in securities;
- the acquisition of control of us in connection with the realization of security granted for a loan or other financial assistance and not for any purpose related to the provisions of the Investment Canada Act; and
- the acquisition of control of us by reason of an amalgamation, merger, consolidation or corporate reorganization following which ultimate direct or indirect control in fact of us, through the ownership of our voting shares, remains unchanged.

Under the new national security regime in the Investment Canada Act, review on a discretionary basis may also be undertaken by the federal government in respect of a much broader range of investments by a non-Canadian to “acquire, in whole or in part, or to establish an entity carrying on all or any part of its operations in Canada.” The relevant test is whether such an investment by a non-Canadian could be “injurious to national security.” The minister responsible for the Investment Canada Act has broad discretion to determine whether an investor is a non-Canadian and may be subject to national security review. Review on national security grounds is at the discretion of the federal government and may occur on a pre- or post-closing basis.

There is no law, governmental decree or regulation in Canada that restricts the export or import of capital or which would affect the remittance of dividends or other payments by us to non-Canadian holders of our common shares or preferred shares, other than withholding tax requirements.

Neither our articles nor by-laws contain any change of control limitations with respect to a merger, acquisition or corporate restructuring that involves us.

This summary is not a comprehensive description of relevant or applicable considerations regarding such requirements and, accordingly, is not intended to be, and should not be interpreted as, legal advice to any prospective purchaser and no representation with respect to such requirements to any prospective purchaser is made. Prospective investors should consult their own Canadian legal advisors with respect to any questions regarding securities law in the provinces and territories of Canada.

-8-

Actions Requiring a Special Majority

Under the CBCA, certain corporate actions require the approval of a special majority of shareholders, meaning holders of shares representing not less than 66 % of those votes cast in respect of a shareholder vote addressing such matter. Those items requiring the approval of a special majority generally relate to fundamental changes with respect to our business, and include among others, resolutions: (i) amending our articles; (ii) approving an amalgamation; (iii) approving a continuance; and (iv) providing for a sale, lease or exchange of all or substantially all of our property.

Advance Notice Procedures and Shareholder Proposals

Under the CBCA, shareholders may make proposals for matters to be considered at the annual general meeting of shareholders. Such proposals must be sent to us in advance of any proposed meeting by delivering a timely written notice in proper form to our registered office in accordance with the requirements of the CBCA. The notice must include information on the business the shareholder intends to bring before the meeting.

In addition, our by-laws require that shareholders provide us with advance notice of their intention to nominate any persons, other than those nominated by management, for election to our board of directors at a meeting of shareholders.

These provisions could have the effect of delaying until the next shareholder meeting the nomination of certain persons for director that are favored by the holders of a majority of our outstanding voting securities.

Ownership and Exchange Controls

There is currently no law, governmental decree or regulation in Canada that restricts the export or import of capital, or which would affect the remittance of dividends, interest or other payments by us to non-resident holders of our common shares, other than withholding tax requirements.

There is currently no limitation imposed by Canadian law or our articles or by-laws on the right of non-residents to hold or vote our common shares, other than those imposed by the Investment Canada Act and the Competition Act (Canada). These acts will generally not apply except where a control of an existing Canadian business or company, which has Canadian assets or revenue over a certain threshold, is acquired and will not apply to trading generally of securities listed on a stock exchange.

Transfer Agent and Registrar

The transfer agent and registrar for our common shares is American Stock Transfer & Trust Company, LLC, or AST. The transfer agent and registrar's address is 6201 15th Avenue, Brooklyn, NY 11219. The transfer agent's telephone number is (800) 937-5449. Additionally, in compliance with the CBCA, we have retained CST Trust Company, an affiliate of AST, to act as our Canadian transfer agent and registrar. CST Trust Company's address is 1066 West Hastings Street, Vancouver, BC V6E 3X1, and its telephone number is (604) 235-3703.

Listing

Our common shares are listed on NASDAQ under the symbol "XENE."

DESCRIPTION OF THE WARRANTS

We may issue warrants for the purchase of our preferred shares or common shares, or any combination thereof. Warrants may be issued independently or together with our preferred shares or common shares and may be attached to or separate from any offered securities. Each series of warrants will be issued under a separate warrant agreement to be entered into between us and a bank or trust company, as warrant agent. The warrant agent will act solely as our agent in connection with the warrants. The warrant agent will not have any obligation or relationship of agency or trust for or with any holders or beneficial owners of warrants.

Equity Warrants

The prospectus supplement relating to a particular series of warrants to purchase our common shares or preferred shares will describe the terms of the warrants, including the following:

- the title of the warrants;
- the offering price for the warrants;
- the aggregate number of warrants offered;

-9-

- the designation and terms of the common shares or preferred shares that may be purchased 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;
- the dates on which the right to exercise the warrants shall commence and expire;
- if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;
- 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 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 comprised of one or more of the other classes of securities 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. Thus, the holder of a unit will have the rights and obligations of a holder of each included security. The units may be issued under unit agreements to be entered into between us and a unit agent, as detailed in the prospectus supplement relating to the units being offered. The prospectus supplement will describe:

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

The descriptions of the units in this prospectus and in any prospectus supplement are summaries of the material provisions of the applicable agreements. These descriptions do not restate those agreements in their entirety and may not contain all the information that you may find useful. We urge you to read the applicable agreements because they, and not the summaries, define your rights as holders of the units. For more information, please review the forms of the relevant agreements, which will be filed with the SEC promptly after the offering of units and will be available as described in the section titled "Where You Can Find More Information."

SELLING SECURITYHOLDERS

This prospectus also relates to the possible resale by certain of our shareholders, who we refer to in this prospectus as the “selling securityholders,” of up to an aggregate maximum amount of 4,394,175 of our common shares that were issued and outstanding prior to the original filing date of the registration statement of which this prospectus forms a part. The selling securityholders originally acquired our common shares that may be offered and sold pursuant to this prospectus and the related prospectus supplement through several private placements of our convertible preferred shares prior to our initial public offering, which convertible preferred shares were converted into common shares in connection with our initial public offering. Information about the selling securityholders, where applicable, including their identities and the number of common shares to be registered on their behalf, will be set forth in the applicable prospectus supplement, documents incorporated by reference or in a free writing prospectus we file with the SEC. The selling securityholders will not sell any common shares pursuant to this prospectus until we have identified such selling securityholders and the shares being offered for resale by such selling securityholders in a prospectus supplement. However, the selling securityholders may sell or transfer all or a portion of their common shares pursuant to any available exemption from the registration requirements of the Securities Act and, if applicable, the prospectus requirement under Canadian securities laws.

PLAN OF DISTRIBUTION

We and/or the selling securityholders, if applicable, 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 underwriting discounts, commissions and other items constituting underwriters' compensation;
- any initial public offering price;
- any discounts or concessions allowed or reallocated or paid to dealers; and
- any commissions paid to agents.

We may engage in at-the-market offerings into an existing trading market in accordance with Rule 415(a)(4). Any at-the-market offering will be through an underwriter or underwriters acting as principal or agent for us.

Sale 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. The underwriters may change from time to time any initial public

offering price and any discounts or concessions allowed or reallocated 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.

-11-

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 or the selling securityholders 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 or the selling securityholders 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 or the selling securityholders. 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 or the selling securityholders 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.

Market Making, Stabilization and Other Transactions

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 or the selling securityholders 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.

Any underwriter may also engage in stabilizing transactions, syndicate covering transactions and penalty bids in accordance with Rule 104 under the Securities Exchange Act of 1934, as amended. Stabilizing transactions involve bids to purchase the underlying security in the open market for the purpose of pegging, fixing or maintaining the price of the securities. Syndicate covering transactions involve purchases of the securities in the open market after the distribution has been completed in order to cover syndicate short positions.

Penalty bids permit the underwriters to reclaim a selling concession from a syndicate member when the securities originally sold by the syndicate member are purchased in a syndicate covering transaction to cover syndicate short positions. Stabilizing transactions, syndicate covering transactions and penalty bids may cause the price of the securities to be higher than it would be in the absence of the transactions. The underwriters may, if they commence these transactions, discontinue them at any time.

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 or the selling securityholders may also make sales through the Internet or through other electronic means. Since we or the selling securityholders 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.

-12-

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 or the selling securityholders against certain liabilities, including liabilities under the Securities Act. Agents, dealers, and underwriters may engage in transactions with or perform services for us in the ordinary course of their businesses.

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 McCarthy Tétrault LLP, Vancouver, British Columbia. As of the date of this prospectus, the members and associates of Wilson Sonsini Goodrich & Rosati, Professional Corporation, as a group, own less than 1% of our outstanding securities and the partners and associates of McCarthy Tétrault LLP, as a group, own less than 1% of our outstanding securities.

EXPERTS

The financial statements of Xenon Pharmaceuticals Inc. as of December 31, 2014 and 2013, and for each of the years in the three-year period ended December 31, 2014, 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. KPMG LLP have confirmed with respect to Xenon Pharmaceuticals Inc., that they are independent within the meaning of the relevant rules and related interpretations

prescribed by the relevant professional bodies in Canada and any applicable legislation or regulations and also that they are independent accountants with respect to the company under all relevant US professional and regulatory standards.

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>. You may also read and copy any document we file at the SEC's Public Reference Room at 100 F Street, NE, Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the Public Reference Room. 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.

-13-

We have filed with the SEC a registration statement under the Securities Act of 1933 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 at the address listed 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.

INFORMATION INCORPORATED BY REFERENCE

The SEC allows us to incorporate by reference into this prospectus certain 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, and information that we file later with the SEC will automatically update and supersede information contained in this prospectus and any accompanying prospectus supplement. We incorporate by reference the documents listed below that we have previously filed with the SEC:

- our Annual Report on Form 10-K for the fiscal year ended December 31, 2014, filed with the SEC on March 12, 2015;
- 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 March 30, 2015;
- our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2015, June 30, 2015 and September 30, 2015, filed with the SEC on May 12, 2015 (as amended on August 13, 2015), August 13, 2015 and November 10, 2015, respectively;
- our Current Reports on Form 8-K filed with the SEC on February 23, March 16, March 23, May 5, May 22, July 1 and August 13, 2015, respectively; 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.

We also incorporate by reference into this prospectus 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 is deemed to be modified or superseded for purposes of this prospectus 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. Neither we nor the selling securityholders have authorized anyone else to provide you with different information. You should not assume that the information in this prospectus is accurate as of any date other than the date of this prospectus or the date of the documents incorporated by reference in this prospectus.

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) 484-3300

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.

Shares

Common Shares

PROSPECTUS SUPPLEMENT

Joint Book-Running Managers

Jefferies

Stifel

Guggenheim Securities

September , 2016