

Confidential Draft Submission Amendment No. 1 submitted to the Securities and Exchange Commission on September 25, 2013.
This draft registration statement has not been filed publicly with the Securities and Exchange Commission
and all information contained herein remains confidential.

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549**

**FORM S-1
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933**

XENON PHARMACEUTICALS INC.

(Exact name of registrant as specified in its charter)

Canada
(State or other jurisdiction of incorporation or organization)

2834
(Primary Standard Industrial Classification Code Number)

98-0661854
(I.R.S. Employer Identification Number)

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Canada
(604) 484-3300**

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

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Approximate date of commencement of proposed sale to the public: As soon as practicable after the effective date of this Registration Statement.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933 check the following box:

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer Accelerated filer Non-accelerated filer (Do not check if a smaller reporting company) Smaller reporting company

CALCULATION OF REGISTRATION FEE

| TITLE OF EACH CLASS OF SECURITIES TO BE REGISTERED | PROPOSED MAXIMUM AGGREGATE OFFERING PRICE ⁽¹⁾ | AMOUNT OF REGISTRATION FEE |
|--|--|----------------------------|
| Common Shares, no par value per share | \$ | \$ |

⁽¹⁾ Estimated solely for the purpose of calculating the amount of the registration fee in accordance with Rule 457(o) under the Securities Act of 1933, as amended. Includes shares that the underwriters have the option to purchase.

The registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the registrant shall file a further amendment that specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933, as amended, or until the Registration Statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

The information in this preliminary prospectus is not complete and may be changed. These securities may not be sold until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell these securities nor does it seek an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED _____, 2013

PRELIMINARY PROSPECTUS

Shares



Xenon Pharmaceuticals Inc. Common Shares

We are offering _____ of our common shares. This is our initial public offering and no public market currently exists for our common shares. We expect the initial public offering price to be between \$ _____ and \$ _____ per share.

We intend to apply to list our common shares on The NASDAQ Global Market under the symbol "XENE". We are an "emerging growth company" as defined by the Jumpstart Our Business Startups Act of 2012 and, as such, we have elected to comply with certain reduced public company reporting requirements for this prospectus and future filings.

Investing in our common shares involves a high degree of risk. See "[Risk Factors](#)" beginning on page 13 of this prospectus.

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

| | <u>PER SHARE</u> | <u>TOTAL</u> |
|---|------------------|--------------|
| Initial Public Offering Price | \$ _____ | \$ _____ |
| Underwriting Discounts and Commissions ⁽¹⁾ | \$ _____ | \$ _____ |
| Proceeds, before expenses, to us | \$ _____ | \$ _____ |

⁽¹⁾ The underwriters will also be reimbursed for certain expenses incurred in this offering. See "Underwriting" for details.

Delivery of the common shares purchased in this offering is expected to be made on or about _____, 2013. We have granted the underwriters an option for a period of 30 days to purchase up to _____ additional common shares. If the underwriters exercise the option in full, the total underwriting discounts and commissions will be \$ _____ and the total proceeds to us, before expenses, will be \$ _____.

Joint Book-Running Managers

Jefferies

Cowen and Company

Co-Managers

Wells Fargo Securities

RBC Capital Markets

Prospectus dated _____, 2013

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We and the underwriters have not authorized anyone to provide any information other than that contained in this prospectus or in any free writing prospectus prepared by or on behalf of us or to which we have referred you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We and the underwriters are not making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus is accurate only as of the date on the front cover of this prospectus. Our business, financial condition, results of operations and prospects may have changed since that date.

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Until [REDACTED], 2013, all dealers that effect transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to the dealers' obligation to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.

In this prospectus, unless otherwise specified or the context otherwise requires, all dollar amounts are expressed in U.S. dollars.

As of June 30, 2013, the exchange rate for the conversion of Canadian dollars into U.S. dollars was 0.9513, based on the Bank of Canada's noon buying rate for one U.S. dollar. Except as otherwise noted, all amounts referred to in this prospectus as "\$ [REDACTED], as converted" shall mean the U.S. dollar amount applying the conversion rate from Canadian dollars as of June 30, 2013.

PROSPECTUS SUMMARY

This summary highlights selected information contained elsewhere in this prospectus and is qualified in its entirety by the more detailed information and financial statements included elsewhere in this prospectus. It does not contain all of the information that may be important to you and your investment decision. You should carefully read this entire prospectus, including the matters set forth under “Risk Factors,” “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and our financial statements and related notes.

Unless the context requires otherwise, in this prospectus the terms “Xenon,” “we,” “us,” “our” and “our company” refer to Xenon Pharmaceuticals Inc.

Xenon Pharmaceuticals Inc.

Overview

We are a biopharmaceutical company focused on the development of novel medicines through the application of our proprietary discovery platform, which we refer to as Extreme Genetics. Our product candidates are based on genetic insights derived from our research of families where individuals exhibit severe traits, or phenotypes. By identifying and characterizing the single-gene defects responsible for such severe phenotypes, we gain valuable insights into their function in human biology and their potential as drug targets. Given that these targets are often involved in diseases beyond the rare genetic disorders in which they are first identified, we are developing proprietary product candidates to treat both orphan as well as more prevalent diseases.

Our Extreme Genetics discovery platform has enabled us to develop a pipeline including one approved product, three development-stage product candidates and four preclinical discovery programs. Of our three development-stage product candidates, XEN701 and the Nav1.7 inhibitor licensed to Genentech, Inc., or Genentech, are in preclinical development. Our platform has also yielded multiple collaborations with leading pharmaceutical companies such as Genentech, Merck Sharp & Dohme GmbH (formerly known as Merck Sharp & Dohme Research Ltd.), an affiliate of Merck & Co., Inc., or Merck, and Teva Pharmaceutical Industries Ltd., or Teva. These collaborations have generated in aggregate over \$140.0 million in non-equity funding to date with the potential to provide us with over \$1.0 billion in future milestone payments.

The following chart summarizes our current product pipeline:

| | Discovery | IND-Enabling | Phase 1 | Phase 2 | Phase 3 | Approved | Commercial Rights |
|---|-----------|--------------|---------|---------|---------|----------|--|
| Glybera LPLD | | | | | | | uniQure |
| XEN402 Erythrometalgia | | | | | | | Teva Xenon US Co-Promote Option |
| XEN402 Common pain indications | | | | | | | Teva Xenon US Co-Promote Option |
| XEN701 Anemia | | | | | | | Xenon |
| Nav1.7 Inhibitor Pain | | | | | | | Genentech |
| SCD1 Inhibitor Acne | | | | | | | Xenon |
| Target for Cardiovascular Disease | | | | | | | Merck |
| Selective Sodium Channel Modulators Dravel Syndrome | | | | | | | Xenon |
| New Pipeline Opportunities | | | | | | | Xenon |

Our Programs

Approved Product

Glybera: Glybera is a gene therapy approved in the European Union, or EU, in October 2012 for the treatment of a subset of patients with the orphan lipid disorder lipoprotein lipase deficiency, or LPLD. Specifically, it is intended to treat LPLD in patients with severe or multiple pancreatitis attacks, despite dietary fat restrictions. In collaboration with the University of British Columbia, or UBC, we demonstrated that a variant of the lipoprotein lipase, or LPL, gene called LPL^{S447X}, resulted in increased LPL enzyme activity leading to reduced triglyceride levels in humans. Glybera contains the LPL^{S447X} gene. Glybera was developed by our licensee, uniQure Biopharma B.V., or uniQure. In a clinical trial, a single administration of Glybera was demonstrated to reduce the incidence of acute pancreatitis over the two-year study period. Glybera is the first product whose active ingredient was derived from our platform to receive commercial approval and is the first gene therapy to be approved in the EU or North America. In July 2013, uniQure announced that it had entered into a partnership with Chiesi Farmaceutici S.p.A, or Chiesi, for the commercialization of Glybera in Europe and more than a dozen other countries including Brazil, China, Mexico and Russia. uniQure has also publicly disclosed that it is preparing to apply for regulatory approval of this product in the U.S., Canada and other markets. Glybera has received orphan drug designation in both the EU and the U.S. We understand that uniQure plans to file an Investigational New Drug application, or IND, with the U.S. Food and Drug Administration, or FDA, in the first half of 2014.

Product Candidates in Development

XEN402: XEN402 is a 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. To select our pain drug target, we discovered that the Nav1.7 protein is deficient in a rare genetic disorder known as congenital indifference to pain, or CIP, a condition where humans cannot feel pain. We have observed evidence of effect for XEN402 in four Phase 2 proof-of-concept clinical trials, including two trials in the orphan disease erythromelalgia, or EM, one trial in postherpetic neuralgia, or PHN, and one trial in dental pain. In December 2012, we entered into a collaborative development and license agreement with Teva through its subsidiary, Ivax International GmbH, or Ivax, pursuant to which we granted Teva an exclusive worldwide license to develop and commercialize XEN402. Prior to our entry into the collaborative development and license agreement with Teva, we submitted INDs to the FDA for oral XEN402 for the indication of dental pain (July 2009) and topical XEN402 for the indication of acute and chronic pain, including neuropathic and inflammatory pain (July 2010). In April 2013, we and Teva announced that XEN402 had received orphan designation from the FDA for the treatment of EM. We are working with the FDA on a regulatory strategy designed to support product approval. We expect to initiate the trial for XEN402 in EM and a Phase 2 trial for a non-orphan indication in 2014. Teva made an upfront payment to us of \$41.0 million, and we are eligible to receive potential milestone payments totaling in aggregate up to \$335.0 million, the majority of which relate to pre-commercial achievements. If XEN402 is approved, we are also eligible to receive royalties in the low teens to low twenties on net sales of the licensed products for the timeframe that such products are covered by the licensed patents and in certain other instances. We also have an option to co-promote products in the U.S. In collaboration with Teva, we are currently developing XEN402 as a topical product to treat the pain associated with EM as well as other, more common forms of pain.

XEN701: XEN701 is a selective antisense oligonucleotide compound designed to be subcutaneously administered and to inhibit the expression of the protein hepcidin in the body by interfering with the messaging function of its ribonucleic acid, or RNA. A compound that interferes with this messaging functioning can limit or prevent the cell from producing proteins. Generally, antisense oligonucleotide compounds are designed to selectively bind to and degrade RNA of a given gene and prevent that gene from producing proteins, including those identified with diseases. To select hepcidin as our anemia drug target, we identified mutations in genes underlying a rare genetic disorder of iron overload or excess known as juvenile

hemochromatosis, or JH. JH is caused by genetic deficiency of hepcidin protein. In anemia of chronic disease, or ACD, the converse is true. Elevated levels of hepcidin cause a restricted iron supply that results in anemia. XEN701 is currently in IND-enabling safety and toxicology studies and we expect to commence Phase 1 studies during the first half of 2014. Initially, our development strategy will focus on treating the anemia associated with chronic kidney disease or end-stage renal disease in niche populations where the use of erythropoietin stimulating agents, the current standard of care, is subject to a black box warning (the FDA's highest level of warning, indicating that a particular drug may lead to death or serious injury) or is contraindicated.

Selective Inhibitor of Nav1.7 for the Treatment of Pain: Chronic pain conditions such as severe cancer pain and neuropathic pain are generally recognized as unmet medical needs providing potential commercial opportunities for a new oral pain drug. Currently available pain drugs often have either a lack of meaningful pain relief or dose-limiting side effects for many patients. An orally administered selective Nav1.7 inhibitor could present a novel mechanism for the treatment of moderate to severe pain. In December 2011, we entered into a collaborative research and license agreement with Genentech and its affiliate, F. Hoffmann-La Roche Ltd, or Roche, to discover and develop inhibitors of Nav1.7 for the treatment of pain. A small-molecule preclinical product candidate was subsequently selected in 2013 for development and is currently in the IND-enabling stage.

Product Candidates in Discovery

We have multiple programs and product candidates in discovery including: (i) selective small-molecule inhibitors of the enzyme SCD1 for acne; (ii) selective small-molecule inhibitors of a target for cardiovascular disease pursuant to a collaboration with Merck; (iii) selective small-molecule sodium channel modulators for Dravet Syndrome, an orphan seizure disorder; and (iv) new pipeline opportunities focused on discovery of novel drug targets for pain.

Our Extreme Genetics Discovery Platform

Our Extreme Genetics discovery platform enables us to identify drug targets that may be more biologically relevant in humans. Our platform is built on the foundation of identifying and studying rare individuals and families with severe phenotypes to discover single-gene defects that have major biological effects in humans. By studying these individuals and families with severe phenotypes, we can obtain critical insights into the genes underlying these diseases and their related biology to develop promising product candidates. We therefore are able to initiate our drug discovery efforts with the advantage of having a greater understanding of the role of the drug target in human disease.

Our reliance on our Extreme Genetics discovery platform for target selection differs from other target selection methods commonly employed in the industry, such as *in vitro* cell biology and screening, tissue and differential expression studies, *in vitro* and animal based pharmacology and the use of animal models, such as gene knock-outs or animal transgenics. Some companies, however, do use human genetics to varying degrees to assist with target identification, such as approaches where larger populations of patients and controls are studied to define associations where a disease and single nucleotide polymorphisms, or SNPs, in certain genes are linked. While SNP associations allow the identifications of genes that show an association with a disease or may increase risk of disease, such associations differ from our Extreme Genetics discovery platform since they do not discover genes that are determinant or causal of a disease. By studying families with rare diseases where individuals present with severe phenotypes, we seek to isolate the genetic cause of such diseases. We then use this causal information as our primary methodology underlying our target discovery and selection.

Our Strategy

Our goal is to apply our Extreme Genetics discovery platform to build a sustainable and profitable biopharmaceutical company that discovers, develops and commercializes innovative therapeutics. Our key strategic initiatives include:

- ⁿ *Discovering Additional Novel Targets.* We are committed to expanding our network of clinical collaborations and access to families with severe phenotypes to identify novel targets for orphan and niche, as well as more prevalent, diseases.
- ⁿ *Expanding Our Proprietary Pipeline of Orphan and Niche Disease Product Candidates.* We will continue to develop product candidates for orphan and niche diseases. This focus may allow us to benefit from both a less costly and expedited development pathway and may provide us with potential commercial benefits, including market exclusivity and premium drug pricing. These benefits may allow us to retain a significantly larger share of the value of such product candidates, as it may be viable for us to develop these assets independently beyond Phase 2 proof-of-concept trials and potentially through commercialization.
- ⁿ *Developing Product Candidates for More Prevalent Diseases through Pharmaceutical Collaborations.* We plan to continue to partner product candidates for more prevalent diseases with pharmaceutical companies to access additional development and commercial resources, expertise and non-dilutive funding to enable the advancement of a broader and more diverse pipeline.
- ⁿ *Independently Commercializing Selected Products.* We intend to develop a specialized sales force in circumstances where we expect to be able to cost-effectively commercialize approved products in orphan and niche markets.

Strategic Alliances

We have implemented our business strategy by entering into multiple collaborations with leading pharmaceutical companies that have provided us with significant funding to date and with the potential for future milestone payments and royalty income.

Agreement with uniQure for Glybera

Effective August 2000, we entered into a sublicense and research agreement with Amsterdam Molecular Therapeutics, or AMT, pursuant to which we granted to AMT an exclusive, worldwide sublicense under certain intellectual property controlled by us to develop and commercialize technology and compounds related to the variant of LPL, called LPL^{S447X}. We collaborated with AMT and UBC on preclinical activities and thereafter AMT developed a LPL gene therapy product, Glybera, which contains this variant. Certain of AMT's assets, including the rights to the intellectual property covered by our agreement, were subsequently acquired by uniQure in April 2012. Under the terms of the agreement, we are eligible to receive mid single-digit royalties on net sales of the licensed products, for sales made by uniQure and its affiliates.

In July 2013, uniQure announced that it had granted Chiesi a sublicense to commercialize Glybera in Europe and more than dozen other countries, including Brazil, China, Mexico and Russia. With respect to uniQure's sublicense to Chiesi, we receive a percentage in the low twenties of all non-royalty compensation relating to the licensed technology or products that uniQure receives from Chiesi (for example upfront payments and milestone payments), a percentage in the low twenties of any royalties that uniQure receives from Chiesi based on sales of technology or products covered by the licensed patents, plus a mid single-digit percentage of certain further royalties that uniQure receives from Chiesi based on sales of the licensed technology or products after the expiration of all licensed patents covering the product.

Agreement with Teva for XEN402

In December 2012, we entered into a collaborative development and license agreement with Teva through its subsidiary, Ivax, pursuant to which we granted Teva an exclusive worldwide license to develop and commercialize certain products, including XEN402.

Under the terms of the agreement, Teva paid us an upfront fee of \$41.0 million. We are collaborating with Teva to further develop XEN402, and Teva is funding all development costs with respect to the licensed products. In addition, we are eligible to receive potential milestone payments totaling up to \$335.0 million, the majority of which relate to pre-commercial activities. If XEN402 is approved, we are also eligible to receive royalties in the low teens to low twenties on net sales of the licensed products for the timeframe that such products are covered by the licensed patents and in certain other instances.

We have an option to a minority co-promotion interest for products incorporating XEN402 in the U.S. Our co-promotion option is exercisable upon the filing of the first NDA with the FDA for a XEN402 product, and we will be obligated to pay an opt-in fee to Teva. If we exercise this option, we will be eligible to receive, in lieu of royalties with respect to such product sales in the U.S., a share of operating profits from such product sales in the U.S. that is equal to our percent interest of detailing activities and co-promotion expenses.

Agreement with Isis for XEN701

In November 2010, we entered into a collaboration and license agreement with Isis Pharmaceuticals, Inc., or Isis. Under this agreement, we received an option to obtain from Isis worldwide exclusive licenses to develop and commercialize antisense products targeting hepcidin and/or hemojuvelin, each of which is a validated target for anemia of chronic disease. We collaborated with Isis on research that led to the selection of XEN701 as the first drug to enter development under the collaboration.

In June 2013, we exercised our option and obtained an exclusive license to develop, manufacture and commercialize antisense products under the collaboration that target hepcidin. Upon the achievement of specific development and regulatory events, we are obligated to pay to Isis pre-commercial milestone payments totaling up to \$88.0 million and sales-based milestone payments totaling up to \$60.0 million. In addition, Isis is eligible to receive royalties in the single-digit range, on net sales of licensed products by us and our affiliates. If we sublicense XEN701 to a third party for development and/or commercialization, then Isis is eligible to receive a percentage of our sublicensing revenue, including milestone payments and royalties we may receive from any sublicensee in lieu of the remaining milestone payments and the royalties described above.

Agreement with Genentech for Selective Nav1.7 Inhibitors

In December 2011, we entered into a collaborative research and license agreement with Genentech to discover and develop small and large molecules that selectively inhibit the Nav1.7 sodium channel as well as companion diagnostics for the potential treatment of pain. Pursuant to this agreement, we granted Genentech a worldwide exclusive license to develop and commercialize compounds directed to Nav1.7 and products incorporating such compounds for all uses.

Under the terms of the agreement, Genentech paid us an upfront payment of \$10.0 million and we subsequently earned a \$5.0 million milestone payment for the selection of a development-stage candidate. In addition, we are eligible to receive pre-commercial and commercial milestone payments with respect to the licensed products totaling up to an additional \$621.0 million. We are also eligible to receive royalties based on net sales of the licensed products, which range from a mid single-digit percentage to ten percent for small-molecule inhibitors for the timeframe that such products are covered by the licensed patents and a low single-digit percentage thereafter, plus a single-digit percentage for large-molecule inhibitors of Nav1.7.

Agreement with Merck for Cardiovascular Disease

In June 2009, we entered into an exclusive collaborative research and option agreement with Merck, pursuant to which we conducted a research program to discover and develop novel small-molecule candidates for the potential treatment of cardiovascular disease. The collaborative research program ended in December 2012.

Under the agreement, Merck had the option to obtain an exclusive license under certain intellectual property controlled by us to develop and commercialize compounds and products directed to targets in the research program, which has now expired. In June 2012, Merck exercised its option to obtain such a worldwide exclusive license to develop and commercialize compound inhibitors of a target that was identified using our Extreme Genetics discovery platform. Through June 30, 2013, we have received milestone payments and an option fee totaling \$9.0 million, and we are eligible for further research, development and regulatory milestone payments of up to \$64.0 million for a product directed to such licensed target as well as royalties from the mid to high single-digit range.

We have an option to co-fund the Phase 1 and first Phase 2 clinical trials of product candidates licensed by Merck by paying Merck 50% of such development costs. Such co-funding option is available at the IND-filing stage for the applicable product candidate. If we exercise our co-funding option then the maximum eligible milestone amounts due to us increase to \$86.5 million and the royalties increase to the high single-digit to the sub-teen double-digit range.

For additional information about our business, please see the section of this prospectus captioned "Business."

Risks Associated with Our Business

Our ability to implement our current business strategy is subject to numerous risks, as more fully described in the section entitled "Risk Factors" immediately following this prospectus summary. These risks include, among others:

- ⌘ We have incurred significant losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future.
- ⌘ We have not generated any revenue from product royalties and may never be profitable.
- ⌘ We will likely need to raise additional funding, which may not be available on acceptable terms, if at all.
- ⌘ Our existing collaborations are important to our business, and future collaborations may also be important to us. If we are unable to maintain any of these collaborations, or if these collaborations are not successful, our business could be adversely affected.
- ⌘ 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.
- ⌘ 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.
- ⌘ We and our collaborators face substantial competition in the markets for our product candidate.
- ⌘ The novelty of gene therapy products and their lack of a commercial track record may hinder market acceptance of Glybera.
- ⌘ Our approach to drug discovery is unproven, and we do not know whether we will be able to develop any products of commercial value.
- ⌘ We could be unsuccessful in obtaining or maintaining adequate patent protection for one or more of our products or product candidates.

- ⁿ The limited patient population for orphan and niche indications may prevent us from accurately estimating the market opportunity for our product candidates or enrolling sufficient patients for our clinical trials.

For additional information about the risks we face, please see the section of this prospectus captioned "Risk Factors."

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:

- ⁿ a requirement to have only two years of audited financial statements and only two years of related management's discussion and analysis;
- ⁿ an exemption from compliance with the auditor attestation requirement on the effectiveness of our internal controls over financial reporting;
- ⁿ 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;
- ⁿ reduced disclosure about our executive compensation arrangements; and
- ⁿ 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:

- ⁿ the last day of the fiscal year during which we have total annual gross revenue of \$1.0 billion or more;
- ⁿ the last day of the fiscal year following the fifth anniversary of the completion of this offering;
- ⁿ the date on which we have, during the previous three-year period, issued more than \$1.0 billion in non-convertible debt; and
- ⁿ the date on which we are deemed to be a "large accelerated filer" under the Securities Exchange Act of 1934, 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).

We may choose to take advantage of some, but not all, of the available benefits under the JOBS Act. We have taken advantage of some reduced reporting requirements in this prospectus. Accordingly, the information contained herein may be different than the information you receive from other public companies in which you hold stock.

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. We may elect to use this extended transition period under the JOBS Act. If we do, our financial statements may not be comparable to the financial statements of issuers who are required to comply with the effective dates for new or revised accounting standards that are applicable to public companies.

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>. We are currently not a reporting issuer, or the equivalent, in any province or territory of Canada and our shares are not listed on any recognized Canadian stock exchange. The information contained in, or that can be accessed through, our website is not part of this prospectus.

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 as is the Xenon corporate name. 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 Biopharma B.V. Solely for convenience, trademarks and trade names referred to in this prospectus, including logos, artwork and other visual displays, may appear without the ® or ™ symbols, but such references are not intended to indicate in any way that we will not assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensor to these trademarks and trade names. We do not intend our use or display of other entities' trade names, trademarks or service marks to imply a relationship with, or endorsement or sponsorship of us by, any other entity.

THE OFFERING

| | |
|---|--|
| Common shares offered by us | common shares |
| Common shares to be outstanding after this offering | common shares (or additional common shares in full) if the underwriters exercise their option to purchase |
| Option to purchase additional common shares | We have granted the underwriters an option for 30 days from the date of this prospectus to purchase up to additional common shares. |
| Use of proceeds | We estimate that the net proceeds from this offering will be approximately \$ million, or approximately \$ million if the underwriters exercise in full their option to purchase additional common shares, at an assumed initial public offering price of \$ per share (the midpoint of the range set forth on the cover page of this prospectus), after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. We currently expect to use the net proceeds from this offering: (1) to fund genetic research, drug discovery and preclinical development activities using our Extreme Genetics discovery platform; (2) to fund our planned development of XEN701, including commencing and advancing a Phase 2b trial; (3) for future success-based milestone payments to current licensors including Isis, should we achieve such milestones; and (4) for working capital and general corporate purposes. We may also use a portion of the net proceeds in connection with any exercise of co-development or co-promotion rights under our strategic alliances; 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 transaction. See "Use of Proceeds." |

Proposed ticker symbol on The NASDAQ Global Market "XENE"

The number of common shares to be outstanding after this offering is based on 39,586,986 common shares outstanding as of June 30, 2013 and excludes the following:

- ⁿ 6,339,591 common shares issuable upon exercise of options outstanding as of June 30, 2013, at a weighted-average exercise price of CAD\$0.79 per common share, or \$0.75 per common share, as converted; and
- ⁿ common shares reserved for future issuance under share-based compensation plans, including common shares reserved for issuance under our 2013 Equity Incentive Plan, which will become effective on the day immediately prior to the date of the completion of this offering and any future automatic increase in common shares reserved for issuance under such plan, and 7,373,338 common shares reserved for issuance under our Amended and Restated Stock Option Plan as of June 30, 2013, which shares will be added to the 2013 Equity Incentive Plan upon effectiveness of such plan.

Except as otherwise indicated, this prospectus:

- n reflects the conversion of all outstanding preferred shares into an aggregate of 33,029,489 common shares upon the closing of this offering;
- n reflects the automatic conversion of 69,356 subscription rights immediately prior to the closing of this offering;
- n assumes the filing of the articles of amendment immediately prior to the closing of this offering;
- n assumes no exercise by the underwriters of their option to purchase additional common shares;
- n reflects a for reverse share split of our common and preferred shares to be effected prior to the closing of this offering; and
- n with respect to financial measures, is presented in accordance with U.S. generally accepted accounting principles, or U.S. GAAP.

SUMMARY FINANCIAL DATA

We have derived the following summary of statements of operations data for the years ended December 31, 2011 and 2012 from audited financial statements appearing elsewhere in this prospectus. We derived the following statements of operations data for the six months ended June 30, 2012 and 2013 and the balance sheet data as of June 30, 2013 from unaudited interim financial statements included elsewhere in this prospectus. In the opinion of management, the unaudited interim financial statements reflect all adjustments, which include only normal recurring adjustments, necessary for a fair presentation of the financial statements. Historical results are not necessarily indicative of the results that may be expected in the future and the results for the six months ended June 30, 2013 are not necessarily indicative of the results that may be expected for the full year or any other period. The summary financial data set forth below should be read together with the financial statements and the related notes to those statements, as well as the sections of this prospectus captioned "Selected Financial Data" and "Management's Discussion and Analysis of Financial Condition and Results of Operations." Our audited annual financial statements and unaudited interim financial statements have been prepared in accordance with U.S. GAAP.

| | YEAR ENDED DECEMBER 31, | | SIX MONTHS ENDED JUNE 30, | |
|--|---------------------------------------|-------------------|------------------------------|----------------|
| | 2011 | 2012 | 2012 | 2013 |
| | (unaudited) | | | |
| | (in thousands, except per share data) | | | |
| Statement of Operations Data: | | | | |
| Revenue: | | | | |
| Collaboration revenue | \$ 6,915 | \$ 14,300 | \$ 8,207 | \$10,985 |
| Royalties | 3 | 8 | 3 | — |
| | <u>6,918</u> | <u>14,308</u> | <u>8,210</u> | <u>10,985</u> |
| Operating expenses: | | | | |
| Research and development | 12,237 | 10,392 | 4,770 | 6,939 |
| General and administrative | 6,795 | 7,069 | 3,561 | 2,872 |
| Total operating expenses | <u>19,032</u> | <u>17,461</u> | <u>8,331</u> | <u>9,811</u> |
| Income (loss) from operations | (12,114) | (3,153) | (121) | 1,174 |
| Other income (expense): | | | | |
| Interest income | 153 | 144 | 56 | 76 |
| Interest expense | (91) | (93) | (46) | (41) |
| Foreign exchange gain (loss) | 60 | (169) | (143) | 1,920 |
| Gain (loss) on write-off and disposal of assets | — | (1,030) | (1,197) | 11 |
| Net income (loss) | <u>(11,992)</u> | <u>(4,301)</u> | <u>(1,451)</u> | <u>3,140</u> |
| Net income (loss) attributable to participating securities | — | — | — | (3,140) |
| Net income (loss) attributable to common shareholders | <u>\$ (11,992)</u> | <u>\$ (4,301)</u> | <u>\$(1,451)</u> | <u>\$ —</u> |
| Net income (loss) per share—basic | <u>\$ (1.86)</u> | <u>\$ (0.67)</u> | <u>\$ (0.23)</u> | <u>\$ 0.00</u> |
| Net income (loss) per share—diluted | <u>\$ (1.86)</u> | <u>\$ (0.67)</u> | <u>\$ (0.23)</u> | <u>\$ 0.00</u> |
| Weighted-average common shares outstanding used in computing basic net income (loss) per share | | | | |
| | <u>6,433</u> | <u>6,452</u> | <u>6,443</u> | <u>6,478</u> |
| Weighted-average common shares outstanding used in computing diluted net income (loss) per share | | | | |
| | <u>6,433</u> | <u>6,452</u> | <u>6,443</u> | <u>6,478</u> |
| Pro forma net income (loss) per share—basic (unaudited) ⁽¹⁾ | | <u>\$ (0.11)</u> | | <u>\$ 0.08</u> |
| Pro forma net income (loss) per share—diluted (unaudited) ⁽¹⁾ | | <u>\$ (0.11)</u> | | <u>\$ 0.07</u> |
| Weighted-average common shares outstanding used in computing the proforma net income (loss) per share—basic (unaudited) ⁽¹⁾ | | | | |
| | | <u>39,536</u> | | <u>39,577</u> |
| Weighted-average common shares outstanding used in computing the proforma net income (loss) per share—diluted (unaudited) ⁽¹⁾ | | | | |
| | | <u>39,536</u> | | <u>41,949</u> |

| | AS OF JUNE 30, 2013 | |
|--|---------------------|--|
| | ACTUAL | PRO FORMA AS ADJUSTED ⁽²⁾ (unaudited) |
| | (In thousands) | |
| Balance Sheet Data: | | |
| Cash, cash equivalents and marketable securities | \$ 49,812 | \$ |
| Working capital | 33,333 | |
| Total assets | 53,458 | |
| Redeemable convertible preferred shares | 102,488 | — |
| Total shareholders' deficit | (87,195) | |

⁽¹⁾ Pro forma net income (loss) per share represents net income (loss) divided by the pro forma weighted-average shares outstanding, and reflects (i) the conversion of all outstanding preferred shares and (ii) the conversion of all outstanding subscription rights, in each case into our common shares, as if the conversions had occurred at the beginning of the period presented.

⁽²⁾ Reflects, on a pro forma basis, the automatic conversion described in footnote (1) and, on an as adjusted basis, the sale and issuance by us of common shares hereunder at an assumed initial price to public of \$ per share, the midpoint of the range set forth on the cover of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses. Each \$1.00 increase (decrease) in the assumed initial price to public of \$ per share, would increase (decrease) each of cash and cash equivalents, working capital, total assets and total shareholders' deficit by approximately \$ million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same, and after deducting estimated underwriting discounts and commissions and estimated offering expenses. We may also increase or decrease the number of shares we are offering. Each increase (decrease) of in the number of shares offered by us would increase (decrease) each of cash and cash equivalents, working capital, total assets and total shareholders' deficit by approximately \$ million, assuming that the assumed initial price to public remains the same, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses. The pro forma as adjusted information discussed above is illustrative only and will adjust based on the actual initial price to public and other terms of this offering determined at pricing.

RISK FACTORS

Investing in our common shares involves a high degree of risk. You should carefully consider the risks and uncertainties described below together with all of the other information contained in this prospectus, including our financial statements and the related notes appearing at the end of this prospectus and "Management's Discussion and Analysis of Financial Condition and Results of Operations," before deciding whether to invest in our common shares. If any of the following risks actually occur, our business, growth prospects, operating results and financial condition could suffer materially, the trading price of our common shares could decline and you could lose all or part of your investment.

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 six months ended June 30, 2013, we have recorded net losses in each reporting period since inception in 1996 and do not expect to have sustained profitability for the foreseeable future. We have incurred net losses of \$12.0 million and \$4.3 million for the years ended December 31, 2011 and 2012. As of June 30, 2013, we had an accumulated deficit of \$125.6 million.

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 and funding received from our licensees and collaborators. We have not generated any 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 Isis Pharmaceuticals, Inc., or Isis, 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.

We have not generated any revenue from product royalties and may never be 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

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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. To date, we have not generated any product royalty revenue from product sales, and do not otherwise anticipate generating revenue from product sales other than from sales of Glybera under our license to uniQure Biopharma B.V., or uniQure, for the foreseeable future, if ever. 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, fails to achieve market acceptance or adequate market share, we may never become profitable. Even if we achieve profitability in the future, 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:

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

The scope of our future revenue will also depend upon the size of any markets in which our product candidates receive approval and the availability of insurance coverage and the availability and amount of reimbursement from third-party payers for 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.

Even if this offering is successful, 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, 2013, we incurred approximately \$6.9 million of costs associated with research and development, exclusive of costs incurred by our collaborators in developing our current product and product candidates.

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The anticipated net proceeds from this offering 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 beyond the expected proceeds of this offering to continue our clinical development and potential commercialization activities. Our future capital requirements depend on many factors, including but not limited to:

- the number and characteristics of the future product candidates we pursue;
- the scope, progress, results and costs of independently researching and developing any of our future product candidates, and conducting preclinical research and clinical trials;
- whether our existing collaborations continue to generate substantial milestone payments and, ultimately, royalties on future products for us;
- the timing of, and the costs involved in, obtaining regulatory approvals for any future product candidates we develop independently;
- the cost of future commercialization activities, including activities required pursuant to our option to co-promote XEN402, if exercised by us, and the cost of commercializing any future products we develop independently that are approved for sale;
- the cost of manufacturing our future products, if any;
- our ability to maintain existing collaborations and to establish new collaborations, licensing or other arrangements and the financial terms of such agreements;
- the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing patents, including litigation costs and the outcome of such litigation; and
- the timing, receipt and amount of sales of, or royalties on, Glybera, and our future products, if any.

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

Upon the completion of this offering, based upon our anticipated operating expenditures, we expect that the net proceeds from this offering, research funding that we expect to receive under our existing collaborations and our existing cash and cash equivalents will be sufficient to fund our current operations for the next 12 to 24 months. However, 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 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 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, and changes in foreign currency exchange rates could impact our results of operations.

Approximately 36% of our cash and cash equivalents as of June 30, 2013 were denominated in U.S. dollars. Historically, a portion of our operating expenses and a substantial portion of our revenue has been denominated in U.S. dollars. Because our functional currency is the Canadian dollar, 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, because of the difference in the amount of our revenue and expenses that are in U.S. dollars relative to Canadian dollars, depreciation in the U.S. dollar relative to the Canadian dollar could result in a material increase in reported expenses relative to revenue, and therefore could cause our operating income (expense) to appear to decline materially, particularly relative to prior periods. The converse is true if the U.S. dollar were to appreciate relative to the Canadian dollar. Fluctuations in foreign currency exchange rates also impact the reporting of our receivables and payables in non-Canadian currencies. Translation gains or losses related to the translation of our net assets from our Canadian functional currency into the U.S. reporting currency are included as a component of accumulated comprehensive income on our balance sheet. 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 our 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 XEN402, XEN701 and our selective Nav1.7 inhibitor and compounds in our discovery pipeline, are in varying stages of development and will require substantial clinical development, testing and regulatory approval prior to commercialization. We currently have two announced product candidates that are, subject to the outcome of current Investigational New Drug application, or IND, enabling safety studies, anticipated to enter Phase 1 clinical trials in the next two years. 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 effected and a decline of our common share price could result.

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 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 Europe and certain other countries outside of North America and Japan. Despite the efforts of uniQure and Chiesi, Glybera may not gain market acceptance among physicians, patients, healthcare payers and the medical community. The commercial success of Glybera will depend on a number of factors, including:

- establishment and demonstration of clinical efficacy and safety and acceptance of the same by the medical community;
- commercialization of competing products;
- sufficient commercial supply of Glybera;
- cost-effectiveness of Glybera;
- the availability of coverage and adequate reimbursement from third parties, including governmental payers, managed care organizations, and private health insurers;
- the relative cost, safety and efficacy of therapies that exist now or may be developed in the future;
- whether the product can be manufactured in commercial quantities at acceptable cost;
- marketing and distribution support for Glybera;
- the effect of current and future healthcare laws;
- the acceptance of gene therapies as a class of treatment; and
- any market or regulatory exclusivities applicable to the product.

To date, the FDA has never approved any gene therapy product as a treatment for any indication in the U.S. and the FDA may never approve Glybera. Any failure of uniQure or its sublicensee to successfully commercialize Glybera could have a material adverse effect on our business, growth prospects, operating results and financial condition and could result in a substantial decline in the price of our common shares.

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 of alternative products; the level of generic competition; and the availability of coverage and adequate reimbursement from government and other third-party payors.

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.

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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 payors.

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.

There are no approved gene therapies currently on the market for 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 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 targeting Nav1.7 inhibitors to develop products to treat various pain indications, including Bioline Rx Ltd., Convergence Pharmaceuticals Limited, Dainippon Sumitomo Co., Ltd. and Pfizer, 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. We are not aware of any drugs or therapies currently approved specifically for treating primary EM.

Our competitors currently market well-known drugs and treatments for anemia, including erythropoietin stimulating agents, or ESAs, such as epogen, and intravenous iron therapy. We are aware of clinical-stage development programs at several major pharmaceutical and biotechnology companies targeting hepcidin for the treatment of cancer associated with anemia, including Eli Lilly and Company and NOXXON Pharma AG. Other companies' clinical-stage development programs do not directly target hepcidin such as prolyl hydroxylase inhibitors and soluble hemojuvelin for the treatment of CKD and ESRD, including Astellas Pharma Inc., AstraZeneca plc, FerruMax Pharmaceuticals, Inc., FibroGen, Inc. and GlaxoSmithKline plc. Another clinical-stage therapy aims to treat anemia by administering iron via dialysate. We are not aware of any drugs or therapies currently approved for treating anemia by inhibiting the production of human hepcidin at the transcriptional level.

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 no gene therapy product has been approved in the U.S. Because Glybera is likely to be the first gene therapy to be marketed, 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 lipoprotein lipase deficiency, or 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. More restrictive government regulations or negative public opinion could have a negative effect on our business or financial condition and may delay or impair the commercialization of Glybera. If Glybera is not successfully commercialized, our ability to generate near term revenue could be impaired.

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, and Teva Pharmaceutical Industries Ltd., or Teva, is responsible for the on-going

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clinical development of XEN402. 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:

- execute our clinical development plans for later-stage product candidates;
- obtain required regulatory approvals in each jurisdiction in which we will seek to commercialize products;
- build and maintain appropriate sales, distribution and marketing capabilities;
- gain market acceptance for our future products, if any; and
- manage our spending as costs and expenses increase due to clinical trials, regulatory approvals and commercialization activities.

If we are unsuccessful in accomplishing these objectives, we 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.

If we are not successful in leveraging our Extreme Genetics discovery platform to discover product candidates in addition to XEN402, XEN701 and our selective Nav1.7 inhibitor, 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 our announced product candidates XEN402, XEN701 and our selective Nav1.7 inhibitor. 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

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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 have recently hired a chief financial officer who is scheduled to join us full-time by November 2013. 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 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.

Dr. Bridger, our Executive Vice President of Research and Development, is a part-time employee who works for us on a three-days-a-week basis. Drs. Pimstone and Goldberg each devote a small amount of their time to clinical work outside of their duties at our company, conducting, on average, 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 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.

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; Dr. Bridger, our Executive Vice President, Research and Development; 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

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obligations with respect to safeguarding the privacy, use, security and transmission of individually identifiable health information such as genetic material. 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 will adopt a code of conduct applicable to all of our employees, which will be effective as of the consummation of this offering, 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.

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. Our collaborator for XEN402, 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:

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

U.S. Holders of our 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 year ending December 31, 2012 and we do not expect to be a PFIC following this offering and for the taxable year ending December 31, 2013.

If we are a PFIC for 2013 or any subsequent year, U.S. Holders (as defined in "United States & Canadian Income Tax Considerations—U.S. Federal Income Tax Information for 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.

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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 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. See “United States and Canadian Income Tax Considerations—U.S. Federal Income Tax Information for U.S. Holders—Passive Foreign Investment Company Consequences.”

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

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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:

- the FDA, EMA or other regulatory authorities may disagree with the design or implementation of our or our collaborators' clinical trials;
- we or our collaborators may be unable to demonstrate to the satisfaction of the FDA, EMA or other regulatory authorities that a product candidate is safe and effective for its proposed indication;
- the results of clinical trials may not meet the level of statistical significance required by the FDA, EMA or other regulatory authorities for approval;
- we or our collaborators may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- the FDA, EMA or other regulatory authorities may disagree with our or our collaborators' interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our product candidates may not be sufficient to support the submission of an NDA or other submission or to obtain regulatory approval in the U.S. or elsewhere;
- the FDA, EMA or other 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 a New Drug Application, or 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;

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- 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, or DSMB, 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.

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 XEN402, XEN701 and selective Nav1.7 inhibitor product candidates for treatment of pain and anemia 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.

In the case 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, 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 XEN402 is 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.

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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 conducting associated preclinical testing and clinical trials, as well as the potential need for additional financing, 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:

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

The limited patient populations in orphan and niche indications present significant recruitment challenges for clinical trials. For example, studies estimate the prevalence of LPLD to be approximately 1:1,000,000 and the prevalence of primary erythromelalgia, or primary EM, to be approximately 43,000 patients in the U.S. Primary EM is a condition of EM that is not caused by another disease or disorder. 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. XEN402 has received orphan drug designation for the treatment of EM by the FDA, and we, in conjunction with our collaborator, Teva, intend to file a corresponding application for regulatory exclusivity in the EU. If we seek orphan drug designations for other indications or in other jurisdictions, such as for XEN402 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

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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 XEN402, 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 effect 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.

Even if we obtain and maintain approval for our product candidates from the FDA, we may never obtain approval for our product candidates outside of the U.S., which would limit our market opportunities and adversely affect our business.

Sales of our approved products outside of the U.S. will be subject to foreign regulatory requirements governing clinical trials and marketing approval, and we plan to seek regulatory approval to commercialize our product candidates both in the 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, such as the EMA for Glybera, does not ensure approval by regulatory authorities in other countries, including by the FDA. 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 providers 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 EEA 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.

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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:

- identify families as potential candidates for study;
- obtain their consent to participate in our research;
- perform medical examinations and gather medical histories;
- conduct the initial analysis of suitability of the families to participate in our research based on the foregoing; and
- 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 XEN402 with Teva in the U.S.

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:

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel to or develop alternative sales channels;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future products;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen 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

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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 good clinical practices, or GCP, 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:

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

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. For example, studies estimate the prevalence of LPLD to be approximately 1:1,000,000 and the prevalence of primary EM to be approximately 43,000 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.

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 payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring

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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.

In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, collectively, PPACA, was enacted, which includes measures that have 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 23.1% 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;

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- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion 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;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new 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 March 31, 2014 and by the 90th day of each subsequent calendar year, and disclosure of such information to be made on a publicly available website beginning in September 2014;
- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians, effective April 1, 2012;
- expansion 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;
- a licensure framework for follow-on biologic products;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- creation of the Independent Payment Advisory Board which, beginning in 2014, will have 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
- establishment 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 on January 1, 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 payors, coverage, an adequate level of reimbursement might not be available for such products and third-party payors' 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

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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 in 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.

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 XEN402, and if our relationship is not successful or is terminated, we may not be able to effectively develop and/or commercialize XEN402, which would have a material adverse effect on our business.

We depend on Teva to collaborate with us to develop and globally commercialize XEN402. Under the agreement, Teva controls all decision-making with respect to the clinical development and commercialization for XEN402. As a result of our dependence on Teva, the eventual success or commercial viability of XEN402 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:

- ⁂ adverse decisions by Teva or the Joint Development Committee regarding the development and commercialization of XEN402;
- ⁂ possible disagreements as to the timing, nature and extent of our development plans, including clinical trials or regulatory approval strategy;
- ⁂ loss of significant rights if we fail to meet our obligations under the agreement;
- ⁂ our limited control over clinical trials of XEN402;
- ⁂ changes in key management personnel at Teva, including in members of the Joint Development Committee; and
- ⁂ possible 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

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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:

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

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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:

- the development of certain of our current or future product candidates may be terminated or delayed;
- our cash expenditures related to development of our product candidates would increase significantly and we may need to seek additional financing sooner than expected;
- we may be required to hire additional employees or otherwise develop expertise, such as clinical, regulatory, sales and marketing expertise, which we do not currently have;
- we will bear all of the risk related to the development of any such product candidates; and
- the competitiveness of any product that is commercialized could be reduced.

We intend to rely on third-party manufacturers to produce our clinical product 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

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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 EEA 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.

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

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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 US in several stages over the lifetime of the patents and/or applications. We employ reputable law firms and other professionals and rely on such third parties to effect payment of these fees with respect to the patents and patent applications that we own, and we rely upon our licensors or our other collaborators to effect payment of these fees with respect to the patents and patent applications that we license. 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
- 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, XEN402, XEN701 and some of our earlier stage product candidates are held by our collaborators.

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 US. 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.

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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.

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.

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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. The patent portfolio for XEN701 is in-licensed from Isis. 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.

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.

Recent patent reform legislation and 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 developed and implemented regulations and procedures to govern administration of the Leahy-Smith Act, and many of the

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substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first to file provisions, were enacted March 16, 2013. The Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our 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. As a consequence of the *Myriad* decision, if any of our future product candidates utilize isolated human DNA as a result of our Extreme Genetics discovery platform that allows us to identify DNA sequences associated with human disease, 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 US 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 US 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.

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. 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 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

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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:

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

We currently carry product liability insurance of \$5,000,000 per occurrence and \$5,000,000 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.

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 payors 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 payors 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

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jurisdictions in which we conduct our business. The applicable federal, state and foreign healthcare laws and regulations that may affect our ability to operate include the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service for which payment may be made under federal and state healthcare programs such as Medicare and Medicaid;
- federal civil and criminal false claims laws 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;
- HIPAA, which imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters;
- HIPAA, 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 behalf of a covered entity, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal Open Payments program, created under Section 6002 of PPACA and its implementing regulations requires 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) to report annually to HHS information related to "payments or other transfers of value" made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, and applicable manufacturers and applicable group purchasing organizations to report annually to HHS ownership and investment interests held by physicians (as defined above) and their immediate family members, with data collection required beginning August 1, 2013, reporting to the Centers for Medicare & Medicaid Services, or CMS, required by March 31, 2014 (and by the 90th day of each subsequent calendar year), and disclosure of such information to be made on a publicly available website beginning in September 2014; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payers, including private insurers; state and foreign laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers; state and foreign laws that require drug manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures; 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.

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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 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. We do not carry insurance for earthquakes or other natural disasters and although our business interruption insurance applies in the event of an earthquake, we may not carry sufficient business interruption insurance to compensate us for all losses that may occur. The disaster recovery and business continuity plans we have in place currently are limited and are unlikely to prove adequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which, particularly when taken together with our lack of earthquake insurance, 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 forgoing could have a material adverse effect on our business.

Risks Related to Our Common Shares and this Offering

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

Our share price could decline as a result of sales of a large number of our common shares after this offering 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.

Holders of approximately common shares, or % of our common shares, will have rights 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 described in the section of the prospectus captioned "Description of Share Capital— Registration Rights." We also intend to register the offer and sale of all common shares that we may issue under our equity compensation plans. Once we register the offer and sale of common shares for the holders of registration rights and option holders, they can be freely sold in the public market upon issuance, subject to the market stand-off and lock-up agreements described in the sections of this prospectus captioned "Shares Eligible for Future Sale—Lock-Up and Market Standoff Agreements" and "Underwriting."

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.

We expect that our trading price will fluctuate significantly and investors may not be able to resell their shares at or above the initial public offering price.

The trading price of our common shares following this offering may be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. As a result of this volatility, you

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may not be able to sell your common shares at or above the initial public offering price, if at all. The market price for our common shares may be influenced by many factors, including:

- ▯ 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 Glybera or 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 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;
- ▯ our dependence on third parties, including our collaborators, CROs, clinical trial sponsors and clinical investigators;
- ▯ regulatory or legal developments in Canada, the U.S. or other countries;
- ▯ developments or disputes concerning patent applications, issued patents or other proprietary rights;
- ▯ the recruitment or departure of key scientific or management personnel;
- ▯ our ability to successfully commercialize our future product candidates we develop independently, if approved;
- ▯ the level of expenses related to any of our product candidates or clinical development programs;
- ▯ actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- ▯ actual or anticipated quarterly variations in our financial results or those of our competitors;
- ▯ any change to the composition of the board of directors or key personnel;
- ▯ expiration of contractual lock-up agreements with our executive officers, directors and security holders;
- ▯ 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.

After this offering, our executive officers, directors and principal shareholders will maintain the ability to control all matters submitted to shareholders for approval.

Upon the closing of this offering, our executive officers and directors and shareholders who owned more than 5% of our outstanding common shares before this offering will, in the aggregate, own or control shares representing

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approximately % of our outstanding common shares or % if investment entities affiliated with certain of our principal shareholders and certain of our other existing shareholders purchase a number of common shares equal to that for which they have expressed an interest in purchasing, of which % will be owned or controlled by our executive officers. As a result, if these shareholders were to choose to act together, they would be able to control all matters submitted to our shareholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, would control the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. The interests of this group of shareholders may not always coincide with our corporate interests or the interests of other shareholders, and they may act in a way in which you may not agree with or in a way that may not be in the best interests of other shareholders. This concentration of voting power could delay or prevent an acquisition of our company on terms that other shareholders may desire or otherwise discourage a potential acquirer from attempting to obtain control of us, which in turn could have a material adverse effect on our share price.

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 that will become effective immediately prior to consummation of this offering, as well as certain provisions under the Canada Business Corporations Act 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 or our by-laws unless such amendment is approved by shareholders holding at least two-thirds of the shares entitled to vote on such approval;
- 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
- shareholders 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 Canada Business Corporations Act or under any applicable Canadian securities law that has the effect of delaying or deterring a change in control could limit the opportunity for our shareholders to receive a premium for their common shares, and could also affect the price that some investors are willing to pay for our common shares.

U.S. civil liabilities may not be enforceable against us, our directors, our officers or certain experts named in this prospectus.

We are governed by the Canada Business Corporations Act and our principal place of business is in Canada. Many of our directors and officers, as well as certain experts named herein, 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, officers and experts 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 Canada Business Corporations Act 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

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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 Canada Business Corporations Act and Delaware General Corporation Law 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, amendments to our articles or our by-laws) the Canada Business Corporations Act generally requires a two-thirds majority vote by shareholders, whereas Delaware General Corporation Law generally only requires a majority vote; (ii) quorum for shareholders meetings under the Canada Business Corporations Act can be set by a corporation's by-laws, and under our by-laws, such quorum only requires the acceptance of one person representing (in person or by proxy) at least 10% of the issued shares, whereas under Delaware General Corporation Law, quorum requires a minimum of one-third of the shares entitled to vote to be present; and (iii) under the Canada Business Corporations Act a holder of 5% or more of our common shares can requisition a special meeting of shareholders at which matters that can be voted on at our annual meeting can be considered, whereas such right does not exist under the Delaware General Corporation Law. Refer to the heading titled "Material Differences between the Canada Business Corporations Act and Delaware General Corporation Law" for more information.

We do not know whether an active and liquid trading market will develop for our common shares or what the market price of our common shares will be and as a result it may be difficult for you to sell your common shares.

Prior to this offering, there has been no public market for our common shares. An active trading market for our shares may never develop or be sustained following this offering, on NASDAQ, on which we intend to apply to have our common shares listed, or otherwise. If an active market for our common shares does not develop, it may be difficult for you to sell common shares you purchase in this offering without depressing the market price for the common shares or you may not be able to sell your shares at all. The initial public offering price for our common shares will be determined through negotiations with the underwriters and the negotiated price may not be indicative of the market price for our common shares after this offering. The initial public offering price may vary from the market price of our common shares after the offering. As a result of these and other factors, you may not be able to sell your common shares at or above the initial public offering price 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 that we did not incur as a private company. 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 British Columbia Securities Commission 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. In addition, we have recently hired a full-time chief financial officer who is scheduled to join us full time in November 2013. 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 will need 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, we expect these rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to accept reduced policy limits and coverage or 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.

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,

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beginning January 1, 2014, Section 404 of the Sarbanes-Oxley Act, or Section 404, will require 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 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 this 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 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. We may elect to use this extended transition period under the JOBS Act. If we do, our financial statements may not be comparable to the financial statements of issuers who are required to comply with the effective dates for new or revised accounting standards that are applicable to public companies, which may make our common shares less attractive to investors.

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

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our reporting obligations. In addition, any testing by us conducted in connection with Section 404 of the Sarbanes-Oxley Act, 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.

We will be required to disclose changes made in our internal controls and procedures on a quarterly basis and our management will be 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. We could be an “emerging growth company” for up to five years. An independent assessment of the effectiveness of our internal controls could detect problems that our management’s assessment might not. In addition, our management and independent registered public accounting firm did not perform an evaluation of our internal control over financial reporting as of December 31, 2012 or December 31, 2011 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.

If you purchase our common shares in this offering, you will incur immediate and substantial dilution in the book value of your shares and 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 additional dilution and could cause our share price to fall.

Investors purchasing common shares in this offering will pay a price per common share that substantially exceeds the net tangible book value per common share as of June 30, 2013. Net tangible book value is our tangible assets after subtracting our liabilities. As a result, investors purchasing common shares in this offering will incur immediate dilution of \$ per common share, based on the initial public offering price of \$ per common share. Further, investors purchasing common shares in this offering will contribute approximately % of the total amount invested by shareholders since our inception, but will own only approximately % of the common shares outstanding after giving effect to this offering.

This dilution is due to our investors who purchased shares prior to this offering having paid substantially less than the price offered to the public in this offering when they purchased their shares. In addition, as of June 30, 2013, options to purchase 6,339,591 of our common shares at a weighted-average exercise price of \$0.79 per common share were outstanding. The exercise of any of these options would result in additional dilution. As a result of the dilution to investors purchasing common shares in this offering, investors may receive significantly less than the purchase price paid in this offering, if anything, in the event of our liquidation. 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 plan(s), 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, including common shares sold in this offering.

For a further description of the dilution that you will experience immediately after this offering, see “Dilution.”

Our management team will have broad discretion to use the net proceeds from this offering and its investment of these proceeds may not yield a favorable return. They may invest the proceeds of this offering in ways with which investors disagree.

Our management team will have broad discretion in the application of the net proceeds from this offering and could spend or invest the proceeds in ways with which our shareholders disagree. Accordingly, investors will need to rely on our management team's judgment with respect to the use of these proceeds. We intend to use the proceeds from this offering to: (1) continue pre-clinical development of product candidates identified using our Extreme Genetics discovery platform; (2) initial IND-enabling studies and clinical development through Phase 2 trials of XEN701, including relevant milestone payments to Isis; (3) fund the development of a sales, marketing and distribution infrastructure to support our co-promotion option with Teva; and (4) for working capital and other general corporate purposes. 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 transaction. These uses may not yield a favorable return to our shareholders.

We cannot specify with certainty all of the particular uses for the net proceeds to be received upon the closing of this offering. In addition, the amount, allocation and timing of our actual expenditures will depend upon numerous factors, including milestone payments received from our collaborations and royalties received on sale of our approved product and any future approved product. Accordingly, we will have broad discretion in using these proceeds. Until the net proceeds are used, they may be placed in investments that do not produce significant income or that may lose value.

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.

We intend to apply to list our common shares on NASDAQ. In order to make a final determination of compliance with their listing criteria, NASDAQ may look to the first trading day's activity and, particularly, the last bid price on such day. In the event the trading price for our common shares drops below NASDAQ's \$1.00 minimum bid requirement, NASDAQ could rescind our initial listing approval. If that were to happen, the liquidity for our common shares would decrease. If we failed to list the common shares on NASDAQ, the liquidity for our common shares would be significantly impaired, which may substantially decrease the trading price of our common shares.

In addition, in the future, 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:

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

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

The trading market for our common shares will be influenced by the research and reports that securities or industry analysts publish about us or our business. Securities and industry analysts do not currently, and may never, publish research on our company. If no or too few securities or industry analysts commence coverage of our company, the trading price for our common shares would likely be negatively impacted. In the event securities or industry analysts initiate coverage, if one or more of the analysts who cover us downgrade our common shares or publish inaccurate or unfavorable research about our business, our 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 price and trading volume to decline.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains forward-looking statements that are based on management's beliefs and assumptions and on information currently available to management. Some of the statements under "Prospectus Summary," "Risk Factors," "Management's Discussion and Analysis of Financial Condition and Results of Operations" and "Business" and elsewhere in this prospectus contain forward-looking statements. In some cases, you can identify forward-looking statements by the following words: "may," "will," "could," "would," "should," "expect," "intend," "plan," "anticipate," "believe," "estimate," "predict," "project," "potential," "continue," "ongoing" or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these words.

These statements involve risks, uncertainties and other factors that may cause actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. Although we believe that we have a reasonable basis for each forward-looking statement contained in this prospectus, we caution you that these statements are based on a combination of facts and factors currently known by us and our projections of the future, about which we cannot be certain. Forward-looking statements in this prospectus 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, including for primary EM or other 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;
- the likelihood of our exercise of our option to co-promote XEN402 in the U.S. under our Teva collaboration and co-fund and co-develop under our Merck collaboration;
- our ability to maintain and establish collaborations;
- our use of proceeds from this offering;

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- our expectations regarding market risk, including interest rate changes and foreign currency fluctuations;
- our belief in the sufficiency of our cash flows to meet our needs for the next 12 to 24 months;
- our expectations regarding the timing during which we will be an emerging growth company under the JOBS Act;
- 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.

In addition, you should refer to the “Risk Factors” section of this prospectus for a discussion of other important factors that may cause actual results to differ materially from those expressed or implied by the forward-looking statements. As a result of these factors, we cannot assure you that the forward-looking statements in this prospectus will prove to be accurate. Furthermore, if the forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all. We undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law. The Private Securities Litigation Reform Act of 1995 and Section 27A of the Securities Act of 1933 do not protect any forward-looking statements that we make in connection with this offering.

MARKET, INDUSTRY AND OTHER DATA

Unless otherwise indicated, information contained in this prospectus concerning our industry and the market in which we operate, including our market position, market opportunity and market size, is based on information from various sources such as industry publications, on assumptions that we have made based on such data and other similar sources and on our knowledge of the markets for our products. These data involve a number of assumptions and limitations. We have not independently verified any third-party information.

In addition, projections, assumptions and estimates of our future performance and the future performance of the industry in which we operate is necessarily subject to a high degree of uncertainty and risk due to a variety of factors, including those described in the section entitled "Risk Factors" and elsewhere in this prospectus. These and other factors could cause results to differ materially from those expressed in the estimates made by the independent parties and by us.

USE OF PROCEEDS

We estimate that the net proceeds to us from the sale of the common shares in this offering will be approximately \$ million, or approximately \$ million if the underwriters exercise their option to purchase additional common shares in full, based upon an assumed initial public offering price of \$ per common share, the mid-point of the estimated price range on the cover page of this prospectus, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us. Each \$1.00 increase (decrease) in the assumed initial public offering price of \$ per common share would increase (decrease) the net proceeds to us from this offering by approximately \$ million, assuming the number of common shares offered by us, as set forth on the cover page of this prospectus, remains the same. We may also increase or decrease the number of common shares we are offering. Each increase (decrease) of one million common shares in the number of common shares offered by us would increase (decrease) the net proceeds to us from this offering by approximately \$ million, assuming that the assumed initial public offering price remains the same, and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. We do not expect that a change in the initial public offering price or the number of common shares by these amounts would have a material effect on uses of the proceeds from this offering, although it may accelerate the time at which we will need to seek additional capital.

We currently expect to use the net proceeds from this offering as follows:

- approximately \$ million to fund genetic research, drug discovery and preclinical development activities using our Extreme Genetics discovery platform;
- approximately \$ million to fund our planned development of XEN701, including commencing and advancing a Phase 2b trial;
- approximately \$ million for future success-based milestone payments to current licensors including Isis, should we achieve such milestones; and
- the remainder for working capital and general corporate purposes.

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 transaction.

This expected use of the net proceeds of this offering represents our intentions based on our current plans and business conditions, which could change in the future as our plans and business conditions evolve. As of the date of this prospectus, we cannot predict with certainty all of the particular uses for the net proceeds to be received upon the closing of this offering or the amounts that we will actually spend on the uses set forth above. The amounts, allocation and timing of our actual expenditures will depend upon numerous factors, including:

- the focus and results of our research, drug discovery and preclinical development activities;
- the type, number, costs and results of any clinical trials for our product candidates;
- regulatory actions relating to our product candidates;
- our ability to achieve milestones and obtain royalty payments from our collaborators;
- whether any co-funding or co-promotion rights under our strategic alliances are exercised;
- competitive and technological developments; and
- the rate of growth, if any, of our business.

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.

CAPITALIZATION

The following table summarizes our capitalization as of June 30, 2013:

- on an actual basis;
- on a pro forma basis to reflect (1) the conversion of all outstanding preferred shares into an aggregate of 33,029,489 common shares upon the closing of this offering; (2) the automatic conversion of all subscription rights outstanding immediately prior to the closing of this offering into an aggregate of 69,356 common shares; and (3) a reverse share split of our common and preferred shares to be effected prior to the closing of this offering; and
- on a pro forma as adjusted basis, to further reflect the sale and issuance by us of common shares in this offering at an assumed initial price to public of \$ per share, the mid-point of the range reflected on the cover page of this prospectus, after deducting underwriting discounts and commissions and estimated offering expenses.

Investors should read the information in this table together with the financial statements and related notes to those statements, as well as the sections of this prospectus captioned "Selected Financial Data" and "Management's Discussion and Analysis of Financial Condition and Results of Operations."

| | AS OF JUNE 30, 2013 | | |
|--|---------------------|-----------------------------|---|
| | ACTUAL | PRO FORMA (unaudited) | PRO FORMA AS ADJUSTED ⁽¹⁾ |
| (in thousands, except per share amounts) | | | |
| Redeemable convertible preferred shares, without par value; issuable in series, 32,102,673 authorized, 31,437,274 preferred shares issued and outstanding, actual; no preferred shares authorized, issued or outstanding, pro forma; no preferred shares authorized, issued or outstanding, pro forma as adjusted | \$ 102,488 | \$ — | \$ — |
| Shareholders' deficit: | | | |
| Common shares, without par value, unlimited common shares authorized, 6,488,141 common shares issued and outstanding, actual; unlimited common shares authorized, common shares issued and outstanding, pro forma; unlimited common shares authorized, common shares issued and outstanding, pro forma as adjusted | 6,035 | | |
| Additional paid-in capital | 29,457 | | |
| Accumulated deficit | (125,644) | | |
| Accumulated comprehensive income | 2,957 | | |
| Total shareholders' deficit | (87,195) | | |
| Total capitalization | <u>\$ 15,293</u> | <u>\$</u> | <u>\$</u> |

⁽¹⁾ Each \$1.00 increase (decrease) in the assumed initial price to public of \$ per common share, the mid-point of the range reflected on the cover page of this prospectus, would increase (decrease) each of additional paid-in capital, total shareholders' deficit and total capitalization by approximately \$ million, assuming that the number of common shares offered by us, as set forth on the cover page of this prospectus, remains the same, and after deducting underwriting discounts and commissions and estimated offering expenses. We may also increase or decrease the number of common shares we are offering. Each increase (decrease) of one million common shares in the number of common shares offered by us would increase (decrease) each of additional paid-in capital, total shareholders' deficit and total capitalization by approximately \$ million, assuming that the assumed initial price to public remains the same, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses. The pro forma as adjusted information discussed above is illustrative only and will adjust based on the actual initial price to public and other terms of this offering determined at pricing.

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The outstanding share information in the table above excludes as of June 30, 2013:

- ⁿ 6,339,591 common shares issuable upon exercise of options outstanding as of June 30, 2013, at a weighted-average exercise price of CAD\$0.79 per share, or \$0.75 per share, as converted; and
- ⁿ common shares reserved for future issuance under share-based compensation plans, including common shares reserved for issuance under our 2013 Equity Incentive Plan, which will become effective on the day immediately prior to the date of the completion of this offering, and any future automatic increase in common shares reserved for issuance under such plan, and 7,373,338 common shares reserved for issuance under our Amended and Restated Stock Option Plan as of June 30, 2013, which shares will be added to the 2013 Equity Incentive Plan upon effectiveness of such plan.

DILUTION

Investors purchasing our common shares in this offering will experience immediate and substantial dilution in the pro forma net tangible book value of their common shares. Dilution in pro forma net tangible book value represents the difference between the price to public per common share and the pro forma net tangible book value per share immediately after the offering.

The historical net tangible book value of our common shares as of June 30, 2013 was \$15.3 million, or \$2.36 per share. Historical net tangible book value (deficit) per common share represents our total tangible assets (total assets less intangible assets) less total liabilities divided by the number of outstanding common shares.

After giving effect to (1) the automatic conversion of the outstanding preferred shares into an aggregate of 33,029,489 common shares immediately prior to the completion of this offering; (2) the automatic conversion into an aggregate of 69,356 common shares of all subscription rights outstanding immediately prior to the closing of this offering; (3) the issuance of common shares in this offering; and (4) receipt of the net proceeds from the sale of common shares in this offering at an assumed initial price to public of \$ per common share (the midpoint of the price range set forth on the cover of this prospectus), after deducting underwriting discounts and commissions and estimated offering expenses, the pro forma as adjusted net tangible book value as of June 30, 2013 would have been approximately \$ million, or \$ per common share. This represents an immediate increase in pro forma as adjusted net tangible book value of \$ per common share to existing shareholders and an immediate dilution of \$ per common share to new investors purchasing common shares in this offering.

The following table illustrates this dilution on a per common share basis to new investors:

| | |
|---|----------|
| Assumed initial price to public per common share | \$ |
| Historical net tangible book value per common share as of June 30, 2013 | \$2.36 |
| Decrease per common share attributable to conversion of redeemable convertible preferred shares | _____ |
| Decrease per common share attributable to the conversion of subscription rights | _____ |
| Pro forma net tangible book deficit per common share before this offering | _____ |
| Increase in net tangible book value per common share attributable to investors participating in this offering | _____ |
| Pro forma as adjusted net tangible book value per common share, as adjusted to give effect to this offering | _____ |
| Pro forma dilution per common share to investors participating in this offering | \$ _____ |

Each \$1.00 increase (decrease) in the assumed initial price to public of \$ per common share would increase (decrease) the pro forma as adjusted net tangible book value by approximately \$ million, or approximately \$ per common share, and increase (decrease) the pro forma dilution per share to investors in this offering by approximately \$ per common share, assuming that the number of common shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting underwriting discounts and commissions and estimated offering expenses. We may also increase or decrease the number of common shares we are offering. An increase of one million in the number of common shares offered by us would increase the pro forma as adjusted net tangible book value by approximately \$, or \$ per common share, and the pro forma dilution per common share to investors in this offering would be \$ per common share, assuming that the assumed initial price to public remains the same, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses. Similarly, a decrease of one million common shares in the number of common shares offered by us would decrease the pro forma as adjusted net tangible book value by approximately \$ million, or \$ per common share, and the pro forma dilution per common share to investors in this offering would be \$ per common share, assuming that the assumed initial price to public remains the same, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses. The pro forma as adjusted information discussed above is illustrative only and will adjust based on the actual initial price to public and other terms of this offering determined at pricing.

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If the underwriters exercise their option in full to purchase additional common shares in this offering, the pro forma as adjusted net tangible book value per common share after the offering would be \$ per common share, the increase in the pro forma net tangible book value per common share to existing shareholders would be \$ per common share and the pro forma dilution to new investors purchasing common shares in this offering would be \$ per common share.

The following table summarizes, on a pro forma basis as of June 30, 2013, the differences between the number of common shares purchased from us, the total consideration and the weighted-average price per share paid by existing shareholders and by investors participating in this offering at an assumed initial price to public of \$ per share, before deducting underwriting discounts and commissions and estimated offering expenses.

| | COMMON SHARES PURCHASED | | TOTAL CONSIDERATION | | WEIGHTED-AVERAGE PRICE PER COMMON SHARE |
|--|-------------------------|---------|---------------------|---------|---|
| | NUMBER | PERCENT | AMOUNT | PERCENT | |
| Existing shareholders before this offering | | % | \$ | % | \$ |
| Investors participating in this offering | | | | | |
| Total | | % | \$ | % | |

Each \$1.00 increase (decrease) in the assumed initial price to public of \$ per common share would increase (decrease) total consideration paid by new investors by approximately \$ million, assuming that the number of common shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting underwriting discounts and commissions and estimated offering expenses. We may also increase or decrease the number of common shares we are offering. An increase (decrease) of in the number of common shares offered by us would increase (decrease) total consideration paid by new investors by \$ million, assuming that the assumed initial price to public remains the same, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses.

The number of common shares to be outstanding following this offering is based on 39,586,986 common shares outstanding as of June 30, 2013, giving effect to the conversion of all outstanding convertible preferred shares into an aggregate of 33,029,489 common shares immediately prior to the closing of this offering and all outstanding subscription rights into an aggregate of 69,356 common shares upon the closing of this offering and reverse share split. The outstanding share information in the table above excludes as of June 30, 2013:

- ¹¹ 6,339,591 common shares issuable upon exercise of options outstanding as of June 30, 2013, at a weighted-average exercise price of CAD\$0.79 per common share, or \$0.75 per common share, as converted;
- ¹² common shares reserved for future issuance under share-based compensation plans, including common shares reserved for issuance under our 2013 Equity Incentive Plan, which will become effective on the day immediately prior to the date of the completion of this offering, and any future automatic increase in common shares reserved for issuance under such plan; and
- ¹³ 7,373,338 common shares reserved for issuance under our Amended and Restated Stock Option Plan as of June 30, 2013, which shares will be added to the 2013 Equity Incentive Plan upon effectiveness of such plan.

Share reserves for our share-based compensation plans will also be subject to automatic annual increase in accordance with the terms of the plans. To the extent that new options are issued under our share-based compensation plans or we issue additional common shares in the future, there will be further dilution to investors participating in this offering.

SELECTED FINANCIAL DATA

We derived the selected statement of operations data for the fiscal years ended December 31, 2011 and 2012 and the balance sheet data as of December 31, 2011 and 2012 from our audited financial statements included elsewhere in this prospectus. The selected statement of operations data for the six months ended June 30, 2012 and 2013 and the balance sheet data as of June 30, 2013 have been derived from unaudited interim financial statements included elsewhere in this prospectus and have been prepared on the same basis as the audited financial statements. In the opinion of management, the unaudited data reflects all adjustments, which include only normal and recurring adjustments, necessary for a fair presentation of the results as of and for the periods. Our historical results are not necessarily indicative of results to be expected in any future period and results for the six months ended June 30, 2013 are not necessarily indicative of results to be expected for the full year ended December 31, 2013. You should read the following selected financial data below in conjunction with our financial statements and related notes included elsewhere in this prospectus and the "Management's Discussion and Analysis of Financial Condition and Results of Operations" section of this prospectus. Our audited annual financial statements and unaudited interim financial statements have been prepared in U.S. dollars and in accordance with U.S. GAAP.

| | <u>YEAR ENDED DECEMBER 31,</u> | | <u>SIX MONTHS ENDED</u> | |
|--|---------------------------------------|-------------------|-------------------------|--------------------------------|
| | <u>2011</u> | <u>2012</u> | <u>2012</u> | <u>JUNE 30,</u> <u>2013</u> |
| | (unaudited) | | | |
| | (in thousands, except per share data) | | | |
| Statement of Operations Data: | | | | |
| Revenue: | | | | |
| Collaboration revenue | \$ 6,915 | \$ 14,300 | \$ 8,207 | \$10,985 |
| Royalties | 3 | 8 | 3 | — |
| | <u>6,918</u> | <u>14,308</u> | <u>8,210</u> | <u>10,985</u> |
| Operating expenses: | | | | |
| Research and development | 12,237 | 10,392 | 4,770 | 6,939 |
| General and administrative | 6,795 | 7,069 | 3,561 | 2,872 |
| Total operating expenses | <u>19,032</u> | <u>17,461</u> | <u>8,331</u> | <u>9,811</u> |
| Income (loss) from operations | (12,114) | (3,153) | (121) | 1,174 |
| Other income (expense): | | | | |
| Interest income | 153 | 144 | 56 | 76 |
| Interest expense | (91) | (93) | (46) | (41) |
| Foreign exchange gain (loss) | 60 | (169) | (143) | 1,920 |
| Gain (loss) on write-off and disposal of assets | — | (1,030) | (1,197) | 11 |
| Net income (loss) | <u>(11,992)</u> | <u>(4,301)</u> | <u>(1,451)</u> | <u>3,140</u> |
| Net income (loss) attributable to participating securities | — | — | — | (3,140) |
| Net income (loss) attributable to common shareholders | <u>\$ (11,992)</u> | <u>\$ (4,301)</u> | <u>\$ (1,451)</u> | <u>\$ —</u> |
| Net income (loss) per share—basic ⁽¹⁾ | <u>\$ (1.86)</u> | <u>\$ (0.67)</u> | <u>\$ (0.23)</u> | <u>\$ 0.00</u> |
| Net income (loss) per share—diluted ⁽¹⁾ | <u>\$ (1.86)</u> | <u>\$ (0.67)</u> | <u>\$ (0.23)</u> | <u>\$ 0.00</u> |
| Weighted-average common shares outstanding used in computing basic net income (loss) per share ⁽¹⁾ | <u>6,433</u> | <u>6,452</u> | <u>6,443</u> | <u>6,478</u> |
| Weighted-average common shares outstanding used in computing diluted net income (loss) per share ⁽¹⁾ | <u>6,433</u> | <u>6,452</u> | <u>6,443</u> | <u>6,478</u> |
| Pro forma net income (loss) per share—basic (unaudited) ⁽²⁾ | | <u>\$ (0.11)</u> | | <u>\$ 0.08</u> |
| Pro forma net income (loss) per share—diluted (unaudited) ⁽²⁾ | | <u>\$ (0.11)</u> | | <u>\$ 0.07</u> |
| Weighted-average common shares outstanding used in computing the proforma net income (loss) per share—basic (unaudited) ⁽²⁾ | | <u>39,536</u> | | <u>39,577</u> |
| Weighted-average common shares outstanding used in computing the proforma net income (loss) per share—diluted (unaudited) ⁽²⁾ | | <u>39,536</u> | | <u>41,949</u> |

| | AS OF DECEMBER 31, | | AS OF |
|--|-----------------------|-----------|---------------------------------|
| | 2011 | 2012 | JUNE 30, 2013 (unaudited) |
| | (in thousands) | | |
| Balance Sheet Data: | | | |
| Cash, cash equivalents and marketable securities | \$ 14,924 | \$ 60,162 | \$ 49,812 |
| Working capital | 20,536 | 41,506 | 33,333 |
| Total assets | 30,465 | 63,305 | 53,458 |
| Note payable | 1,586 | 1,665 | — |
| Redeemable convertible preferred shares | 102,488 | 102,488 | 102,488 |
| Total shareholders' deficit | (86,316) | (89,865) | (87,195) |

⁽¹⁾ See Note 2 to our financial statements appearing elsewhere in this prospectus for an explanation of the method used to calculate basic and diluted net income (loss) per common share and the weighted-average number of common shares used in computation of the per common share amounts.

⁽²⁾ Pro forma net income (loss) per share represents net income (loss) divided by the pro forma weighted-average shares outstanding, and reflects (i) the conversion of all outstanding preferred shares and (ii) the conversion of all outstanding subscription rights, in each case into our common shares, as if the conversions had occurred at the beginning of the period presented.

MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis of our financial condition and results of operations together with our financial statements and related notes appearing in this prospectus. Some of the information contained in this discussion and analysis or set forth in other parts of this prospectus, including information with respect to our plans and strategy for our business, includes forward-looking statements that involve risks and uncertainties. You should read the "Risk Factors" section of this prospectus for a discussion of important factors that could cause actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a biopharmaceutical company focused on the development of novel medicines through the application of our proprietary discovery platform, which we refer to as Extreme Genetics. Our product candidates are based on genetic insights derived from our research of families where individuals exhibit severe traits, or phenotypes. By identifying and characterizing the single-gene defects responsible for such severe phenotypes, we gain valuable insights into their function in human biology and their potential as drug targets. Given that these targets are often involved in diseases beyond the rare genetic disorders in which they are first identified, we are developing proprietary product candidates to treat both orphan as well as more prevalent diseases.

We were incorporated in 1996 under the British Columbia Business Corporations Act and, federally, in 2000 under the Canada Business Corporation Act. We commenced active operations in 1999 and, to date, have devoted substantially all of our resources to the discovery and development of novel medicines through the application of our proprietary Extreme Genetics discovery platform. We initially focused on genetic discovery research, and subsequently expanded our efforts into drug discovery and preclinical and clinical development. To support our development activities, we also engage in supporting activities such as manufacturing and formulation development.

Our current pipeline includes the following product, product candidates and discovery-stage programs:

- ⁿ Glybera, a gene therapy product approved in the European Union, or EU, which utilizes the LPL^{S447X} gene as an active ingredient for the treatment of a subset of patients with the orphan lipid disorder LPLD, exclusive rights to which we have licensed to uniQure Biopharma B.V., or uniQure;
- ⁿ XEN402, a small-molecule inhibitor of the sodium channel Nav1.7 and other sodium channels for the treatment of the orphan disorder erythromelalgia, or EM, and other more common forms of pain, which is being funded by, and developed in collaboration with Teva Pharmaceutical Industries Ltd., or Teva, through its subsidiary, Ivax International GmbH, or Ivax;
- ⁿ XEN701, a subcutaneously administered antisense oligonucleotide compound for the treatment of anemia of chronic disease, which we are funding and developing internally pursuant to a license from Isis Pharmaceuticals, Inc., or Isis;
- ⁿ A selective Nav1.7 inhibitor for the treatment of pain, which is being funded by and developed in collaboration with Genentech, Inc., or Genentech, and its affiliate, F. Hoffmann-La Roche Ltd, or Roche; and
- ⁿ Four discovery-stage programs including (i) selective small-molecule inhibitors of the enzyme SCD1 for acne, (ii) selective small-molecule inhibitors of a target for cardiovascular disease which is partnered with Merck Sharp & Dohme GmbH (formerly known as Merck Sharp & Dohme Research Ltd.), an affiliate of Merck & Co., Inc., or Merck, (iii) selective small-molecule sodium channel modulators for Dravet Syndrome, an orphan seizure disorder, and (iv) new pipeline opportunities focused on discovery of novel drug targets for pain.

In keeping with our business strategy and as noted above, we have entered into multiple collaborations with pharmaceutical collaborators, including Genentech, Merck and Teva. These collaborations have generated in aggregate over \$140.0 million in non-equity funding through June 30, 2013. This includes approximately \$70.0 million in upfront payments, \$20.0 million in milestone payments and option fees, and \$50.0 million in research and development funding. We are eligible to receive more than \$1.0 billion of research, development, regulatory and sales-based milestone payments, as well as royalties on net product sales.

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We have funded our operations primarily through payments received from our pharmaceutical collaborators and government funding as well as through the sale of convertible preferred shares in various financing transactions. Through June 30, 2013, we have received an aggregate of approximately \$262.0 million to fund our operations, of which approximately \$140.0 million was non-equity funding pursuant to collaboration and license agreements, approximately \$17.0 million was pursuant to government funding, and approximately \$105.0 million was pursuant to the sale of our preferred shares, including approximately \$28.0 million related to share sales to collaborators. For 2011 and 2012 and the six months ended June 30, 2013, we recognized revenue for an aggregate of approximately \$7.0 million, \$14.0 million and \$11.0 million, respectively, related to funding from our collaborators.

Though our revenue from our collaboration and license agreements has resulted in net income for the six-months ended June 30, 2013 of \$3.1 million, we have incurred net losses on an annual basis since inception and do not expect to have sustained profitability for the foreseeable future. We had net losses of \$12.0 million and \$4.3 million for the years ended December 31, 2011 and 2012, respectively, and had an accumulated deficit of \$87.2 million as of June 30, 2013, from expenses incurred in connection with our research programs and from general and administrative costs associated with our operations.

We have not generated any royalties or other revenue from product sales, and we expect that our revenue in the near term will be substantially dependent on our collaboration agreements. Given the uncertain nature of clinical development of our current and future product candidates and the commercialization of current and future products, we cannot predict when or whether we will receive further milestone payments under our current or future collaboration agreements or whether we will be able to report either revenue or net income in future years.

We expect to continue to incur significant expenses and operating losses for the next 12 to 24 months. We anticipate that our expenses will increase substantially as we:

- continue our research and preclinical and clinical development of our product candidates;
- seek regulatory and marketing approvals for any of our product candidates that successfully complete clinical trials;
- make milestone and other payments under our in-license agreements;
- maintain, protect and expand our intellectual property portfolio;
- attract, hire and retain skilled personnel; and
- create additional infrastructure to support our operations as a public company and otherwise.

Financial Operations Overview

Revenue

To date, our revenue has been primarily derived from collaboration and licensing agreements as well as, to a lesser extent, government funding. In addition, we have received nominal royalties from a diagnostic license. To date, we have not generated any product royalty revenue from product sales, and do not otherwise anticipate generating revenue from product sales other than from sales of Glybera under our license to uniQure for the foreseeable future, if ever. We have entered into several collaboration agreements, the most significant of which, with respect to revenue, are described below.

uniQure. Effective August 2000, we entered into a sublicense and research agreement with Amsterdam Molecular Therapeutics, or AMT, pursuant to which we granted to AMT an exclusive, worldwide sublicense under certain intellectual property controlled by us to develop and commercialize compounds related to the variant of LPL, called LPL^{S447X}. In collaboration with the University of British Columbia, or UBC, we demonstrated that the LPL^{S447X} variant resulted in increased LPL enzyme activity leading to reduced triglyceride levels in humans. Under our sublicense and research agreement with AMT, we collaborated with AMT and UBC on preclinical activities, and thereafter AMT developed a LPL gene therapy product, Glybera, which contains the LPL^{S447X} variant. Certain of AMT's assets, including the rights to the intellectual property covered by our agreement, were subsequently acquired by uniQure in April 2012. Under the terms of the agreement, we are eligible to receive mid single-digit royalties for sales made by uniQure and its affiliates. The royalty rates are reduced to a low single-digit for sales made by uniQure and its affiliates in countries where a licensed technology or a licensed product is not covered by a valid patent claim. In

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July 2013, uniQure announced that it had entered into a partnership with Chiesi Farmaceutici S.p.A., or Chiesi, for the commercialization of Glybera in Europe and more than a dozen other countries including Brazil, China, Mexico and Russia. With respect to uniQure's sublicense to Chiesi, we receive a percentage in the low twenties of all non-royalty compensation relating to the licensed technology or products that uniQure receives from Chiesi (for example upfront payments and milestone payments), a percentage in the low twenties of any royalties that uniQure receives from Chiesi based on sales of products covered by the licensed patents, plus a mid single-digit percentage of certain further royalties that uniQure receives from Chiesi based on sales of the licensed technology or products after the expiration of all licensed patents covering the product.

Teva. In December 2012, we entered into a collaborative development and license agreement with Teva pursuant to which we granted Teva an exclusive worldwide license to develop and commercialize certain products, including XEN402. Under the terms of the agreement, Teva paid us an upfront fee of \$41.0 million and is funding all development costs with respect to the products licensed under the agreement. In addition, we are eligible to receive potential milestone payments totaling in aggregate up to \$335.0 million, comprised of up to \$20.0 million in clinical milestone payments, up to \$285.0 million in regulatory milestone payments, and up to \$30.0 million in sales-based milestone payments. If approved, we are also eligible to receive royalties in the low teens to low twenties on net sales of the licensed products for the timeframe that such products are covered by the licensed patents and in certain other instances.

We have an option to a minority co-promotion interest for products incorporating XEN402 in the U.S. Our co-promotion option is exercisable upon the filing of the first New Drug Application, or NDA, for a XEN402 product with the FDA and we will be obligated to pay an opt-in fee to Teva, which is calculated by multiplying our co-promotion interest (as a percentage) by the amount of certain milestones paid or payable by Teva, to which is added certain past and future development costs incurred by Teva with respect to the product for the U.S. Our co-promotion interest is in the twenty to thirty percent range, and equals our percentage share of detailing activities and co-promotion expenses. Such opt-in fee is payable as a reduction to the milestone payments or our share of operating profits that Teva would otherwise owe to us or a combination of the two. If we exercise this option, we will be eligible to receive, in lieu of royalties with respect to such product sales in the U.S., a share of operating profits from such product sales in the U.S. that is equal to our percent interest of detailing activities and co-promotion expenses.

Genentech. We entered into a collaborative research and license agreement with Genentech in December 2011, to discover and develop small and large molecules that selectively inhibit the Nav1.7 sodium channel as well as companion diagnostics for the potential treatment of pain. Under the terms of the agreement, Genentech paid us an upfront fee of \$10.0 million and we have subsequently earned a \$5.0 million milestone payment for the selection of a development-stage candidate. As of June 30, 2013, we were eligible to receive further pre-commercial and commercial milestone payments with respect to the licensed products totaling in aggregate up to \$626.0 million, comprised of up to \$58.5 million in preclinical and clinical milestone payments, up to \$387.5 million in regulatory milestone payments, and up to \$180.0 million in sales-based milestone payments for multiple products and indications. Genentech is also funding certain of our FTEs performing the research collaboration plan. We are also eligible to receive royalties based on net sales of the licensed products, which range from a mid single-digit percentage to ten percent for small-molecule inhibitors for the timeframe that such products are covered by the licensed patents and a low single-digit percentage thereafter, plus a low single-digit percentage for large-molecule inhibitors of Nav1.7.

Merck. In June 2009, we entered into an exclusive collaborative research and option agreement with Merck, pursuant to which the parties conducted a research program to discover and develop novel small-molecule candidates for the potential treatment of cardiovascular disease. Merck exercised its option to obtain an exclusive license to cardiovascular target and compound inhibitors that were discovered during the collaboration research program, which program ended in December 2012.

As of June 30, 2013, we had received milestone payments and an option fee from Merck totaling \$9.0 million and we are eligible for further research, development and regulatory milestone payments of up to \$64.0 million, comprised of \$21.0 million in preclinical and clinical milestone payments and up to \$43.0 million in regulatory milestone payments for products directed to the licensed target, or as much as \$86.5 million if we exercise our option to co-fund the Phase 1 and Phase 2 clinical trials.

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Genome BC. We entered into a research funding agreement with Genome BC in January 2009. Under the agreement with Genome BC, we carried out certain research activities with partial funding from Genome BC provided on a quarterly basis in arrears over the term of the research program. This agreement terminates in September 2013.

The following table is a summary of revenue recognized from our current collaboration and licensing agreements for the years ended December 31, 2011 and 2012 and the six months ended June 30, 2012 and 2013:

| | YEAR ENDED DECEMBER 31, | | SIX MONTHS ENDED JUNE 30, | |
|--|-------------------------|------------------|---------------------------|-----------------|
| | 2011 | 2012 | 2012 | 2013 |
| | (in thousands) | | | |
| uniQure: | | | | |
| Milestone payment | — | \$ 198 | — | — |
| Teva: | | | | |
| Recognition of upfront payment | — | 927 | — | \$ 6,607 |
| Research funding | — | — | — | 294 |
| Genentech: | | | | |
| Recognition of upfront payment | \$ 94 | 3,431 | \$1,685 | 1,659 |
| Research funding | 93 | 3,517 | 1,647 | 2,257 |
| Merck: | | | | |
| Recognition of initial milestone payment | 2,145 | 1,060 | 1,054 | — |
| Option fee | — | 2,060 | 2,047 | — |
| Research funding | 3,206 | 2,442 | 1,688 | — |
| Milestone payment | 1,038 | — | — | — |
| Genome BC: | | | | |
| Research funding | 339 | 665 | 86 | 168 |
| Total collaboration revenue | <u>\$ 6,915</u> | <u>\$ 14,300</u> | <u>\$8,207</u> | <u>\$10,985</u> |

Through June 30, 2013, we had received upfront fees and milestone payments totaling CAD\$575,000, pursuant to our agreement with uniQure. We are eligible to receive certain additional milestone payments of less than CAD\$1.0 million for Glybera and for each subsequent product, if any, developed pursuant to the agreement.

Under the terms of our agreement with Teva, we received an upfront payment of \$41.0 million. We determined that the various deliverables under this agreement should be considered as one single unit of accounting. As such, the \$41.0 million upfront payment is being recognized as revenue ratably over the expected period of research performance of pre-commercial activities, which is the three-year period from December 2012 through December 2015.

Under the terms of our agreement with Genentech, we received an upfront payment of \$10.0 million. We determined that the various deliverables under this agreement should be considered as one single unit of accounting. As such, the \$10.0 million upfront payment is being recognized as revenue ratably over the expected period of research performance, which is the three-year period from December 2011 through December 2014.

Under the terms of our agreement with Merck, we received an initial milestone payment of \$5.0 million in February 2010. We determined that this initial milestone payment was not substantive and should not be considered a separate element. As such, we are recognizing the initial milestone payment of \$5.0 million as revenue ratably over the expected period of research performance of pre-commercial activities, which is the period from February 2010 through June 2012. Since the beginning of 2011, we have received both an option fee and two milestone payments from Merck. Each of these payments was determined to be substantive and at risk at the inception of the agreement and as such have been recognized as revenue in the period received.

As our other internal and partnered products are in various stages of clinical and preclinical development, we do not expect to generate any revenue from product sales other than from our share of revenue related to our agreement

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with uniQure for at least the next several years. We expect that revenue for the next several years will be derived from our agreement with uniQure and our eligibility to receive a share of the compensation received by uniQure relating to the technology or products licensed by us, and full-time employees and milestone payments under our current collaboration agreements and any additional collaboration agreements that we may enter into in the future. We cannot provide any assurance as to the extent or timing of future milestone payments or royalty payments or that we will receive any future payments at all.

We expect that any revenue we generate will fluctuate quarter to quarter as a function of the timing and amount of milestones and other payments from our existing collaborations and any future collaborations.

The following table is a summary of our deferred revenue for our collaboration and licensing agreements as of December 31, 2011 and 2012, and June 30, 2013:

| | DECEMBER 31, | | JUNE 30, |
|------------------------|------------------|------------------|---------------------|
| | 2011 | 2012 | 2013 (unaudited) |
| | | (in thousands) | |
| Teva | — | \$ 39,907 | \$ 31,388 |
| Genentech | \$ 9,949 | 6,745 | 4,782 |
| Merck | 1,155 | — | — |
| Total deferred revenue | <u>\$ 11,104</u> | <u>\$ 46,652</u> | <u>\$ 36,170</u> |

We expect such deferred revenue remaining as of June 30, 2013 to be recognized as revenue in the applicable period during the three fiscal years ending December 31, 2015 based on our accounting policy for revenue recognition indicated for each collaboration agreement.

Operating Expenses

The following table summarizes our operating expenses for the years ended December 31, 2011 and 2012, respectively and for the six months ended June 30, 2012 and 2013:

| | YEAR ENDED DECEMBER 31, | | SIX MONTHS ENDED JUNE 30, | |
|----------------------------|-------------------------|------------------|------------------------------|-----------------|
| | 2011 | 2012 | 2012 | 2013 |
| | | (in thousands) | | (unaudited) |
| Research and development | \$ 12,237 | \$ 10,392 | \$ 4,770 | \$ 6,939 |
| General and administrative | 6,795 | 7,069 | 3,561 | 2,872 |
| Total operating expenses | <u>\$ 19,032</u> | <u>\$ 17,461</u> | <u>\$ 8,331</u> | <u>\$ 9,811</u> |

Research and Development Expenses

Research and development expenses represent costs incurred to conduct research on our product candidates in collaboration with Teva, Genentech and Merck, as well as further research and development of our other proprietary product candidates.

Research and development expenses consist of costs incurred in performing research and development activities, including salary, related benefits and share-based compensation for employees engaged in scientific research and development, third-party contract costs relating to research, formulation, manufacturing, preclinical studies and clinical trial activities, third-party license and collaboration fees, laboratory consumables and allocated facility-related costs.

Project-specific expenses reflect costs directly attributable to our clinical development candidates and our preclinical candidates once nominated and selected for further development. All remaining research and

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development expenses are reflected in early-stage discovery programs. At any given time, we have several active early-stage research and drug discovery programs. Our personnel and infrastructure are typically deployed over multiple projects and are not directly linked to any individual internal early-stage research or drug discovery program. Therefore, we do not maintain financial information for our internal early-stage research and internal drug discovery programs on a project-specific basis.

We expense all research and development costs as incurred. We expect that our research and development expenses will increase in the future as we advance our product candidate XEN701 into clinical development, conduct our development activities under our agreements with Teva and Genentech, advance our internal drug discovery programs into preclinical development and continue our early-stage research. The increase in expense will likely include added personnel and third-party contracts related to research, formulation, manufacturing, preclinical studies and clinical trial activities as well as third-party license and collaboration fees and laboratory consumables.

Clinical development timelines, likelihood of regulatory approval and commercialization and associated costs are uncertain and difficult to estimate and can vary significantly. We anticipate determining which research and development projects to pursue as well as the level of funding available for each project based on the scientific research and preclinical and clinical results of each product candidate and related regulatory action. We expect our research and development expenses to continue to represent our largest category of operating expense for the next 12 to 24 months.

General and Administrative Expenses

General and administrative expenses consist primarily of salary, related benefits and share-based compensation of our executive, finance, business development and administrative functions, travel expenses, allocated facility-related costs not otherwise included in research and development expenses, and professional fees for auditing, tax and legal services, including legal expenses for intellectual property protection.

We expect that general and administrative expenses will increase in the future as we expand our operating activities to support increased research and development activities, and build our commercial infrastructure for the potential option for co-promotion of XEN402 in the U.S., if and when regulatory approval is received.

We also anticipate incurring additional general and administrative expenses as a public company, including costs of additional personnel, additional professional fees for audit, accounting and legal services, director fees, enhanced business and accounting systems, costs related to investor relations and increased premiums for directors' and officers' liability insurance.

Other Income (Expense)

Interest Income. Interest income consists of income earned on our cash and investment balances. Our interest income has not been significant due to the low level of cash and investment balances and low interest earned on such balances. We anticipate that our interest income will increase in the future due to higher cash and investment balances than existed previously as a result of the upfront payment of \$41.0 million received from Teva in December 2012 and the receipt of the anticipated net cash proceeds from this offering.

Interest Expense. Interest expense consists of interest accrued on the note payable held by Isis Pharmaceuticals, Inc., or Isis, related to our collaboration agreement for XEN701. As we have fully repaid the note payable to Isis in June 2013 and now have no other debts outstanding, we expect to have little or no interest expense in the future.

Foreign Exchange Gain (Loss). Our functional currency is the Canadian dollar. For presentation purposes, our assets and liabilities are translated to U.S. dollars at exchange rates at the reporting date. Any resulting exchange gains and losses resulting from the translation of U.S. denominated transactions are recorded in current operations.

Gain (Loss) on Write-off and Disposal of Assets. During the year ended December 31, 2012, we wrote-off leasehold improvements at our leased facility which had a net book value of \$1.0 million in connection with a lease extension and modification agreement made effective April 1, 2012.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which have been prepared in conformity with generally accepted accounting principles in the U.S., or U.S. GAAP. The preparation of our financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the revenue and expenses incurred during the reported periods. We base estimates on our historical experience, known trends and various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are more fully described in the notes to our financial statements appearing in this prospectus, we believe that the following accounting policies are the most critical to understanding and evaluating our reported financial results.

Revenue Recognition

We have generated revenue primarily through collaboration agreements.

Under these collaboration agreements, we may receive non-refundable upfront payments, funding for research and development services, milestones, other contingent payments and royalties. In addition to receiving upfront payments, we may also be eligible to receive research funding, milestone and other contingent payments based on achieving pre-determined milestones. Research funding is recorded as revenue over the period of the research commitment. Milestone and other contingent payments are recorded as revenue when the underlying milestone is achieved if there is substantive uncertainty at the date the collaboration arrangement is entered into that the event will be achieved. In assessing the appropriate revenue recognition related to a collaboration agreement, we first determine whether an arrangement includes multiple elements, such as the delivery of intellectual property rights and research and development services. Upfront payments are recorded as deferred revenue in the balance sheet and are recognized as collaboration revenue over the estimated period of research performance that is consistent with the terms of the research and development obligations contained in the collaboration agreement. We periodically review the estimated period of performance based on the progress made under each arrangement.

In January 2011, the Financial Accounting Standards Board, or FASB, adopted new authoritative guidance on revenue recognition for multiple element arrangements, Accounting Standards Update, or ASU, No. 2009-13, *Multiple-Deliverable Revenue Arrangements*, or ASU 2009-13. This guidance, which applies to multiple element arrangements entered into or materially modified on or after January 1, 2011, amends the criteria for separating and allocating consideration in a multiple element arrangement by modifying the fair value requirements for revenue recognition and eliminating the use of the residual method. The selling prices of deliverables under an arrangement may be derived using third-party evidence, or TPE, or a best estimate of selling price, or BESP, if vendor-specific objective evidence of fair value, or VSOE, is not available.

Deliverables under the arrangement will be separate units of accounting provided that a delivered item has value to the customer on a stand-alone basis and if the arrangement does not include a general right of return relative to the delivered item and delivery or performance of the undelivered items is considered probably and substantially in the control of the vendor. The update also provided new guidance regarding how to apply the standard to arrangements that are materially modified following adoption of the update. The potential future impact of the adoption of this update will depend on the nature of any new agreements entered into or material modifications to existing arrangements.

Under a collaboration agreement, a steering committee is sometimes responsible for overseeing the general working relationships, determining the protocols to be followed in the research and development performed, and evaluating the results from the continued development of the product. We intend to evaluate whether our participation in any joint steering committees is a substantive obligation or whether the services are considered inconsequential or perfunctory.

The factors we would consider in determining if our participation in a joint steering committee is a substantive obligation include: (i) which party negotiated or requested the steering committee, (ii) how frequently the steering

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committee meets, (iii) whether or not there are any penalties or other recourse if we do not attend the steering committee meetings, (iv) which party has decision making authority on the steering committee and (v) whether or not the collaborator has the requisite experience and expertise associated with the research and development of the licensed intellectual property.

Incentive milestone payments may be triggered either by the results of our research efforts or by events external to us, such as regulatory approval to market a product. We recognize consideration that is contingent upon achievement of a milestone in its entirety as revenue in the period in which the milestone is achieved, but only if the consideration earned from the achievement of a milestone meets all the criteria for the milestone to be considered substantive at the inception of the arrangement. For a milestone to be considered substantive, the consideration earned by achieving the milestone must be commensurate with either our performance to achieve the milestone or the enhancement of the value of the item delivered as a result of a specific outcome resulting from our performance to achieve the milestone, relate solely to our past performance and be reasonable relative to all deliverables and payment terms in the collaboration agreement.

We generally recognize revenue from upfront payments ratably over the term of our estimated period of performance of research under our collaboration agreements in the event that such arrangements represent a single unit of accounting.

In January 2011, we also adopted the guidance (ASU No. 2010-17, *Milestones Method of Revenue Recognition*, or ASU 2010-17) that permits the recognition of revenue contingent upon our achievement of a milestone in its entirety, in the period the milestone is achieved, only if the milestone meets certain criteria and is considered to be substantive.

We made judgments which affect the periods over which we recognized revenue, including modifying such periods based on any amendments to our collaboration agreements.

Foreign Currency

Reporting Currency

For presentation purposes, our assets and liabilities are translated to U.S. dollars at exchange rates at the reporting date. The income and expenses are translated to U.S. dollars at the average exchange rate for the period in which the transaction arose. Equity transactions are translated at the spot exchange rates on which the transactions occur. Exchange differences arising are recognized in a separate component of equity titled accumulated other comprehensive loss. The financial statements have been presented in a currency other than our functional currency of the Canadian dollar, as management has determined that the U.S. dollar is the common currency in which our peers, being international drug and pharmaceutical companies, present their financial statements.

Transactions and Balances

Foreign currency transactions are translated into the Canadian functional currency using the exchange rates prevailing at the dates of the transactions. Foreign exchange gains and losses resulting from the settlement of foreign currency transactions and from the re-measurement of monetary assets and liabilities denominated in currencies other than our functional currency are recognized in the other income (expense).

Accrued Expenses

As part of the process of preparing our financial statements, we are required to estimate accrued expenses. This process involves communicating with our applicable personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of actual cost. The majority of our service providers invoice us monthly in arrears for services performed. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us. Examples of estimated accrued expenses include:

- ⁿ fees paid to contract research organizations in connection with preclinical and toxicology studies and clinical trials;
- ⁿ fees paid to investigative sites in connection with clinical trials;

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- fees paid to contract manufacturers in connection with the production of clinical trial materials; and
- fees paid for professional services.

There have been no material adjustments to our estimates of accrued expenses for any of the periods presented herein, and we do not anticipate that our payment of actual expenses will differ materially from our estimates at June 30, 2013.

Share-Based Compensation

Compensation expense related to share-based awards to employees, directors and other service providers is measured and recognized in our financial statements based on the fair value method with a corresponding increase in additional paid-in capital. Any consideration we receive from the exercise of stock options is credited to share capital.

We measure the fair value of each option awarded to employees on the grant date using the Black-Scholes option-pricing model and a single option award approach for options issued. The fair value of the award determined at grant is amortized over the vesting period.

We measure the fair value of each option awarded to non-employees on the date of grant and periodically re-measure during the grant period as the options are earned.

We expense the value of the options, net of forfeitures, over the vesting periods of the awards, which is typically three to four years. Prior to the completion of this offering, we used the methodology described below to determine fair value. Following completion of this offering, the fair value of our common shares will be determined based on the quoted market price.

Our use of the Black-Scholes option-pricing model requires the input of highly subjective assumptions, including the fair value of the underlying common shares, risk-free interest rates, the expected term of the option, the expected volatility of the price of our common shares and the expected dividend yield of our common shares. The assumptions used in our option-pricing model represent management's best estimates. These estimates involve inherent uncertainties and the application of management's judgment. If factors change and different assumptions are used, our share-based compensation expense could be materially different in the future.

Our assumptions and estimates are as follows:

- *Fair Value of Common Shares.* Because our common shares are not yet publicly traded, we must estimate their fair value, as discussed in "Valuation of Common Shares" below.
- *Risk-Free Interest Rate.* We base the risk-free interest rate used in the Black-Scholes option-pricing model on the implied yield available on the long-term U.S. Treasury note rate.
- *Expected Term.* The expected term is our estimate of when share-based awards are expected to become liquid. We use the simplified method to determine the expected term of options. Under this method the expected term represents the average of the vesting period and the contractual term.
- *Expected Volatility.* We determine the price volatility factor based on the historical volatilities of our publicly-traded peer group as we do not have a trading history for our common shares. Industry peers consist of several public companies in the life sciences industry that are similar to us in size, stage of life cycle, and financial leverage. We did not rely on implied volatilities of traded options in our industry peers' common shares because the volume of activity was relatively low. Following completion of the offering, we intend to continue to consistently apply this process using the same or similar public companies until a sufficient amount of historical information regarding the volatility of our own common shares price becomes available, or unless circumstances change such that the identified companies are no longer similar to us, in which case, more suitable companies whose share prices are publicly available would be utilized in the calculation.
- *Expected Dividend Yield.* We have never declared or paid cash dividends and based on our current expectation we do not expect to pay dividends in the foreseeable future. Consequently, we used an expected dividend yield of zero.

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The assumptions we used to determine the fair value of stock options granted during the periods presented are as follows, presented on a weighted-average basis:

| | YEAR ENDED DECEMBER 31, | | SIX MONTHS ENDED JUNE 30, | |
|--------------------------|-------------------------|-------|---------------------------|-------|
| | 2011 | 2012 | 2012 (unaudited) | 2013 |
| Risk-free interest rate | 2.36% | 1.14% | 1.15% | 1.03% |
| Expected term (in years) | 6.2 | 6.2 | 6.2 | 6.2 |
| Expected volatility | 70% | 70% | 70% | 70% |
| Expected dividend yield | — | — | — | — |

In addition to the assumptions used in the Black-Scholes option-pricing model, we must also estimate a forfeiture rate to calculate the share-based compensation expense for our awards. Our forfeiture rate is based on an analysis of our actual forfeitures. We will continue to evaluate the appropriateness of the forfeiture rate based on actual forfeiture experience, analysis of employee turnover, and other factors, such as historical experience with option exercises. Quarterly changes in the estimated forfeiture rate can have a significant impact on our share-based compensation expense as the cumulative effect of adjusting the rate is recognized in the period the forfeiture estimate is changed. If a revised forfeiture rate is higher than the previously estimated forfeiture rate, an adjustment is made that will result in a decrease to the share-based compensation expense recognized in the financial statements. If a revised forfeiture rate is lower than the previously estimated forfeiture rate, an adjustment is made that will result in an increase to the share-based compensation expense recognized in the financial statements.

We will continue to use judgment in evaluating the assumptions related to our share-based compensation on a prospective basis. As we continue to accumulate additional data related to our common shares, we may have refinements to our estimates, which could impact our future share-based compensation expense.

Valuation of Common Shares

We are required to estimate the fair value of the common shares underlying our share-based awards when performing the fair value calculations with the Black-Scholes option-pricing model. The fair value of our common shares was determined by our board of directors, with input from management, and takes into account our most recently available valuation of common shares and our assessment of additional objective and subjective factors we believed were relevant and which may have changed between the date of the most recent valuation and the date of the grant. We believe that our audit committee, or the Committee, and our board of directors, or our Board, has the relevant experience and expertise to determine the fair value of our common shares.

Because there has been no public market for our common shares, the Committee and our Board considers numerous objective and subjective factors to determine its best estimate of the fair value of our common shares as of each grant date, including, among other things, the following:

- the lack of marketability of our common shares;
- the rights of the preferred shares and the common shares in a liquidation scenario;
- current market conditions applicable at the time of the assessment;
- our financial condition;
- our business performance;
- the latest sales and issuances of our preferred shares to third parties;
- prevailing industry trends;
- the stage of development of our product candidates; and
- with respect to grants made on or following January 1, 2013, valuation reports prepared by an independent third-party valuation firm.

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Option Grants

The following table summarizes by grant date the number of shares subject to options granted between January 1, 2012 and the date of this prospectus, the per share exercise price of the options and the fair value of common shares underlying the options on the date of grant:

| GRANT DATE | NUMBER OF COMMON SHARES UNDERLYING OPTIONS GRANTED | OPTION EXERCISE PRICE (CAD \$) | OPTION EXERCISE PRICE (U.S. \$) | FAIR VALUE PER SHARE (U.S. \$) |
|--------------------|---|---|--|---|
| January 1, 2012 | 610,750 | 0.77 | 0.76 | 0.76 |
| January 7, 2012 | 7,000 | 0.77 | 0.75 | 0.75 |
| March 8, 2012 | 2,000 | 0.77 | 0.78 | 0.78 |
| March 19, 2012 | 500 | 0.77 | 0.78 | 0.78 |
| April 1, 2012 | 10,000 | 0.77 | 0.77 | 0.77 |
| April 29, 2012 | 10,000 | 0.77 | 0.79 | 0.79 |
| May 16, 2012 | 1,000 | 0.77 | 0.76 | 0.76 |
| July 1, 2012 | 10,000 | 0.77 | 0.76 | 0.76 |
| August 20, 2012 | 2,500 | 0.77 | 0.78 | 0.78 |
| September 17, 2012 | 7,500 | 0.77 | 0.79 | 0.79 |
| September 24, 2012 | 50,000 | 0.55 | 0.56 | 0.56 |
| October 29, 2012 | 15,000 | 0.55 | 0.55 | 0.55 |
| November 5, 2012 | 2,000 | 0.55 | 0.55 | 0.55 |
| December 14, 2012 | 1,000 | 0.55 | 0.56 | 0.56 |
| December 21, 2012 | 250 | 0.55 | 0.55 | 0.55 |
| January 1, 2013 | 823,400 | 0.55 | 0.55 | 1.07 |
| January 2, 2013 | 1,500 | 0.55 | 0.55 | 1.07 |
| January 7, 2013 | 500 | 0.55 | 0.56 | 1.07 |
| January 14, 2013 | 200,000 | 0.55 | 0.56 | 1.07 |
| January 28, 2013 | 3,000 | 0.55 | 0.55 | 1.07 |
| February 10, 2013 | 3,000 | 0.55 | 0.55 | 1.07 |
| February 11, 2013 | 5,000 | 0.55 | 0.55 | 1.07 |
| March 10, 2013 | 150,000 | 0.55 | 0.54 | 1.07 |
| April 1, 2013 | 750 | 0.55 | 0.54 | 1.91 |
| April 25, 2013 | 20,000 | 0.55 | 0.54 | 1.91 |
| April 28, 2013 | 5,000 | 0.55 | 0.54 | 1.91 |
| June 16, 2013 | 2,000 | 0.55 | 0.54 | 1.91 |
| August 1, 2013 | 207,000 | 2.01 | 1.94 | 1.91 |

The exercise prices of our options are denominated in Canadian dollars. The exercise prices in the chart above have been translated to U.S. dollars at the exchange rate in effect on the applicable grant date.

With respect to the January 1, 2012 stock options grants, our Board set the option exercise price with reference to its assessment of the market price, as such term is defined in our Amended and Restated Stock Option Plan, of our common shares. Our Board had previously received and considered an internally-prepared valuation report presented to the Committee. Our Board determined that the valuation provided for in the report represented the Company's market value as of January 1, 2012, the date of grant, CAD \$0.77 per common share. On January 9, 2012, our Board concluded that this price was appropriate as of January 1, 2012, the date of grant of the options.

From January 2012 through September 24, 2012, our Board determined that there had been no material change in overall market conditions generally and the biotechnology sector in particular. Our Board further determined that we had not experienced a material change in the market price of our common shares. Among the reasons for this conclusion were the following:

- ⁿ the Genentech collaboration, which was an early-stage discovery program that we had entered into in December 2011, had not materially progressed;

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- we did not materially progress our product candidates;
- we did not raise any additional equity through private placements and our cash balances generally continued to decline; and
- we had no plans for an initial public offering, or IPO, in the near term because we did not believe that the public markets presented a favorable environment at the time for an early-stage biotechnology company such as ours.

In September 2012, we prepared an internal valuation report by estimating our enterprise value using a comparable group of public companies. We considered an average of enterprise values and metrics of a multiple of book value to enterprise value for the comparable companies based on their published financial statements as of June 30, 2012. The average metric of multiple of book value to enterprise value was applied to our book value, and a common share value was then computed by dividing the gross equity value, less the estimated amount to redeem all outstanding preferred shares, by the number of common shares outstanding. The Committee and our Board considered this valuation together with management input and other factors in making a determination of the common share valuation as of September 24, 2012. Our Board determined that the market price as of the date of the valuation was CAD\$0.55.

Among the factors considered in reaching this determination were the fact that some of our clinical assets had not advanced since the date of the Company's last valuation and the fact that the collaborative research component of one of the Company's collaboration agreements in place at the time of the last valuation was winding down and due to expire with the loss of concomitant revenue.

In December 2012, we entered into a collaboration agreement with Teva for our lead program, XEN402, based on the results of four Phase 2 clinical trials. Under the Teva agreement, we received an upfront license fee of \$41.0 million which substantially improved our financial position. In addition, several life sciences public offerings were completed in the fourth quarter of 2012 as market conditions improved for biotechnology companies.

The fair value determinations as of January 1, 2013 and June 30, 2013 were determined retrospectively by the Committee and our Board having considered and with reference to a report prepared by an independent third-party valuation firm utilizing the option pricing method, or OPM. In connection with the assessment, we performed a probability-weighted analysis of the different valuations expected for the common shares in the event that we complete an IPO as well as in the alternative. Such an analysis may be considered to be part of the PWERM methodology.

OPM analyzes the value of each class of security by treating it as a call option on a portion of the future value of a business. Under this method, the common shares have value only if the funds available for distribution to shareholders exceed the value of the liquidation preference at the time of a liquidity event (for example, in a merger or sale), assuming the enterprise has funds available to make a liquidation preference meaningful and collectible by the shareholders. OPM values each equity class by creating a series of call options on our equity value, with exercise prices based on the liquidation preferences, participation rights, and strike prices of derivatives. This method is generally preferred when future outcomes are difficult to predict and dissolution or liquidation is not imminent.

With respect to our determination of fair value as of January 1, 2013, our Board determined the fair value with reference to a valuation report which was based on a blend of the income and market approach with a two-thirds weighting for the income approach and a one-third weighting for the market approach. In the report, the equity value was allocated using a time to sale event of three years and time to IPO of one year, using a discount rate of 33.8%, determined, in part, with reference to a company-specific risk premium accounting for the fact that we had not, among other things: (i) completed clinical trials for our product candidates, (ii) received needed regulatory approvals for commercial sale in important markets and (iii) demonstrated large-scale commercial viability of our products. The report assumed volatility of 70% based on historical trading volatility for our peer group of companies. A discount for lack of marketability, to account for the illiquidity of the common shares, was applied to the indicated common share value to determine the fair value of the shares. The discount was 35% for the sale scenario and 10% for the IPO scenario. The discount for lack of marketability was determined based on qualitative factors such as our expectation of the timing of the liquidity event under both the sale and IPO scenarios, our ability to access additional capital and the resulting dilution, and the degree of risk in the biotechnology industry. Based on these factors, our Board concluded that our common shares had a fair value of \$1.07 per share on January 1, 2013.

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For our June 30, 2013 determination of fair value, we and our valuation firm considered a number of factors including:

- the improving market receptivity for early-stage biotechnology companies, which caused us to consider an IPO;
- the grant by the FDA of orphan drug designation to XEN402;
- our decision to exercise our license option on XEN701 and commence IND-enabling studies for this product candidate;
- progress towards our IPO, including engagement of investment bankers, lawyers and accountants and our initial organizational meeting.

For our June 30, 2013 valuation, we estimated enterprise value using a blend of the income and market approaches. We adjusted our valuation model to increase the probability of an IPO from 30% to 50% to account for an increased probability of an IPO scenario, in light of continued favorable market conditions and the progress we achieved towards a potential initial public offering of our common shares. Additionally, we discounted the common shares using a discount rate of 24.3% and reduced the discount for lack of marketability for the IPO scenario from 10% to 5% given that we believed that we were moving close to a potential exit event through an IPO. We believe that the reduction in discount rate for lack of marketability from the valuation as at January 1, 2013 was consistent with the reduction of the risk and other qualitative factors. We reduced the expected time to IPO from 12 months to 6 months for this valuation while maintaining the expected time to sale scenario at three years. We assumed volatility remained at 70% as in the prior valuation.

Based on the revised assumptions underlying the valuation model and the changes in our business and in the market values of early-stage biotechnology companies, as well as the impact of an increasing enterprise value on the relative value of our common shares as compared to our convertible preferred shares, the Committee and our Board, together with management input determined that the fair value of our common shares had increased to \$1.91 per share as of June 30, 2013. For financial reporting purposes, given the lack of company milestones in the second quarter of 2013 that would be expected to materially influence common share value, and given the fact that the concentration of IPO preparation activities and market receptivity improvement occurred in the second quarter of 2013, we conservatively applied this \$1.91 value for computation of stock-based compensation expense to our option grants between April 1, 2013 and June 30, 2013. In connection with the stock option grant on August 1, 2013, our Board determined that there had been no material change to the fair value of our common stock as of such date.

During the quarter ended June 30, 2013, we granted 27,750 options granted resulting in share-based compensation expense of \$2,448.

Based on the assumed initial public offering price of \$ per share, which is the midpoint of the estimated price range set forth on the cover page of this prospectus, the aggregate intrinsic value of stock options outstanding as of June 30, 2013 was \$ million, of which \$ million relate to vested options and \$ million to unvested options.

The following table summarizes the share-based compensation expense recorded for the periods shown (in thousands):

| | YEAR ENDED DECEMBER 31, | | SIX MONTHS ENDED JUNE 30, | |
|----------------------------|-------------------------|--------|------------------------------|--------|
| | 2011 | 2012 | 2012 (unaudited) | 2013 |
| Research and development | \$ 145 | \$ 112 | \$ 58 | \$ 70 |
| General and administrative | 290 | 294 | 146 | 203 |
| Total | \$ 435 | \$ 406 | \$ 204 | \$ 273 |

[Table of Contents](#)**Results of Operations****Comparison of Six Months Ended June 30, 2012 and 2013****Revenue**

The following table summarizes the results of our operations for the six months ended June 30, 2012 and 2013, together with changes in those items (in thousands):

| | SIX MONTHS ENDED JUNE 30, | | CHANGE 2012 VS. 2013 INCREASE/(DECREASE) |
|---|---------------------------|-----------|--|
| | 2012 | 2013 | |
| | (unaudited) | | |
| Collaboration revenue | \$ 8,207 | \$ 10,985 | \$ 2,778 |
| Royalties | 3 | — | (3) |
| Research and development expenses | 4,770 | 6,939 | 2,169 |
| General and administrative expenses | 3,561 | 2,872 | (689) |
| Other: | | | |
| Interest income | 56 | 76 | 20 |
| Interest expense | 46 | 41 | (5) |
| Foreign exchange gain (loss) | (143) | 1,920 | 2,063 |
| Gain (loss) on write-off and disposal of assets | (1,197) | 11 | 1,208 |

We recognized revenue of \$11.0 million for the six months ended June 30, 2013 compared to \$8.2 million for the six months ended June 30, 2012, an increase of \$2.8 million. The increase was primarily attributable to the recognition of \$6.9 million of the upfront payment and research funding from Teva, and the \$0.6 million in additional FTE funding we received from Genentech. This was partially offset by the \$4.7 million decrease in revenue from Merck compared to the six months ended June 30, 2012 in which we received \$1.6 million in FTE funding related to the research agreement with Merck that ended in December 2012, a \$2.0 million option fee payment received from Merck in June 2012, and \$1.1 million for the recognition of the initial milestone payment received in February 2010.

Research and Development Expenses

The following table summarizes our research and development expenses for the six months ended June 30, 2012 and 2013, together with changes in those items (in thousands):

| | SIX MONTHS ENDED JUNE 30, | | CHANGE 2012 VS. 2013 INCREASE/(DECREASE) |
|---|---------------------------|----------|--|
| | 2012 | 2013 | |
| | (unaudited) | | |
| XEN402 | \$ 1,149 | \$ 479 | \$ (670) |
| XEN701 | 306 | 3,190 | 2,884 |
| Product and discovery programs | 3,176 | 2,431 | (745) |
| Early stage research | 139 | 839 | 700 |
| Total research and development expenses | \$ 4,770 | \$ 6,939 | \$ 2,169 |

Research and development expenses were \$6.9 million for the six months ended June 30, 2013 as compared to \$4.8 million for the six months ended June 30, 2012, an increase of \$2.2 million. The increase was primarily attributable to a \$2.9 million increase in spending for XEN701 and a \$0.7 million increase in spending for our early stage research programs. The increases were offset in part by a \$0.7 million decrease in spending for XEN402 related to Teva's assumption of the development costs of that product candidate as of January 1, 2013, and a \$0.7 million decrease in spending related to our product and discovery programs.

[Table of Contents](#)*General and Administrative Expenses*

The following table summarizes our general and administrative expenses for the six months ended June 30, 2012 and 2013, together with changes in those items (in thousands):

| | SIX MONTHS ENDED JUNE 30, | | CHANGE 2012 VS. 2013 INCREASE/(DECREASE) |
|-------------------------------------|---------------------------|----------|--|
| | 2012 | 2013 | |
| | (unaudited) | | |
| General and administrative expenses | \$ 3,561 | \$ 2,872 | \$ (689) |

General and administrative expenses were \$2.9 million for the six months ended June 30, 2013 compared to \$3.6 million for the six months ended June 30, 2012. This decrease was primarily due to a reduction in intellectual property expenses, the majority of which have been assumed by our collaborators.

Other Income (Expense)

The following table summarizes our other income (expense) for the six months ended June 30, 2012 and 2013, together with changes in those items (in thousands):

| | SIX MONTHS ENDED JUNE 30, | | CHANGE 2012 VS. 2013 INCREASE/(DECREASE) |
|-------------------------|---------------------------|----------|--|
| | 2012 | 2013 | |
| | (unaudited) | | |
| Other income (expense): | \$ (1,330) | \$ 1,966 | \$ 3,296 |

Interest income increased slightly for the six months ended June 30, 2013 compared to the six months ended June 30, 2012. The increase was primarily attributable to our increased cash and investment balances from our receipt of \$41.0 million in December 2012 from Teva.

We recognized a foreign exchange gain of \$1.9 million for the six months ended June 30, 2013 as compared to a foreign exchange loss of \$0.1 million for the six months ended June 30, 2012. The foreign exchange gain in 2013 was related to our increased cash balances and due to the increased Canadian dollar to U.S. dollar exchange rate.

We wrote-off leasehold improvements with a net book value of \$1.0 million for the six months ended June 30, 2012 in connection with a lease extension and modification agreement made effective April 1, 2012. No such item was recorded in the six months ended June 30, 2013.

Comparison of Years Ended December 31, 2011 and 2012*Revenue*

The following table summarizes the results of our operations for the years ended December, 2011 and 2012 together with changes in those items (in thousands):

| | YEAR ENDED DECEMBER 31, | | CHANGE 2011 VS. 2012 INCREASE/(DECREASE) |
|---|-------------------------|-----------|--|
| | 2011 | 2012 | |
| Collaboration revenue | \$ 6,915 | \$ 14,300 | \$ 7,385 |
| Royalties | 3 | 8 | 5 |
| Research and development expenses | 12,237 | 10,392 | (1,845) |
| General and administrative expenses | 6,795 | 7,069 | 274 |
| Other: | | | |
| Interest income | 153 | 144 | (9) |
| Interest expense | 91 | 93 | 2 |
| Foreign exchange gain (loss) | 60 | (169) | (229) |
| Gain (loss) on write-off and disposal of assets | — | (1,030) | (1,030) |

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We recognized revenue of \$14.3 million for the year ended December 31, 2012 as compared to \$6.9 million for the year ended December 31, 2011, an increase of \$7.4 million. The increase during 2012 was primarily due to an upfront payment and research funding pursuant to our collaboration agreement with Genentech.

Research and Development Expenses

The following table summarizes research and development expenses for the years ended December, 2011 and 2012 together with changes in those items (in thousands):

| | YEAR ENDED DECEMBER 31, | | CHANGE 2011 VS. |
|---|-------------------------|-----------|-----------------------------|
| | 2011 | 2012 | 2012 INCREASE/(DECREASE) |
| XEN402 | \$ 2,443 | \$ 1,940 | \$ (503) |
| XEN701 | 739 | 2,666 | 1,927 |
| Product and discovery programs | 7,057 | 5,336 | (1,721) |
| Early stage research | 1,998 | 450 | (1,548) |
| Total research and development expenses | \$ 12,237 | \$ 10,392 | \$ (1,845) |

Research and development expenses were \$10.4 million for the year ended December 31, 2012 compared to \$12.2 million for the year ended December 31, 2011. The decrease was primarily due to a smaller number of personnel working in research and development as we experienced normal attrition in the department without replacing the departed employees in the year.

General and Administrative Expenses

The following table summarizes general and administrative expenses for the years ended December 31, 2011 and 2012 together with changes in those items (in thousands):

| | YEAR ENDED DECEMBER 31, | | CHANGE 2011 VS. |
|-------------------------------------|-------------------------|----------|-----------------------------|
| | 2011 | 2012 | 2012 INCREASE/(DECREASE) |
| General and administrative expenses | \$ 6,795 | \$ 7,069 | \$ 274 |

General and administrative expenses were \$7.1 million for the year ended December 31, 2012 compared to \$6.8 million for the year ended December 31, 2011, an increase of \$0.3 million. The increase was primarily due to an increase in intellectual property expenses associated with our discovery and development programs.

Other Income (Expense)

The following table summarizes our other income (expense) for the year ended December 31, 2011 and 2012 together with changes in those items (in thousands):

| | YEAR ENDED DECEMBER 31, | | CHANGE 2011 VS. |
|--------------------------|----------------------------|-----------|-----------------------------|
| | 2011 | 2012 | 2012 INCREASE/(DECREASE) |
| Other income (expenses): | \$ 122 | \$(1,148) | \$ (1,270) |

Interest income for the year ended December 31, 2012 was comparable to interest income for the year ended December 31, 2011 due to similar levels of cash and investment balances for both years.

Interest expense for the year ended December 31, 2012 was comparable to interest expense for the year ended December 31, 2011 due to the similar amount of principal of the note payable to our collaborator, Isis, pursuant to our agreement with them.

We recognized a foreign exchange loss of \$169,000 for the year ended December 31, 2012 compared to a foreign exchange gain of \$60,000 for the year ended December 31, 2011 due to unfavorable exchange rate fluctuation.

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We wrote-off leasehold improvements with a net book value of \$1.0 million during the year ended December 31, 2012 in connection with a lease extension and modification agreement made effective April 1, 2012. No such item was recorded in the year ended December 31, 2011.

Liquidity and Capital Resources

To date, we have financed our operations primarily through funding received from collaborator and license agreements and private placements of our common and preferred shares, as well as government funding. Through June 30, 2013, we have received an aggregate of approximately \$262.0 million to fund our operations, of which approximately \$140.0 million was non-equity funding pursuant to collaboration and license agreements, approximately \$17.0 million was pursuant to government funding, and approximately \$105.0 was pursuant to the sale of our preferred shares. As of June 30, 2013, we had \$49.8 million in cash and cash equivalents.

We have incurred significant operating losses since inception. Our net loss was \$12.0 million for the year ended December 31, 2011 and \$4.3 million for the year ended December 31, 2012. Although we posted net income for the six months ended June 30, 2013, we had an accumulated deficit of \$125.6 million through that date. We expect to continue to incur significant expenses in excess of our sublicensing and royalty revenue from Glybera and expect to incur operating losses over the next several years. Our net losses may fluctuate significantly from quarter to quarter and year to year. We expect to continue to incur significant expenses and 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 current clinical studies for our 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 Isis Pharmaceuticals, Inc., or Isis, UBC, and the Memorial University of Newfoundland, or MUN; maintain, protect and expand our intellectual property portfolio; attract and retain skilled personnel; establish a sales, marketing and distribution infrastructure to commercialize any products for which we or one of our collaborators may obtain marketing approval, and maintain 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.

Until such time as we can generate substantial product revenue, if ever, we expect to finance our cash needs through a combination of collaboration agreements and equity or debt financings. Except for any obligations of our collaborators to reimburse us for research and development expenses or to make milestone payments under our agreements with them, upon completion of this offering, we will not have any committed external sources of capital. To the extent that we raise additional capital through the future sale of equity or debt, the ownership interest of our shareholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our existing common shareholders. If we raise additional funds through collaboration agreements in the future, we may have to relinquish valuable rights to our technologies, future revenue streams or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Our future capital requirements are difficult to forecast and will depend on many factors, including:

- whether our existing collaborations continue to generate research funding, milestone payments and royalties to us;
- the number and stage of development of future product candidates that we choose to pursue;
- the scope, progress, results and costs of research and development of our future product candidates independently, and conducting preclinical research and clinical studies;
- the timing and costs involved in obtaining regulatory approvals for any future product candidates we develop independently;

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- the cost associated with exercising our co-promotion option for XEN402 in the U.S., should the opportunity arise and we choose to do so;
- the cost of commercialization activities, if any, of any future product candidates we develop independently that are approved for sale, including marketing, sales and distribution costs;
- the cost of manufacturing our future product candidates and any products we successfully commercialize independently;
- our ability to maintain existing collaborations and to establish new collaborations, licensing or other arrangements and the financial terms of such arrangements;
- the costs of preparing, filing, prosecuting, maintaining, defending and enforcing patents, including litigation costs and the outcome of such litigation; and
- the timing, receipt and amount of sales, or royalties on Glybera, XEN402, XEN701, a selective Nav1.7 inhibitor and our future product candidates, if any.

Based on our research and development plans and our timing expectations related to the progress of our programs, we expect that the net proceeds from this offering, together with our existing cash and cash equivalents as of the date of this prospectus 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 the next 12 to 24 months. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we expect. Additionally, the process of testing drug candidates in clinical trials is costly, and the timing of progress in these trials remains uncertain.

Cash Flows

The following table shows a summary of our cash flows for the years ended December 31, 2011 and 2012 and for the six months ended June 30, 2012 and 2013 (in thousands):

| | YEAR ENDED DECEMBER 31, | | SIX MONTHS ENDED JUNE 30, | |
|---|-------------------------|-----------|------------------------------|-----------|
| | 2011 | 2012 | 2012 | 2013 |
| Net cash provided by (used in) operating activities | \$ (13,689) | \$ 45,573 | \$6,146 | \$(5,614) |
| Net cash provided by (used in) investing activities | 13,889 | 491 | 910 | (68) |
| Net cash provided by (used in) financing activities | 2 | — | — | (1,697) |

Operating Activities

During the six months ended June 30, 2013, net cash used in operating activities totaled \$5.6 million. Our net income of \$3.1 million was offset by a significant decrease in deferred revenue and decrease in other operating assets.

During the six months ended June 30, 2012, operating activities provided \$6.1 million of cash. The collection of the receivable for \$10.0 million upfront payment from the Genentech collaboration offset our net loss and a decrease in operating liabilities.

During the year ended December 31, 2012, operating activities provided \$45.6 million of cash. This cash flow from operations resulted from the \$41.0 million payment received from Teva and the collection of the receivable for the \$10.0 million upfront payment from the Genentech collaboration, partially offset by our net loss of \$4.3 million. Our accounts payable and accrued liabilities were affected by the timing of payments to our vendors and additional accruals for our research activities.

During the year ended December 31, 2011, operating activities used \$13.7 million of cash, primarily as a result of our net loss for the year of \$12.0 million and the net impact of the Genentech collaboration and our recording of the receivable and deferred revenue of the upfront payment of \$10.0 million.

Investing Activities

During the six months ended June 30, 2013, net cash used in investing activities was \$0.1 million and consisted primarily of purchases of research and computer equipment.

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During the six months ended June 30, 2012, net cash provided by investing activities was \$0.9 million. Net cash provided by investing activities during the period consisted primarily of cash received from the sale of marketable securities of \$1.0 million, partially offset by cash used to purchase research and computer equipment.

For the year ended December 31, 2012, net cash provided by investing activities was \$0.5 million and consisted primarily of cash received from the sale of marketable securities of \$1.0 million, partially offset by purchases of research and computer equipment of \$0.5 million.

For the year ended December 31, 2011, net cash provided by investing activities was \$13.9 million and consisted primarily of cash received from the sale of marketable securities of \$14.2 million, partially offset by purchases of research and computer equipment of \$0.3 million.

Financing Activities

During the six months ended June 30, 2013, net cash used for financing was \$1.7 million, which can be attributed to repayment of the note we issued to Isis in connection with our collaboration agreement.

Net cash provided by financing activities for the six months ended June 30, 2012 as well as the years ended December 31, 2011 and 2012 were related to the exercise of stock options and was less than \$2,000 for each period.

Contractual Obligations and Commitments

The following summarizes our significant contractual obligations as of December 31, 2012:

| <u>CONTRACTUAL OBLIGATIONS</u> | <u>TOTAL</u> | <u>LESS THAN 1 YEAR</u> | <u>1 TO 3 YEARS</u> | <u>3 TO 5 YEARS</u> | <u>MORE THAN 5 YEARS</u> |
|---------------------------------|------------------|-----------------------------|---------------------|---------------------|------------------------------|
| Operating leases ⁽¹⁾ | \$ 8,784 | \$ 924 | \$ 1,860 | \$ 1,896 | \$ 4,104 |
| Long term debt ⁽²⁾ | 1,665 | — | 1,665 | — | — |
| Total obligations | \$ 10,449 | \$ 924 | \$ 3,525 | \$ 1,896 | \$ 4,104 |

⁽¹⁾ Represents future minimum lease payments under non-cancelable operating leases in effect as of June 30, 2013 including the remaining lease payments for our current facilities in Burnaby, British Columbia, Canada. The minimum lease payments above do not include common area maintenance charges or real estate taxes.

⁽²⁾ We issued a promissory note of \$1.5 million to Isis pursuant to our collaboration and license agreement. The note bears interest, with interest compounded annually and interest payable at the time the note becomes due, which is the earlier of occurrence of certain future financing events or at a time during late 2014. Included in the balance is interest payable calculated up to December 31, 2012. The note was paid in full in June 2013.

The contractual obligations table above does not include any potential future milestone or royalty payments we may be required to make under our license agreement with Isis, under which we were granted an exclusive worldwide license to XEN701, due to the uncertainty of the occurrence of the events requiring payment under that agreement. To the extent that we continue to develop and ultimately commercialize XEN701, we may be obligated to pay Isis up to \$148.0 million in milestone payments plus single-digit royalties on net sales. The table also excludes potential future payments we may be required to make if we elect to opt into the co-development arrangement under our collaboration with Merck or the co-promotion arrangement provided for XEN402 under our collaboration with Teva. Our potential payment obligations in the single-digit percentage range to UBC related to amounts we receive from sales of Glybera are also excluded from the table. Additionally, the table does not include our potential royalty obligation to MUN pursuant to the Restated Collaborative Research & License Agreement by and between us and MUN dated December 2006. Pursuant to this agreement, we are obligated to pay MUN certain milestone payments and a single-digit percentage royalty of net sales for products that we sell directly and a single-digit percentage of royalties we receive from sales on products under our pain program.

Inflation

We do not believe that inflation had a material effect on our business, financial condition or results of operations in the last two fiscal years. If our costs were to become subject to significant inflationary pressures, we may be able to offset higher costs through revenue increases. Our inability to do so could harm our business, financial condition and results of operations.

Off-Balance Sheet Arrangements

We do not engage in any off-balance sheet financing activities. We do not have any interest in entities referred to as variable interest entities, which include special purposes entities and other structured finance entities.

Related Party Transactions

For a description of our related party transactions, see "Certain Relationships and Related Party Transactions."

Recent Accounting Pronouncements

In May 2011, in an effort to assist in the convergence of U.S. GAAP and International Financial Reporting Standards, or IFRS, the Financial Accounting Standards Board, or FASB, issued an Accounting Standards Update related to "Fair Value Measurements: Amendments to Achieve Common Fair Value Measurements and Disclosure Requirements in U.S. GAAP and IFRS." The standard expands existing disclosure requirements for fair value measurements and makes certain other amendments, including a requirement to categorize, by level in the fair value hierarchy, items that are required to be disclosed, but not measured, at fair value. The standard is effective for fiscal years, and interim periods within those years, beginning after December 15, 2011, and should be applied prospectively. We adopted this standard as of January 1, 2012 and its adoption did not have a material effect on our financial statements for the year ended December 31, 2012.

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 allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We can elect to take advantage of the ability to delay the adoption of new or revised accounting standards, and as a result, we may not comply with new or revised accounting standards on the relevant dates on which adoption of such standards is required for public companies that are not emerging growth companies and our financial statements may not be comparable to the financial statements of those companies. No such elections have been made for the years ended December 31, 2011 and 2012.

Quantitative and Qualitative Disclosure About Market Risk

We are exposed to various market risks in the ordinary course of our business, including changes in interest rates and currency exchange rates. Market risk is the potential loss arising from adverse changes in interest rates and exchange rates.

Foreign Currency Exchange Risk

The principal market risk we face is foreign currency exchange rate risk. We face this risk, in part, as a result of entering into transactions denominated in currencies other than Canadian dollars, particularly those denominated in U.S. dollars and Euros. We also hold non-Canadian dollar denominated cash, accounts receivable and accounts payable, which are primarily denominated in U.S. dollars.

Changes in foreign currency exchange rates can create significant foreign exchange gains or losses to us. Our current foreign currency risk is primarily with the U.S. dollar as a majority of our non-Canadian dollar denominated expenses are denominated in U.S. dollars. To limit our exposure to volatility in currency markets, we estimate our anticipated expenses that will be denominated in currencies other than the Canadian dollar and then purchase a corresponding amount of the relevant foreign currency at the current spot rate. Once these estimated expense amounts are acquired, we do not hedge our exposure and thus assume the risk of future gains or losses on the amounts of foreign currency held. The impact of an adverse change in foreign exchange rates may be offset in the event we receive a milestone payment from a foreign collaborator. At June 30, 2013, we held cash of \$18.0 million denominated in U.S. dollars. A hypothetical 10% increase (decrease) in the value of the U.S. dollar would result in a foreign exchange gain (loss) of \$1.8 million (\$1.8 million) being recorded in the Statement of Operations on the translation of these U.S. dollar cash balances into the Canadian dollar functional currency.

Interest Rate Risk

An additional market risk we face is interest rate risk. We had cash and cash equivalents of \$49.8 million as of June 30, 2013, which consisted of bank deposits. The goals of our investment policy are liquidity and capital preservation; we do not enter into investments for trading or speculative purposes and have not used any derivative financial instruments to manage our interest rate exposure. We believe that we do not have any material exposure to changes in the fair value of these assets as a result of changes in interest rates due to the short term nature of our cash and cash equivalents. Declines in interest rates, however, would reduce future investment income. A 10% change in interest rates during any of the periods presented would not have had a material impact on our financial statements. Such interest-earning instruments carry a degree of interest rate risk. We had no outstanding debt as of June 30, 2013.

BUSINESS

Overview

We are a biopharmaceutical company focused on the development of novel medicines through the application of our proprietary discovery platform, which we refer to as Extreme Genetics. Our product candidates are based on genetic insights derived from our research of families where individuals exhibit severe traits, or phenotypes. We apply our expertise to predict which phenotypes are caused by single-gene defects. By identifying and characterizing the single-gene defects responsible for such severe phenotypes, we gain valuable insights into their function in human biology and their potential as drug targets. Given that these targets are often involved in diseases beyond the rare genetic disorders in which they are first identified, we are developing proprietary product candidates to treat both orphan as well as more prevalent diseases.

To date, our Extreme Genetics discovery platform has yielded collaborations with multiple pharmaceutical companies, one approved product and a pipeline of novel product candidates, including:

- Glybera, the first gene therapy approved by the European Medicines Agency, or EMA, for the treatment of the orphan disorder lipoprotein lipase deficiency, or LPLD;
- XEN402, a product candidate with Phase 2 proof-of-concept data for the orphan disorder erythromelalgia, or EM, and other more common forms of pain;
- XEN701, a preclinical product candidate in Investigational New Drug application, or IND, enabling studies for the treatment of anemia of chronic kidney disease, or CKD, and end-stage renal disease, or ESRD;
- an oral preclinical product candidate in IND-enabling studies for the treatment of pain; and
- drug discovery programs for acne, cardiovascular disease and for the orphan disorder Dravet Syndrome, or DS.

With respect to XEN402, in December 2012 we entered into a collaborative development and license agreement with Teva Pharmaceutical Industries Ltd., or Teva, through its subsidiary, Ivax International GmbH, or Ivax, pursuant to which we granted Teva an exclusive worldwide license to develop and commercialize this product candidate. Prior to our entry into the collaborative development and license agreement with Teva, we submitted INDs to the U.S. Food and Drug Administration, or FDA, for oral XEN402 for the indication of dental pain (July 2009) and topical XEN402 for the indication of acute and chronic pain, including neuropathic and inflammatory pain (July 2010). Under the terms of the agreement, Teva paid us an upfront fee of \$41.0 million. We are collaborating with Teva to further develop XEN402, and Teva is funding all the related development costs. In addition, we are eligible to receive potential milestone payments totaling in aggregate up to \$335.0 million, the majority of which relate to pre-commercial activities. If XEN402 is approved, we are also eligible to receive royalties in the low teens to low twenties on net sales of the licensed products for the timeframe that such products are covered by the licensed patents and in certain other instances. We also have an option to co-promote products in the U.S.

A key aspect of our business model is to provide to the drug target selection process the often-missing human validation using our Extreme Genetics discovery platform. By carefully selecting families with severe phenotypes, we can enhance the likelihood of discovering a drug target that may have a major effect in humans. From this knowledge, we can gain an improved understanding of how a drug that modulates the target might act when given to a human.

The selection of suitable families with rare phenotypes is integral to our successful identification of single-gene defects. Such families are rare and dispersed throughout the world, which makes accessing and studying such families a challenge. We have developed internal clinical genetics expertise allowing us to identify and access rare families. To date, we have established a global network that has included more than 30 clinical collaborations in multiple countries. We collect DNA and detailed clinical information from the selected families to which we then apply our in-house genetics, molecular biology and bioinformatics capabilities to identify the single-gene defect. Using these genetic insights, we apply our in-house small-molecule expertise as well as access other therapeutic modalities, such as antisense or gene therapy, with the goal of developing novel medicines.

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Our business strategy is to advance a broad portfolio of product candidates while maintaining an efficient organization. We intend to achieve this by:

- selectively developing and commercializing products for orphan and niche diseases independently where high unmet medical needs exist (where we define a niche disease as a sub-population of a larger indication); and
- collaborating with major pharmaceutical companies to leverage our discoveries for more prevalent diseases representing larger market opportunities.

We have implemented our business strategy by entering into multiple alliances with key industry collaborators, including Genentech, Inc., Merck Sharp & Dohme GmbH (formerly known as Merck Sharp & Dohme Research Ltd.), an affiliate of Merck & Co., Inc., or Merck, and Teva that have in aggregate generated more than \$140.0 million in non-equity funding through June 30, 2013 and provide us with research funding and the potential for more than \$1.0 billion of research, development, regulatory and sales-based milestone payments, as well as royalties on net product sales.

Our Pipeline

The following is a summary of our current product pipeline:

| | Discovery | IND-Enabling | Phase 1 | Phase 2 | Phase 3 | Approved | Commercial Rights |
|---|-----------|--------------|---------|---------|---------|----------|--|
| Glybera LPLD | | | | | | | uniQure |
| XEN402 Erythromelalgia | | | | | | | Teva Xenon US Co-Promote Option |
| XEN402 Common pain indications | | | | | | | Teva Xenon US Co-Promote Option |
| XEN701 Anemia | | | | | | | Xenon |
| Nav1.7 Inhibitor Pain | | | | | | | Genentech |
| SCD1 Inhibitor Acne | | | | | | | Xenon |
| Target for Cardiovascular Disease | | | | | | | Merck |
| Selective Sodium Channel Modulators Dravet Syndrome | | | | | | | Xenon |
| New Pipeline Opportunities | | | | | | | Xenon |

Approved Product

Glybera

Glybera is a gene therapy approved in the European Union, or EU, in October 2012 for the treatment of a subset of patients with the orphan lipid disorder LPLD. Specifically, it is intended to treat LPLD in patients with severe or multiple pancreatitis attacks, despite dietary fat restrictions. LPLD is a severe metabolic disease of elevated blood triglycerides resulting in pancreatitis and in some cases, death. Together with collaborators from the University of British Columbia, or UBC, we demonstrated that a variant of the lipoprotein lipase, or LPL, gene called LPL^{S447X} resulted in increased LPL enzyme activity leading to reduced triglyceride levels in humans. Under our sublicense and research agreement with AMT, we collaborated with AMT and UBC on preclinical activities, and thereafter AMT developed a LPL gene therapy product, Glybera, which contains the LPL^{S447X} variant. We believe that the introduction of the therapeutic LPL^{S447X} gene through administration of Glybera provides a clinical benefit for a

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subset of LPLD patients. Glybera is the first product whose active ingredient was derived from our platform to receive commercial approval and is the first gene therapy to be approved in the EU or North America. The goal of Glybera therapy is to chronically treat LPLD in order to achieve sustained improvement of clearance of triglyceride-rich lipid particles known as chylomicrons, and a significantly reduced risk of pancreatitis attacks in patients suffering from multiple recurrent pancreatitis and abdominal pain events. Glybera was developed by our licensee, uniQure Biopharma B.V., or uniQure. In July 2013, uniQure announced that it had entered into a partnership with Chiesi Farmaceutici S.p.A., or Chiesi, for the commercialization of Glybera in Europe and more than a dozen other countries including Brazil, China, Mexico and Russia. uniQure has also publicly disclosed that it is preparing to apply for regulatory approval of this product in the U.S., Canada and other markets. We understand that uniQure plans to file an IND with the FDA in the first half of 2014. We are eligible to receive mid single-digit royalties on net sales of the licensed products, for sales made by uniQure and its affiliates. The royalty rates are reduced to a low single-digit for sales made by uniQure and its affiliates in countries where a licensed technology or a licensed product is not covered by a valid patent claim. With respect to uniQure's sublicense to Chiesi, we are eligible to receive a percentage in the low twenties of all non-royalty compensation relating to the licensed technology or products that uniQure receives from Chiesi (for example upfront payments and milestone payments), a percentage in the low twenties of any royalties that uniQure receives from Chiesi based on sales of technology or products covered by the licensed patents, plus a mid single-digit percentage of certain further royalties that uniQure receives from Chiesi based on sales of our licensed technology or products after the expiration of all licensed patents covering the product.

Product Candidates in Development

XEN402

XEN402 is a 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. To select our pain target, we discovered that the Nav1.7 protein is deficient in a rare genetic disorder known as congenital indifference to pain, or CIP, a condition where humans cannot feel pain. We have observed evidence of effect for XEN402 in four Phase 2 proof-of-concept clinical trials, including two trials in the orphan disorder EM, one trial in postherpetic neuralgia, or PHN, and one trial in dental pain. In December 2012, we entered into a collaborative development and license agreement with Teva, through its subsidiary, Ivax, pursuant to which we granted Teva an exclusive worldwide license to develop and commercialize XEN402. Prior to our entry into the collaborative development and license agreement with Teva, we submitted INDs to the FDA for oral XEN402 for the indication of dental pain (July 2009) and topical XEN402 for the indication of acute and chronic pain, including neuropathic and inflammatory pain (July 2010). In collaboration with Teva, we are currently developing XEN402 as a topical product to treat the pain associated with EM, as well as for other more common forms of pain. In April 2013, we and Teva announced that XEN402 had received orphan designation from the FDA for the treatment of EM. We are working with the FDA on a regulatory strategy designed to support product approval. We expect to initiate the trial for XEN402 in EM and a Phase 2 trial for a non-orphan indication in 2014. Under the terms of the agreement, Teva paid us an upfront fee of \$41.0 million and we are eligible to receive potential milestone payments totaling up to \$335.0 million, the majority of which relate to pre-commercial achievements. If XEN402 is approved, we are also eligible to receive royalties in the low teens to low twenties on net sales of the licensed products for the timeframe that such products are covered by the licensed patents and in certain other instances. We also have an option to co-promote products in the U.S.

XEN701

XEN701 is a selective antisense oligonucleotide compound designed to be subcutaneously administered and to inhibit the expression of the protein hepcidin. To select hepcidin as our anemia drug target, we identified mutations in genes underlying a rare genetic disorder of iron overload, or excess, known as juvenile hemochromatosis, or JH. JH is caused by single-gene defects the consequences of which is deficiency of the hepcidin protein. This deficiency of hepcidin causes the iron overload in JH patients. In anemia of chronic disease, or ACD, the converse is true. Elevated levels of hepcidin cause a restricted iron supply that results in low hemoglobin, or anemia. XEN701 is the first drug to enter development in our collaboration with Isis Pharmaceuticals, Inc., or Isis, to develop antisense drugs that target the hepcidin-hemojuvelin pathway. We have exclusive worldwide rights for development and commercialization of XEN701. Neither we nor Isis has submitted an IND to the FDA for XEN701. XEN701 is currently in IND-enabling safety and toxicology studies and we expect to commence Phase 1 studies during the first half of 2014. Initially, our development strategy will focus on treating the anemia associated with CKD or ESRD in

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niche populations where the use of erythropoietin stimulating agents, or ESAs, the current standard of care, is subject to a black box warning (the FDA's highest level of warning, indicating that a particular drug may lead to death or serious injury) or is contraindicated. For example, we estimate there are 115,000 CKD and ESRD patients in the U.S. who are anemic and currently have cancer or have had cancer within the last five years. Despite this, some of these patients continue to receive ESAs even though ESA labels contain a black box warning for patients with cancer. As the mechanism of XEN701 is distinct from that of ESAs, we anticipate XEN701 may provide an alternative in these niche populations.

Selective Inhibitor of Nav1.7 for the Treatment of Pain

Chronic pain conditions such as severe cancer pain and neuropathic pain are generally recognized as unmet medical needs providing potential commercial opportunities for a new oral pain drug. Currently available pain drugs such often have either a lack of meaningful pain relief or dose-limiting side effects for many patients. An orally administered selective Nav1.7 inhibitor could present a novel mechanism for the treatment of moderate to severe pain. This mechanism contrasts with our non-selective sodium channel inhibition approach taken with XEN402. In December 2011, we entered into a collaborative research and license agreement with Genentech, Inc., or Genentech, and its affiliate, F. Hoffmann-La Roche Ltd, or Roche, to discover and develop inhibitors of Nav1.7 for the treatment of pain. The goal of the collaboration is to discover and develop orally active products that selectively inhibit this sodium channel. A small-molecule preclinical product candidate was selected in 2013 for development and is currently in the IND-enabling stage. Neither we nor Genentech has submitted an IND to the FDA for the selective inhibitor of Nav1.7 for the treatment of pain. Under the terms of the agreement, Genentech paid us an upfront fee of \$10.0 million and we have subsequently earned a \$5.0 million milestone payment for the selection of the development-stage product candidate. We are also eligible to receive pre-commercial and commercial milestone payments with respect to the licensed products totaling up to an additional \$621.0 million. In addition, we are also eligible to receive royalties based on net sales of the licensed products, which range from a mid single-digit percentage to ten percent for small-molecule inhibitors for the timeframe that such products are covered by the licensed patents and a low single-digit percentage thereafter, plus a low single-digit percentage for large-molecule inhibitors of Nav1.7.

Product Candidates in Discovery

Selective Small-Molecule Inhibitors of SCD1 for Acne

SCD1 is an enzyme involved in lipid synthesis that is expressed in sebaceous glands in the skin. Mice deficient in SCD1 have a marked phenotype of sebaceous gland atrophy suggesting that inhibition of SCD1 activity in the skin may provide a novel treatment option for acne and seborrhea. We have developed novel small-molecule SCD1 inhibitors. In animal models, we have shown that our topical small-molecule SCD1 inhibitors can reduce sebaceous gland size and number. We have identified multiple compounds that have properties suitable for topical administration including adequate skin penetration and photostability.

Selective Small-Molecule Inhibitors of Targets for Cardiovascular Disease

We entered into a collaborative research and option agreement with Merck in June 2009 to discover novel targets and compounds for the treatment of cardiovascular disease using our Extreme Genetics discovery platform. In 2012, Merck exercised its option to obtain an exclusive license to a cardiovascular target and compound inhibitors that were discovered during the research collaboration.

Selective Small-Molecule Sodium Channel Modulators for DS

DS is a severe form of childhood epilepsy in which the majority of cases results from deficiency of the Nav1.1 sodium channel. Nav1.1 plays a critical role in neuronal inhibitory pathways. When it is deficient, the brain becomes hyper-excitabile leading to the intermittent and often severe seizures characteristic of DS. Thus, we believe selective sodium channel modulators may reduce brain hyper-excitability and limit or prevent the seizures of DS.

New Pipeline Opportunities

Using our Extreme Genetics discovery platform, we are currently working to identify new drug targets for the treatment of pain. In addition, we are evaluating other opportunities in multiple indications outside of pain.

Our Strategy

Our goal is to apply our Extreme Genetics discovery platform to build a sustainable and profitable biopharmaceutical company that discovers, develops and commercializes innovative therapeutics. Our key strategic initiatives include:

- *Discovering Additional Novel Targets.* We are committed to expanding our network of clinical collaborations and access to families with severe phenotypes to identify novel targets for orphan and niche, as well as more prevalent, diseases. To support this strategy, we will continue to invest in personnel with clinical genetics expertise and in technologies and methods that we believe will enhance our Extreme Genetics discovery platform.
- *Expanding Our Proprietary Pipeline of Orphan and Niche Disease Product Candidates.* We will continue to develop product candidates for orphan and niche diseases. This focus may allow us to benefit from both a less costly and expedited development pathway and may provide us with potential commercial benefits, including market exclusivity and premium drug pricing. These benefits may allow us to retain a significantly larger share of the value of such product candidates, as it may be viable for us to develop these assets independently beyond Phase 2 proof-of-concept trials and potentially through commercialization.
- *Developing Product Candidates for More Prevalent Diseases through Pharmaceutical Collaborations.* We plan to continue to partner programs, including product candidates for more prevalent diseases with pharmaceutical companies to access additional development and commercial resources, expertise and non-dilutive funding to enable the advancement of a broader and more diverse pipeline.
- *Independently Commercializing Selected Products.* We intend to develop a specialized sales force in circumstances where we expect to be able to cost-effectively commercialize approved products in orphan and niche indications. This capability would enable us to co-promote XEN402, if we exercise our option to do so, as well as market any approved products that we may independently commercialize.

Our Extreme Genetics Discovery Platform

Despite advances in medical sciences and the pharmaceutical industry's understanding of diseases, research and development productivity in the industry has declined over the years. We believe that a contributor to this problem is the industry's reliance on drug discovery approaches that are sometimes based on targets that do not necessarily have a major biological effect in humans. Consequently, it is fairly common for a pharmaceutical company to invest substantial time, resources and funds into drug development only to realize in late-stage clinical trials that a product candidate may be directed to a target that is either not biologically relevant to the disease or that may have diverse functions or effects in humans, thereby leading to poor efficacy or safety.

Our Extreme Genetics discovery platform enables us to identify drug targets that may be more biologically relevant in humans. Our platform is built on the foundation of identifying and studying rare individuals and families with severe phenotypes to discover single-gene defects that have major biological effects in humans. By studying these individuals and families with severe phenotypes, we can obtain critical insights into the genes underlying these diseases and their related biology to develop promising product candidates. We therefore are able to initiate our drug discovery with the advantage of having a greater understanding of the role of the drug target in human disease.

Our reliance on our Extreme Genetics discovery platform for target selection differs from other target selection methods commonly employed in the industry, such as *in vitro* cell biology and screening, tissue and differential expression studies, *in vitro* and animal based pharmacology and the use of animal models, such as gene knock-outs or animal transgenics. Some companies, however, do use human genetics to varying degrees to assist with target identification, such as approaches where larger populations of patients and controls are studied to define associations where a disease and single nucleotide polymorphisms, or SNPs, in certain genes are linked. While SNP associations allow the identifications of genes that show an association with a disease or may increase risk of disease, such associations differ from our Extreme Genetics discovery platform since they do not discover genes that are determinant or causal of a disease. By studying families with rare diseases where individuals present with severe phenotypes, we seek to isolate the genetic cause of such diseases. We then use this causal information as our primary methodology underlying our target discovery and selection.

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The key components of our Extreme Genetics discovery platform include:

- an established global network that has included more than 30 clinical collaborators in multiple countries, and which has provided us with access to rare individuals and families with severe phenotypes dispersed throughout the world;
- clinical geneticists and genetic counselors with a deep understanding of clinical phenotypes. These experts identify the rare genetic disorders with severe phenotypes that we study;
- years of experience and extensive know-how in successfully navigating through regulations in multiple countries in order to obtain the approvals necessary to collect and use detailed clinical information and DNA samples from individuals and families with severe phenotypes;
- internal capabilities in genome sequencing, molecular biology and bioinformatics to enable identification of single-gene defects and validation of these as potential drug targets; and
- expertise in small-molecule drug discovery to design promising product candidates that effectively modulate the identified drug targets. Our drug discovery capabilities include medicinal and synthetic chemistry, assay development and *in vitro* and *in vivo* pharmacology.

Our Extreme Genetics discovery platform has proven to be a valuable asset for our company over the years. It has led to a robust pipeline, including an approved product, three development-stage product candidates and four preclinical discovery programs. Of our three development-stage product candidates, XEN701 and the Nav1.7 inhibitor licensed to Genentech are in preclinical development. Our platform has also allowed us to attract numerous collaborations with leading pharmaceutical companies, including Genentech, Merck and Teva, that have in aggregate generated more than \$140.0 million in non-equity funding through June 30, 2013 and provide us with research funding and the potential for more than \$1.0 billion of research, development, regulatory and sales-based milestone payments, as well as royalties on net product sales.

Programs

Glybera (alipogene tiparvovec): A Gene Therapy for the Orphan Disease LPLD

Glybera is a gene therapy approved in the European Union, or EU, in October 2012 for the treatment of a subset of patients with the orphan lipid disorder LPLD. Specifically, it is intended to treat LPLD in patients with severe or multiple pancreatitis attacks, despite dietary fat restrictions. LPLD is a severe metabolic disease of elevated blood triglycerides resulting in pancreatitis and in some cases, death. In collaboration with UBC we demonstrated that a variant of the LPL gene called LPL^{S447X} resulted in increased LPL enzyme activity leading to reduced triglyceride levels in humans. Under our sublicense and research agreement with AMT, we collaborated with AMT and UBC on preclinical activities, and thereafter AMT developed a LPL gene therapy product, Glybera, which contains the LPL^{S447X} variant. We believe that the introduction of the therapeutic LPL^{S447X} gene through administration of Glybera provides a clinical benefit for LPLD patients. Glybera is the first product whose active ingredient was derived from our platform to receive commercial approval and is the first gene therapy to be approved in the EU or North America. The goal of Glybera therapy is to chronically treat LPLD in order to achieve sustained improvement of clearance of triglyceride-rich lipid particles known as chylomicrons, and a significantly reduced risk of pancreatitis attacks in patients suffering from multiple recurrent pancreatitis and abdominal pain events. Glybera was developed by our licensee, uniQure. In July 2013, uniQure announced that it had entered into a partnership with Chiesi Farmaceutici S.p.A., or Chiesi, for the commercialization of Glybera in Europe and more than a dozen other countries including Brazil, China, Mexico and Russia. uniQure has also publicly disclosed that it is preparing to apply for regulatory approval of this product in the U.S., Canada and other markets. We understand that uniQure plans to file an IND with the FDA in the first half of 2014. We are eligible to receive mid single-digit royalties on net sales of the licensed products, for sales made by uniQure and its affiliates. The royalty rates are reduced to a low single-digit for sales made by uniQure and its affiliates in countries where a licensed technology or a licensed product is not covered by a valid patent claim. With respect to uniQure's sublicense to Chiesi, we are eligible to receive a percentage in the low twenties of all non-royalty compensation relating to the licensed technology or products that uniQure receives from Chiesi (for example upfront payments and milestone payments), a percentage in the low twenties of any royalties that uniQure receives from Chiesi based on sales of technology or products covered by the licensed patents, plus a mid single-digit percentage of certain further royalties that uniQure receives from Chiesi based on sales of our licensed technology or products after the expiration of all licensed patents covering the product.

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About LPLD

Familial LPLD is a rare autosomal-recessive disorder of lipoprotein metabolism. LPLD is characterized by severe hypertriglyceridemia caused by the absence of LPL activity, and, as a consequence, certain triglyceride-rich lipoproteins accumulate in the plasma. The population frequency of LPLD in the U.S. has been reported to be approximately one in a million individuals by the National Library of Medicine.

LPLD typically manifests early in childhood, with repeated episodes of abdominal pain and acute pancreatitis that can be life-threatening. There is currently no approved gene therapy for 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 believe effective therapeutic strategies are therefore needed for this condition.

About LPL^{S447X}

Together with our collaborators at UBC and using our Extreme Genetics discovery platform, we demonstrated that the LPL^{S447X} variant resulted in reduced triglyceride levels in humans, as this single-gene defect results in and elevated LPL enzyme activity and we further demonstrated that LPL^{S447X} in an adenovirus gene therapy could treat hypertriglyceridemia in animal models of LPLD.

Clinical Development of Glybera

In a scientific publication, a single dose of Glybera was well-tolerated with no material safety concerns and was demonstrated to reduce the incidence of acute pancreatitis and abdominal pain events over the two-year study period.

Commercialization of Glybera

Glybera was approved for commercialization in the EU in October 2012. uniQure publicly disclosed entry into a commercialization agreement with Chiesi in July 2013. uniQure has also publicly disclosed that it is preparing to apply for regulatory approval of this product in the U.S., Canada and other markets. Glybera has received orphan drug designation in both the EU and the U.S.

XEN402: A Small Molecule for the Treatment of the Orphan Disease EM and Other Pain Disorders

XEN402 is a novel 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. We discovered that the Nav1.7 protein is deficient in a rare genetic disorder known as congenital indifference to pain, or CIP, a condition where humans cannot feel pain. We have observed evidence of effect for XEN402 in four Phase 2 proof-of-concept clinical trials, including two trials in primary erythromelalgia, or primary EM, one trial in postherpetic neuralgia, or PHN, and one trial in dental pain. In December 2012, we entered into a collaborative development and license agreement with Teva pursuant to which we granted Teva an exclusive worldwide license to develop and commercialize XEN402. In collaboration with Teva, we are currently developing XEN402 as a topical product to treat the pain associated with the orphan disorder EM, as well as for other more common forms of pain. In April 2013, we and Teva announced that XEN402 had received orphan designation from the FDA for the treatment of EM. We are working with the FDA on a regulatory strategy designed to support product approval. We expect to initiate the trial for XEN402 in EM and a Phase 2 trial for a non-orphan pain indication in 2014. Under the terms of the agreement, Teva paid us an upfront fee of \$41.0 million and we are eligible to receive potential milestone payments totaling up to \$335.0 million, the majority of which relate to pre-commercial achievements. If XEN402 is approved, we are also eligible to receive royalties in the low teens to low twenties on net sales of the licensed products for the timeframe that such products are covered by the licensed patents and in certain other instances. We also have an option to co-promote products in the U.S. Prior to our entry into the collaborative development and license agreement with Teva, we submitted INDs to the FDA for oral XEN402 for the indication of dental pain (July 2009) and topical XEN402 for the indication of acute and chronic pain, including neuropathic and inflammatory pain (July 2010).

Discovery of XEN402

Using our Extreme Genetics discovery platform, we discovered Nav1.7 by studying families with a rare disorder called CIP. CIP patients are unable to feel pain for painful events including fractures, childbirth, osteomyelitis and osteoarthritis, severe burns, ulcers, wounds and tooth abscesses. Based on this severe phenotype of absence of pain in humans, we predicted that the single-gene defect causing CIP could define an important novel human drug target for treating pain. We showed that defects in the CIP gene result in deficiency of the sodium channel Nav1.7.

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Nav1.7 is highly expressed in peripheral nerves and transmits pain signals. We believe that inhibition of Nav1.7 may reduce these pain signals. XEN402 was designed to be a non-selective small-molecule inhibitor of Nav1.7 such that it also can inhibit additional sodium channels, including those that we believe play a role in pain signaling. We believe this mixed sodium channel inhibition may enhance the potential efficacy of XEN402 in chronic pain. XEN402 is currently being developed as a topical product as its chemical properties are consistent with topical administration, including high local skin and underlying tissue concentrations in tandem with maintenance of low plasma levels. With these properties, we believe we can target the site of generation of peripherally-based pain without unnecessarily exposing other tissues to significant levels of this compound, such as the central nervous system where we might expect to observe side-effects when multiple sodium channels are inhibited. We have demonstrated efficacy with this compound in multiple animal models for pain. Topical XEN402 in animal models has been shown to exhibit anti-inflammatory properties and may be suited to peripherally-based inflammatory pain such as joint arthritic pain. The non-selective sodium channel inhibition and primary topical administration are in contrast to our selective Nav1.7 inhibitors licensed to Genentech, which are selective for the Nav1.7 sodium channel and are oral formulations.

In contrast to the absence of pain in CIP, when Nav1.7 is deficient, overactivity of Nav1.7 can cause the spontaneous pain of primary EM. Therefore, we believe that XEN402, which inhibits Nav1.7, has a relevant mechanistic rationale as a treatment for primary EM.

About EM

EM is a disorder of severe neuropathic pain where, in certain families, mutations causing increased activity of the Nav1.7 sodium channel have been identified. The disorder is characterized by recurrent flares of intense burning pain with redness of the skin in the feet, hands or both. Although there is a range in age of onset and age of diagnosis, the typical diagnosis for EM is between 50 and 60 years. These painful flares are triggered by a variety of factors including heat exposure, exercise and humidity. Most EM patients experience several painful flares a day and for some, these flares may progress into a state of chronic severe burning pain. Many EM patients seek relief by modulating their environment because they do not respond well to existing pharmacotherapies. For example, patients may seek relief by immersing their limbs in cold or ice water, sometimes for many hours a day. Because of complications related to this method of cooling, some EM patients require amputation of their extremities. While the condition is variable in nature, normal daily functioning such as walking, standing, working, socializing, exercising and sleeping is generally significantly impaired. For example, in a study of 32 pediatric EM patients published by the Mayo Clinic, 13% of these EM patients were wheelchair bound due to the severity of their EM symptoms.

The incidence rate that has been reported in studies of EM ranges from 0.36 per 100,000 person-years in Sweden to 1.3 per 100,000 person-years in the U.S. An additional study estimated EM prevalence in Dunedin, New Zealand to be 15 of every 100,000 individuals. With assumed average disease duration of 20 years, these incidence and prevalence data, when extrapolated, would predict approximately 50,000 patients in the U.S. with EM. Of these, we estimate approximately 43,000 may have primary EM, with the remainder having EM that is secondary to another disorder. These estimates of prevalence comprise patients of all ages (from infants to the elderly) and at all stages of disease severity. Furthermore, the prevalence of EM in the U.S. has not to our knowledge been directly determined. In addition, a number of EM patients might not currently be diagnosed or be followed by a specialist physician. Given the above, this prevalence estimate may not represent the number of patients that might be eligible for our clinical trials or that might represent the eligible treatment population for a commercial product.

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XEN402 EM Clinical Development

XEN402 has been studied in both a topical formulation and an oral formulation in Phase 1 clinical trials in healthy volunteers and small, exploratory Phase 2 proof-of-concept clinical trials in primary EM. The table below summarizes the results of these XEN402 trials:

Topical Phase 2 EM Trial

| <u>DESIGN</u> | <u>KEY SAFETY DATA</u> | <u>KEY EFFICACY DATA</u> |
|---|---|---|
| n Double-blind, randomized, placebo-controlled | n Safe and well tolerated | n Three of seven patients (43%) on XEN402 showed consistent clinically meaningful reductions in induced and daily pain compared to baseline |
| n Eight primary EM patients randomized | n Low plasma exposures | n Four of six (67%) patients on XEN402 who used rescue cooling showed a reduction in cooling usage compared to baseline |
| n 8% ointment or placebo was dosed twice daily for two or three weeks | n No meaningful central nervous system side effects | n Six of seven (86%) patients on XEN402 had an improvement in sleep interference scores compared to baseline |
| | n No drug-related serious adverse events, or SAEs, or deaths, with local application site reactions being the most common drug-related adverse event reported | |

Topical Phase 1 Trial

| <u>DESIGN</u> | <u>KEY SAFETY DATA</u> | <u>KEY EFFICACY DATA</u> |
|--|---|--------------------------|
| n Cumulative irritation, double-blind, randomized, placebo, positive and negative controlled | n No clinically meaningful difference was observed between cumulative skin irritation scores for 4% and 8% ointment, placebo and the negative control | n Not applicable |
| n 20 healthy volunteers | n The positive control showed greater skin irritation | |
| n 4% and 8% ointment and placebo and positive and a 0.9% saline negative control were dosed once daily for 21 days | n No SAEs or deaths | |

Oral Phase 2 EM Trial

| <u>DESIGN</u> | <u>KEY SAFETY DATA</u> | <u>KEY EFFICACY DATA</u> |
|--|--|--|
| n Double-blind, randomized, placebo-controlled crossover | n Most common adverse events, or AEs, were dizziness and drowsiness that ranged from mild (no interference in daily activities) to severe (significant interference in daily activities) | n A significant (42%) reduction in EM pain was observed in the three patients where pain was induced (p=0.014) |
| n Four primary EM patients randomized | n No SAEs or deaths, with the most frequently reported AEs being dizziness, headache, sedation and drowsiness | |
| n 400 mg or placebo was dosed twice daily for 2 days | | |

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Oral Phase 1 Trial

| DESIGN | KEY SAFETY DATA | KEY EFFICACY DATA |
|---|--|-------------------|
| n Double-blind, randomized, placebo-controlled | n Maximal tolerated dose, or MTD, for SAD study was 500 mg | n Not applicable |
| n Single-ascending dose, or SAD, study in 38 healthy volunteers up to 800 mg | n Dose-limiting toxicity included dizziness and drowsiness observed at 800 mg single dose | |
| n Multi-ascending dose, or MAD, study in 32 healthy volunteers up to 400mg twice daily for 5.5 days | n Occasional short-lived AEs of mild to moderate dizziness, drowsiness and tremor were reported by some subjects in the 500 mg single dose | |
| | n MTD in MAD study was not achieved | |
| | n Occasional short-lived AEs of mild to moderate dizziness and drowsiness were reported by some subjects in the 400 mg twice daily dose | |

Topical XEN402 Phase 2 Trial in EM

We conducted a small Phase 2 proof-of-concept trial with XEN402 ointment in patients with primary EM. This exploratory trial was a randomized, double-blind, placebo-controlled design with eight subjects (seven XEN402 and one placebo) comparing 8% XEN402 to placebo applied two times per day to the feet for a duration of 14 or 21 days. We evaluated multiple endpoints for each subject to increase our understanding of the effect of XEN402, including the amount of pain in response to a heat stimulus, the frequency and duration of cooling to provide relief from their painful flares, changes in daily pain scores and the degree of sleep interference. Throughout the trial, XEN402 plasma concentrations were low and XEN402 was well-tolerated. Consistent with these low plasma levels, there was no treatment-related dizziness and drowsiness and there were no treatment-related SAEs. Dizziness and drowsiness are common side effects for many currently prescribed centrally-acting analgesics. Local application site reactions were the most common drug-related AEs observed.

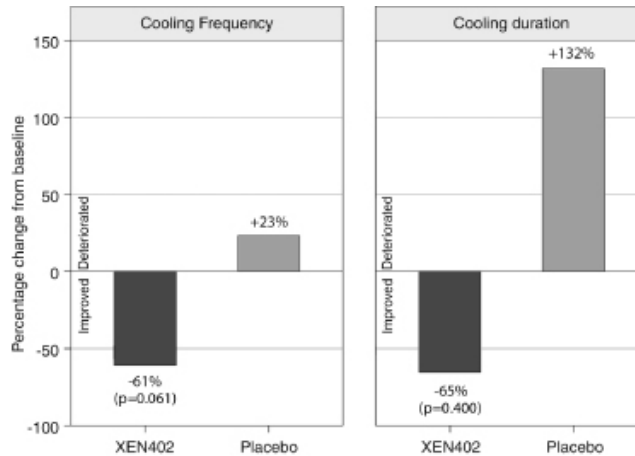
In this trial, three of the seven (43%) XEN402-treated subjects responded positively based on the magnitude and consistency of improvement across the measured efficacy parameters. While the four remaining XEN402-treated subjects were considered to be non-responders based on their magnitude of response or inconsistent response or both, some improvements were seen in certain efficacy parameters, in particular, sleep and rescue cooling. Similarly, the placebo-treated subject did not show a consistent pattern of response.

We developed a novel pain induction method for assessing the response of XEN402 using an electric heater placed at a standardized distance from the subject's feet. Four of the seven (57%) subjects receiving XEN402 treatment responded better to the standard heat inductions compared to pre-treatment. Three of these seven (43%) subjects showed greater than 50% improvements in their ability to tolerate and/or recover from the heat inductions. In addition, these three subjects demonstrated clinically meaningful improvements (a one-point, or 30% or greater reduction) in the level of daily pain experienced during the outpatient treatment period compared to pre-treatment. The remaining XEN402-treated subjects and the placebo-treated subject responded inconsistently or demonstrated deteriorations in their responses compared to baseline.

EM patients may seek relief by immersing their limbs in cold or ice water to help manage their painful flares. If a patient uses less cooling when on XEN402, this may indicate the product is reducing the number and/or intensity of their EM flares. Four of the six (67%) XEN402-treated subjects who used cooling at baseline showed a meaningful reduction in cooling usage while on treatment. In contrast, the placebo-treated subject cooled for substantially longer during the outpatient period compared to pre-treatment.

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Unlike the placebo-treated subject, subjects on XEN402 used less rescue cooling compared to their baseline measurements. The amount of daily cooling usage, including cooling frequency and cooling duration, for subjects on XEN402 or placebo as a percentage change from baseline is shown below.



EM flares often wake patients several times each night and an improvement in the sleep interference scores could indicate that XEN402 may reduce the number and/or intensity of the flares during sleep. Six of the seven (86%) subjects receiving XEN402 treatment showed improvements in their daily sleep interference scores during treatment compared to baseline, with three subjects demonstrating at least 50% improvements. In five of the six (83%) subjects this was associated with less or no cooling usage. The placebo-treated subject also demonstrated a reduction in sleep interference; however, as with the daily pain scores, the interpretation of this response is confounded by the greater cooling usage by this subject.

Oral XEN402 Phase 2 Trial in EM

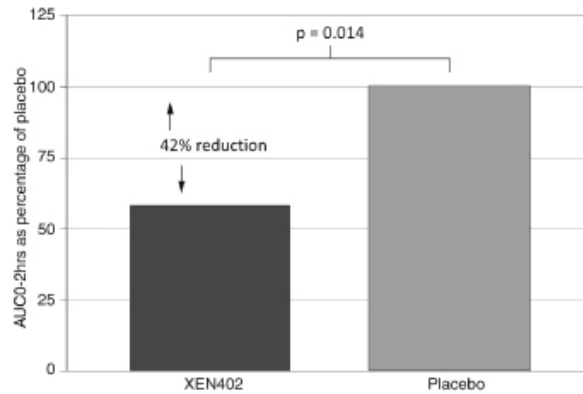
We conducted a small Phase 2 proof-of-concept trial with oral XEN402 in patients with primary EM. This exploratory trial, which was published in the journal *Pain*, Goldberg, Y.P. et al *Pain* 153 (2012) 80-85, was a randomized, double-blind, placebo-controlled, two-period crossover design with four subjects comparing oral XEN402 to placebo each administered twice per day for a duration of two days. In one treatment period, subjects received XEN402 (400 mg bid), and in the other treatment period, subjects received placebo. The order in which the subjects received each treatment was randomized.

Three patients with episodic EM pain were subjected to heat or exercise on up to six occasions during each treatment period to induce a controlled painful flare. One patient who was in constant, severe pain was not induced.

Improvements in pain efficacy measures in all four subjects were observed, with statistically significant reductions in pain scores in the three subjects in whom pain was induced. The amount of pain in the two hours following induction was reduced by 21% ($p = 0.011$), 33% ($p = 0.004$) and 88% ($p = 0.031$) in these three patients, respectively. Overall, in these three subjects, pain was reduced by 42% on XEN402, compared to placebo ($p = 0.014$). The subject who was in constant pain and was not induced, showed a mild reduction in pain at various time points during the XEN402 dosing period.

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Mean total pain intensity scores were measured for the two hours following each pain induction over the two day treatment period with either XEN402 or placebo. The amount of pain following induction was calculated by quantifying the area under the pain intensity curve for two hours following induction, or AUC_{0-2hrs} . Data are presented as a mean AUC_{0-2hrs} for the three subjects who underwent pain induction either by step exercise or by heat. A 42% reduction in the amount of induced pain was observed on average with XEN402 compared to placebo ($p=0.014$).



Teva is conducting work in an attempt to improve on the oral formulation.

Future Development Plans for XEN402 in EM

We are collaborating with Teva on the development of topical XEN402 for EM. The rationale for selecting topical XEN402 for treating EM includes the following:

- EM pain is generally localized to the feet and hands, making application of topical XEN402 a practical method of administration;
- EM pain appears to have a peripheral component;
- Nav1.7, which is the target for XEN402, is expressed in peripheral nerve endings in the skin and there is scientific data supporting a role of this target in primary EM; and
- topical XEN402 provides high local concentrations of drug in the skin and underlying tissue with limited exposure of the compound to non-target tissues, which we believe may reduce systemic side effects.

XEN402 Clinical Development for Other Pain Indications

We believe that XEN402 may have broader potential applicability as a pain drug beyond its use in the treatment of EM. The types of pain that CIP patients cannot perceive suggest that Nav1.7 may be involved in pain signaling for different types of painful stimuli including both neuropathic and inflammatory pain.

Many chronic pain conditions have unmet medical need providing additional market opportunities for novel pain drugs. The current standards of care for more common forms of pain such as osteoarthritis, chronic low back pain and diabetic neuropathic pain, are often lacking in robust efficacy and may result in common side effects, such as nausea, dizziness and sleepiness. Certain anti-inflammatory pain medications have FDA black box warnings for gastrointestinal bleeding and cardiovascular events, both of which can be fatal. Despite these currently available treatments, we believe that there may be subpopulations of pain patients with unmet medical needs, which XEN402 may be able to address given its novel mechanism of action.

Prior to our collaboration with Teva, we had concluded two Phase 2 proof-of-concept trials, one for acute inflammatory dental pain with oral XEN402 and another for the neuropathic pain of PHN with topical XEN402. These trials were performed to better understand the potential for XEN402 to treat more common forms of pain.

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Topical XEN402 Phase 2 Trial in PHN

| DESIGN | | KEY SAFETY DATA | KEY EFFICACY DATA |
|--------|---|--|---|
| n | Double-blind, randomized, placebo-controlled, cross-over | n Safe and well tolerated | n There was a reduction in the primary efficacy endpoint (change from baseline in mean daily pain score) for XEN402 and placebo, but the difference between treatments was not statistically significant |
| n | 70 subjects randomized | n The most frequent AEs (greater than 5% frequency) included local application site reactions, nasopharyngitis and urinary tract infections, or UTIs | n Significantly increased proportion of XEN402-treated patients reported 30% or greater (p=0.049) and 50% or greater (p=0.0078) reduction in their pain compared to placebo |
| n | 8% ointment or placebo administered twice daily for three weeks | n Fewer related treatment emergent AEs for XEN402 (18%) versus placebo (30%) | n A retrospective exploratory analysis not described in the study protocol showed that a significant increased proportion of XEN402-treated patients reported 30% or greater improvement in sleep (p=0.034) compared to placebo |
| | | n Low plasma exposure | |
| | | n No meaningful central nervous system side effects | |
| | | n Less application site pain for XEN402 (16% placebo versus 3% XEN402) and pruritis, or itch, (13% placebo versus 3% XEN402) | |
| | | n No drug-related SAEs | |

Oral XEN402 Phase 2 Trial in Dental Pain

| DESIGN | | KEY SAFETY DATA | KEY EFFICACY DATA |
|--------|---|--|--|
| n | Double-blind randomized, placebo-controlled | n Safe and well tolerated | n No statistical difference in the primary efficacy variable evaluated was observed |
| n | 61 subjects randomized | n The most frequently reported AEs were nausea, dizziness, headache and drowsiness, which were mild or moderate in intensity | n The primary and secondary endpoints showed consistent trends in favor of reduced pain for XEN402 versus placebo |
| n | Single oral dose of 500 mg or placebo | n No SAEs | n Certain secondary endpoints achieved statistical significance |
| | | | n In a post-hoc analysis, significantly increased proportion of XEN402-treated patients reported 30% or greater and 50% or greater reduction in their pain compared to placebo |

XEN402 Trial in Postherpetic Neuralgia, or PHN

We conducted a Phase 2 proof-of-concept trial of topical XEN402 in 70 PHN patients. On average, patients enrolled into the study had refractory PHN and their average disease duration was 76.6 months. This study was a double-blind, placebo-controlled, crossover trial where topical XEN402 was administered twice daily with each patient receiving either XEN402 or placebo for three weeks, then after a washout period, the subjects received the alternative treatment.

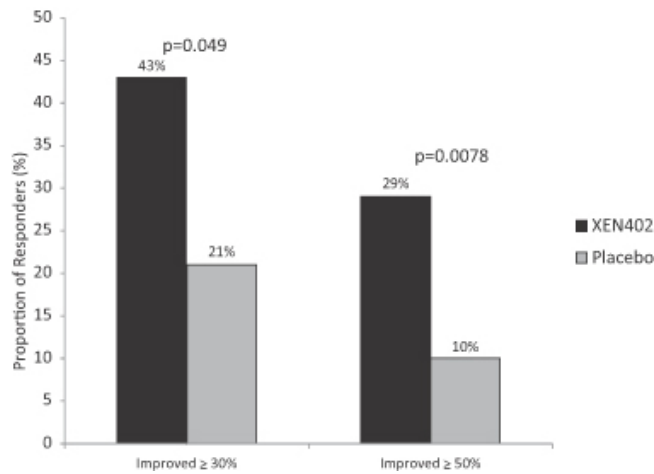
Topical XEN402 was well-tolerated with no drug-related SAEs. No drug-related centrally mediated side effects of dizziness and drowsiness were observed in this study. In addition, while on topical XEN402, PHN patients reported reduced site application pain (3% XEN402 versus 16% placebo) and less pruritis, or itch, (3% XEN402 versus 13% placebo) compared to while on placebo treatment. Chronic itch is an important co-morbidity for many PHN patients. The most frequently reported AEs included local application site reactions, nasopharyngitis and UTIs.

There was a reduction in the primary efficacy endpoint (change from baseline in mean daily pain score) for XEN402 and placebo, but the difference between treatments was not statistically significant. Multiple secondary endpoints were studied, including the proportion of subjects achieving at least 30% and 50% improvements in pain, the use of rescue analgesic medications, and the change in Daily Sleep Interference Scale score. A greater proportion of subjects on XEN402 experienced a clinically meaningful reduction in their pain during the trial, which is a 30% or

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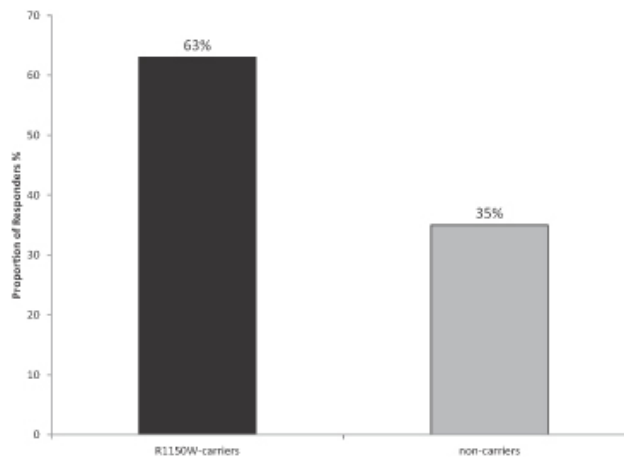
greater reduction in pain. A statistically significant larger proportion of subjects on topical XEN402 exhibited a 30% or greater ($p=0.049$) and a 50% or greater ($p=0.0078$) reduction in pain compared to placebo. A greater proportion of subjects on topical XEN402 exhibited a statistically significant 30% or greater ($p=0.034$) improvement in sleep compared to placebo. Importantly, a trend to reduced use of rescue pain medication in the responders on XEN402 was observed, suggesting rescue use did not explain the greater response in these subjects.

XEN402 demonstrated a statistically significant increase in the proportion of clinically meaningful responders (30% or greater and 50% or greater reduction in pain) compared to placebo.



There is a relatively common variant within Nav1.7 called R1150W. We estimate that this variant has a frequency of 6% to 30% in different ethnic populations. Publications have reported that subjects with this variant who suffer from various painful disorders may experience a greater amount of pain compared to those subjects who do not have this variant. Cell-based assays suggest this variant may increase the activity of the Nav1.7 channel and this increased activity may explain why such patients feel more pain. In our PHN trial there were eight carriers of this R1150W variant who were among the evaluable subjects. Of these carriers, five out of eight (63%) had a 30% or greater reduction in their pain when on topical XEN402. Although it was not a pre-selected endpoint of the trial, a trend towards greater response to XEN402 was observed in R1150W-carriers versus non-carriers.

A greater proportion of Nav1.7 R1150W-carriers had a clinically meaningful 30% or greater response to XEN402 than non-carriers.



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Future Development Plans for Topical XEN402

Teva plans to perform pain trials in non-orphan pain indications with topical XEN402 with the goal of broadening its market potential to other pain indications beyond EM.

Further analysis of the R1150W variant described above is planned to better understand the potential of this variant to predict response to XEN402.

Oral XEN402 Trial in Dental Pain

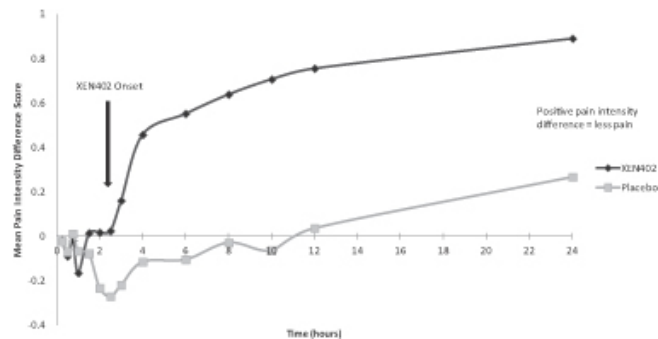
The third molar tooth extraction is an established model of inflammatory pain. We performed a randomized, double-blind, placebo-controlled, Phase 2 proof-of-concept trial in 61 healthy male subjects. 41 subjects received a single oral 500 mg dose of XEN402 and 20 subjects received placebo. XEN402 was generally safe and well-tolerated. There were no SAEs. The most frequently reported AEs were dizziness, nausea, drowsiness and headache, all of which were mild or moderate in intensity.

The primary and all secondary endpoints showed consistent trends in favor of reduced pain for XEN402 versus placebo.

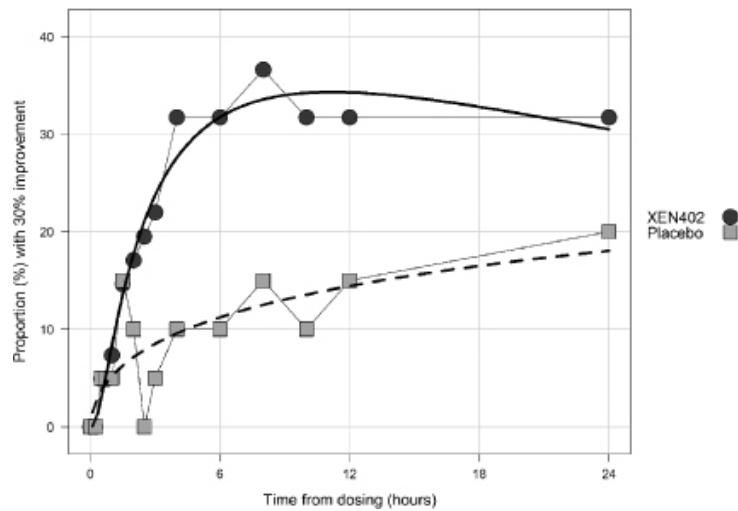
The primary efficacy endpoint was the change in total pain relief at six hours post-dose, or TOTPAR-6. For this endpoint, XEN402-treated subjects experienced greater pain relief compared to subjects who received placebo, although the difference did not achieve statistical significance. Multiple secondary endpoints were studied including Categorical Pain Relief Rating Scale, or REL, a numerical five-point scale ranging from no pain to complete pain and Pain Intensity Difference, or PID, compared to baseline. Certain secondary endpoints for the REL achieved predefined statistical significance for this trial.

Pain intensity was reduced on XEN402 compared to placebo, however, these results did not reach statistical significance. The mean XEN402 PID curve starts to separate from the placebo at approximately two hours (see arrow included in figure below). Prior to the onset of efficacy there was a relatively high rescue rate of approximately 40% of XEN402-treated subjects and approximately 50% of placebo-treated subjects. The high rescue rate reduced the power of the trial to show statistical significance.

XEN402 showed a 0.8 point separation from placebo in pain intensity difference at 12 hours. Note the separation marked by the arrow indicating time of onset of XEN402-effect at approximately 2.0 hours after dosing.



Post-hoc exploratory analyses demonstrated a statistically significant proportion of subjects on XEN402 exhibited a 30% or greater ($p < 0.05$) (see figure below) and 50% or greater ($p < 0.05$) reduction in pain compared to placebo. These improvements were observed from approximately 1.5 to 19 hours post-dosing, suggestive of an extended clinical effect after a single oral dose.



We concluded that these data suggest XEN402 may be a candidate for further study in inflammatory pain.

XEN701: An Antisense Oligonucleotide for the Treatment of Anemia of Chronic Kidney Disease

XEN701 is a subcutaneously administered selective antisense oligonucleotide compound designed to inhibit the expression of the protein hepcidin. To select hepcidin as our anemia drug target, we identified mutations in genes underlying a rare genetic disorder of iron overload, or excess, known as juvenile hemochromatosis, or JH, that presents at an early age. JH is caused by single-gene defects the consequences of which is deficiency of the hepcidin protein. This deficiency of hepcidin causes the iron overload in JH patients. In anemia of chronic disease, or ACD, the converse is true. Elevated levels of hepcidin cause a restricted iron supply that results in low hemoglobin or anemia. XEN701 is the first drug to enter development in our collaboration with Isis to develop antisense drugs that target the hepcidin-hemojuvelin pathway. We have exclusive worldwide rights for development and commercialization of XEN701. Neither we nor Isis has submitted an IND to the FDA for XEN701. XEN701 is currently in IND-enabling safety and toxicology studies and we expect to commence Phase 1 studies during the first half of 2014. Initially, our development strategy will focus on treating the anemia associated with chronic kidney disease, or CKD, or end stage renal disease, or ESRD, in niche populations where the use of erythropoietin stimulating agents, or ESAs, the current standard of care, is subject to a black box warning (the FDA's highest level of warning, indicating that a particular drug may lead to death or serious injury) or is contraindicated. For example, we estimate there are 115,000 CKD and ESRD patients in the U.S. who are anemic and currently have cancer or have had cancer within the last five years. Despite this, some of these patients continue to receive ESAs even though ESA labels contain a black box warning for patients with cancer. As the mechanism of XEN701 is distinct from that of ESAs, we anticipate XEN701 may provide an alternative in these niche populations.

Discovery of XEN701

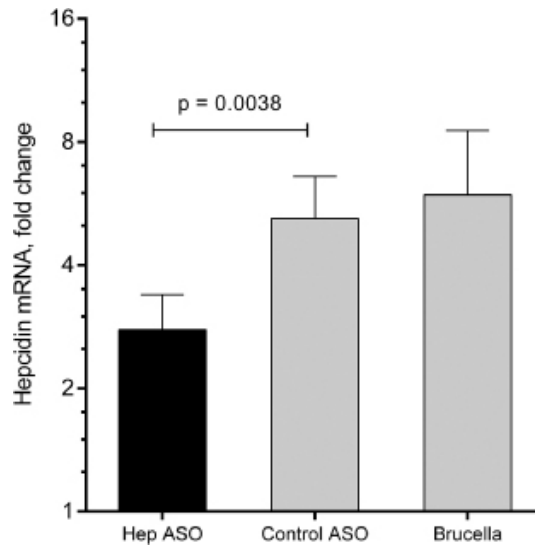
XEN701 is a selective antisense oligonucleotide compound designed to be subcutaneously administered and to inhibit the expression of the protein hepcidin in the body by interfering with the messaging function of its ribonucleic acid, or RNA. A compound that interferes with this messaging functioning can limit or prevent the cell from producing proteins. Generally, antisense oligonucleotide compounds are designed to selectively bind to and degrade RNA of a given gene and prevent that gene from producing proteins, including those identified with diseases.

JH is a rare genetic disorder of iron overload. We showed that JH is caused by genetic defects that result in a deficiency of the protein hepcidin. Hepcidin is now recognized as an important regulator of iron metabolism in humans. Multiple published studies have demonstrated that elevated circulating hepcidin is a characteristic of ACD. This increase in hepcidin expression is in response to chronic inflammation and associated with declining renal function. It is the excess hepcidin in ACD that results in restricted iron availability impairing red blood cell production resulting in anemia. XEN701 is designed to lower hepcidin levels, which we believe may reverse the restricted iron availability and thereby reverse the anemia.

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XEN701 is the first drug to enter development in our collaboration with Isis, and uses Isis' second generation MOE-Gapmer chemistry. The discovery of XEN701 utilized a screening process that, according to Isis, results in an improved human side effect profile for newer second-generation antisense oligonucleotides. In non-human primate studies, XEN701 was generally well-tolerated and after six weeks of weekly subcutaneous dosing the liver reduction of hepcidin mRNA was 75% with a corresponding decrease in plasma hepcidin protein levels of 66%. Furthermore, we have demonstrated, using mouse-specific antisense oligonucleotides targeting hepcidin, that we can reduce elevated hepcidin levels in the presence of inflammation.

Brucella antigen causes an inflammatory response that induces hepcidin liver expression. Mouse-specific hepcidin ASO, or Hep ASO, is able to significantly reduce hepcidin liver messenger RNA, or mRNA, induction by Brucella antigen, whereas the control ASO does not have this effect.



We believe that the antisense approach offers distinct advantages as a therapeutic strategy to lower hepcidin, including the following:

- hepcidin is primarily expressed in the liver and antisense compounds distribute readily to the liver;
- the suppression of gene expression at the level of RNA may be a more effective therapeutic intervention strategy given the relatively large (up to 100 fold or more) range of hepcidin protein in humans depending on the underlying inflammatory state; and
- we are not aware of any reported drug-drug metabolism interactions with antisense compounds, which may be beneficial as CKD and ESRD patients generally take multiple medications.

About Anemia in Niche CKD and ESRD Populations

The anemia associated with CKD and ESRD has many of the characteristics of ACD, but the condition is exacerbated by renal insufficiency which causes a decrease in the production of erythropoietin. Erythropoietin is a hormone produced by the kidney that interacts with the EPO receptor in bone marrow to stimulate red blood cell production. As a direct result, ESAs are used to successfully treat anemia in many CKD and ESRD patients.

Despite their success in treating anemia of CKD and ESRD, ESAs have a FDA black box warning of increased mortality and/or increased risk of tumor progression or reoccurrence in patients with cancer, and increased risk of death, myocardial infarction, stroke, venous thromboembolism and thrombosis of vascular access. ESAs are also contraindicated in patients with uncontrolled hypertension. A new anemia drug targeting a distinct mechanism to ESAs could offer an alternative for treating anemia in CKD and ESRD patients, where warnings exist for the use of currently available ESAs.

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We have estimated from the U.S. Renal Data System that approximately 460,000 CKD and ESRD patients in the U.S. have their anemia treated with ESAs. Approximately 8% to 10% of these patients are estimated to have cancer, and may be at risk of increased mortality and/or increased risk of tumor progression or reoccurrence. Furthermore, cardiovascular disease is even more common in CKD and ESRD patients compared to the general population. Up to 25% of such patients have been reported to have poorly-controlled hypertension. The incidence of acute coronary syndrome in ESRD has been reported to be 2.9% per year and approximately 40% of patients initiating dialysis have been reported to have ischemic heart disease at the onset of dialysis. In addition, an estimated 5% of CKD and ESRD patients do not have their anemia adequately treated by currently available therapies. We believe these niche populations represent potential development opportunities for XEN701.

Future Development Plans for XEN701

We plan to initiate a Phase 1 single-ascending and multi-ascending dose study in human volunteers in the first half of 2014. Thereafter, we plan to initiate a Phase 2 proof-of-concept trial in CKD or ESRD patients with anemia.

Selective Inhibitors of Nav1.7 for Pain

Chronic pain conditions such as severe cancer pain and neuropathic pain are generally recognized as significant unmet medical needs, therefore providing commercial opportunities for a new oral pain drug. Currently available pain drugs such as narcotics often have either a lack of meaningful pain relief for many patients or dose limiting side effects. An oral selective Nav1.7 inhibitor could present a novel mechanism for the treatment of moderate to severe pain. This mechanism contrasts with our non-selective sodium channel inhibition approach taken with XEN402. We believe that the selective inhibition of Nav1.7 may lower the potential for dose-limiting central nervous system side-effects and allow for an improved side-effect profile for oral administration of such an inhibitor, which could potentially allow for the treatment of pain that has a central or deep tissue component, including cancer pain and neuropathic pain. In December 2011, we entered into a collaborative research and license agreement with Genentech and its affiliate, Roche, to discover and develop inhibitors of Nav1.7 for the treatment of pain. The goal of the collaboration is to discover and develop orally active products that selectively inhibit this sodium channel. In collaboration with Genentech, we have created a novel family of potent and selective Nav1.7 inhibitors that have pharmacokinetic profiles suitable for oral administration. A small-molecule preclinical product candidate was selected in 2013 for development and is currently in the IND-enabling stage. Neither we nor Genentech has submitted an IND to the FDA for the selective inhibitor of Nav1.7 for the treatment of pain. Under the terms of the agreement, Genentech paid us an upfront fee of \$10.0 million and subsequently we have earned a \$5.0 million milestone payment for the selection of the development-stage product candidate. We are also eligible to receive pre-commercial and commercial milestone payments with respect to the licensed products totaling up to an additional \$621.0 million. In addition we are also eligible to receive royalties based on net sales of the licensed products, which range from a mid single-digit percentage to ten percent for small-molecule inhibitors for the timeframe that such products are covered by the licensed patents and a low single-digit percentage thereafter, plus a low single-digit percentage for large-molecule inhibitors of Nav1.7.

Programs in Discovery

Selective Small-Molecule Inhibitors of SCD1 for Acne

SCD1 is an enzyme involved in lipid synthesis that is expressed in sebaceous glands in the skin. Mice deficient in SCD1 have a marked phenotype of sebaceous gland atrophy suggesting that inhibition of SCD1 activity in the skin may provide a novel treatment option for acne and seborrhea. We have developed novel small-molecule SCD1 inhibitors. In animal models, we have shown that our topical small-molecule SCD1 inhibitors can reduce sebaceous gland size and number. We have identified multiple compounds that have properties suitable for topical administration including adequate skin penetration and photostability.

Acne affects 40 to 50 million people in the U.S., with 10% to 20% of adolescents having a moderate to severe form of the condition. In keeping with our business strategy, our preference is to partner our SCD1 inhibitor program for further development for acne.

Selective Small-Molecule Inhibitors of Targets for Cardiovascular Disease

We entered into a collaborative research and option agreement with Merck in June 2009 to discover novel targets and compounds for the treatment of cardiovascular disease using our Extreme Genetics discovery platform. In 2012, Merck exercised its option to obtain an exclusive license to a target for cardiovascular disease and compound

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inhibitors that were discovered during the research collaboration. The target, when inhibited, is predicted to provide a beneficial lipid profile with the goal of protecting from cardiovascular disease.

Selective Small-Molecule Sodium Channel Modulators for DS

DS is a severe form of childhood epilepsy in which the majority of cases result from deficiency of the Nav1.1 sodium channel. Nav1.1 plays a critical role in neuronal inhibitory pathways. When it is deficient, the brain becomes hyper-excitabile leading to the intermittent and often severe seizures characteristic of DS. Thus, we believe selective sodium channel modulators may reduce brain hyper-excitability and limit or prevent the seizures of DS.

We have developed substantial expertise in sodium-channel biology and selective chemistries from our pain program. We intend to leverage this expertise for the development of selective sodium channel modulators for DS. The frequency of DS in the U.S. has been estimated to be one in 20,000 to 40,000 births with approximately 7,500 to 15,000 patients in the U.S. based on federal census data. Given the nature of this orphan disorder, we believe that DS may represent an attractive opportunity for us to advance independently.

New Pipeline Opportunities

Using our Extreme Genetics discovery platform, we are currently working to identify new drug targets for the treatment of pain. For example, we are working on additional CIP families that are not explained by Nav1.7 deficiency as well as families with severe pain phenotypes such as paroxysmal extreme pain disorder. In addition, we are evaluating other opportunities in multiple indications outside of pain.

Strategic Alliances

Agreement with uniQure for Glybera

Effective August 2000, we entered into a sublicense and research agreement with Amsterdam Molecular Therapeutics, or AMT, pursuant to which we granted to AMT an exclusive, worldwide sublicense under certain intellectual property controlled by us to develop and commercialize technology and compounds related to the variant of LPL, called LPL^{S447X}. Together with collaborators from UBC, we demonstrated that the LPL^{S447X} variant resulted in increased LPL enzyme activity leading to reduced triglyceride levels in humans. Under our sublicense and research agreement with AMT, we collaborated with AMT and UBC on preclinical activities, and thereafter AMT developed a LPL gene therapy product, Glybera, which contains the LPL^{S447X} variant. Certain of AMT's assets, including the rights to the intellectual property covered by our agreement, were subsequently acquired by uniQure in April 2012. Glybera was approved in the EU in October 2012 to treat LPLD. uniQure conducted the clinical trials and is responsible for the commercialization of Glybera.

Under the terms of the agreement, we are eligible to receive mid single-digit royalties on net sales of the licensed products, for sales made by uniQure and its affiliates. The royalty rates for sales made by uniQure and its affiliates are reduced to a low single-digit when the licensed patents expire. In July 2013, uniQure announced that it had entered into a partnership with Chiesi for the commercialization of Glybera in Europe and more than a dozen other countries including Brazil, China, Mexico and Russia. uniQure has also publicly disclosed that it is preparing to apply for regulatory approval of this product in the U.S., Canada and other markets. With respect to uniQure's sublicense to Chiesi for the commercialization of Glybera in Europe and more than a dozen other countries including Brazil, China, Mexico and Russia, we are eligible to receive a percentage in the low twenties of all non-royalty compensation relating to the licensed technology or products that uniQure receives from Chiesi (including, for example, upfront payments and milestone payments), a percentage in the low twenties of any royalties that uniQure receives from Chiesi based on sales of technology or products covered by the licensed patents, plus a mid single-digit percentage of certain further royalties that uniQure receives from Chiesi based on sales of our licensed technology or products after the expiration of all licensed patents covering the product. If uniQure grants a sublicense to a third party other than to Chiesi, then we are eligible to receive a percentage in the low twenties of all non-royalty compensation relating to the licensed technology or products that uniQure receives from such sublicensee (for example upfront payments and milestone payments), plus a percentage in the low twenties of any royalties that uniQure receives from such sublicensee based on sales of technology or products covered by the licensed patents.

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Through June 30, 2013, we have received upfront fees and milestone payments totaling CAD\$575,000, and are eligible to receive certain additional milestone payments of less than CAD\$1.0 million for Glybera and for each subsequent product, if any, developed pursuant to the agreement with uniQure. We, in turn, have certain payment obligations to our licensor, UBC, based on amounts received from uniQure or otherwise based on the exploitation of the licensed intellectual property.

Our sublicense agreement with uniQure expires on the date of the expiration of the UBC license agreement. Either party may terminate the agreement in the event of the other party's default under the agreement that remains uncured for 20 days after receipt of notice from the non-breaching party.

Agreement with UBC for Glybera

Effective August 2000, we entered into a license agreement with UBC pursuant to which UBC granted to us an exclusive, worldwide license under UBC's interest in certain intellectual property controlled by UBC to develop and commercialize technology and compounds in the field of gene therapy, including products that related to the variant of LPL, called LPL^{S447X}.

Under the terms of the agreement, UBC is eligible to receive low single-digit royalties on net sales of the licensed products made by us, and is also eligible to receive certain pre-commercial milestone payments. UBC is also eligible to receive a mid single-digit percentage of certain compensation that we receive based on sublicenses granted by us to a third party relating to the licensed technology or products, including in connection with our sublicensing agreement with uniQure for Glybera.

Through June 30, 2013, we have paid to UBC upfront fees and milestone payments totaling CAD\$230,000 and are obligated to pay a certain additional milestone payment of approximately CAD\$200,000 for Glybera and further milestone payments of CAD\$322,500 for each subsequent product, if any, developed pursuant to our sublicensing agreement with uniQure.

Our license agreement with UBC expires on the date of the expiration of the last patent granted under such license. In the event that our sublicense with uniQure is terminated, we may terminate the agreement with 30 days advance notice to UBC. Either party may terminate the agreement in the event of the other party's default under the agreement that remains uncured for 30 days after receipt of notice from the non-breaching party, and UBC may terminate without such cure period in the event of certain types of breach by us.

Agreement with Teva for XEN402

In December 2012, we entered into a collaborative development and license agreement with Teva, through its subsidiary, Ivax, pursuant to which we granted Teva an exclusive worldwide license to develop and commercialize certain products, including XEN402.

Under the terms of the agreement, Teva paid us an upfront fee of \$41.0 million. We are collaborating with Teva to further develop XEN402, and Teva is funding all development costs with respect to the licensed products. Teva is providing funding to us for certain of our full-time equivalents, or FTEs, performing the research collaboration plan. In addition, we are eligible to receive potential milestone payments totaling up to \$335.0 million, comprised of up to \$20.0 million in clinical milestone payments, up to \$285.0 million in regulatory milestone payments, and up to \$30.0 million in sales-based milestone payments. If XEN402 is approved, we are also eligible to receive royalties in the low teens to low twenties on net sales of the licensed products for the timeframe that such products are covered by the licensed patents and in certain other instances.

We have an option to a minority co-promotion interest for products incorporating XEN402 in the U.S. Our exercise of this option is subject to meeting objective financial conditions, staffing requirements and compliance standards to be determined in Teva's reasonable discretion in accordance with standard industry practice. Our co-promotion option is exercisable upon the filing of the first NDA for a XEN402 product with the FDA and we will be obligated to pay an opt-in fee to Teva, which is calculated by multiplying our co-promotion interest (as a percentage) by the amount of certain milestones paid or payable by Teva, to which is added certain past and future development costs incurred by Teva with respect to the product for the U.S. Our co-promotion interest is in the twenty to thirty percent range, and equals our percentage share of detailing activities and co-promotion expenses. Such opt-in fee is payable

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as a reduction to the milestone payments or our share of operating profits that Teva would otherwise owe to us or a combination of the two. If we exercise this option, we will be eligible to receive, in lieu of royalties with respect to such product sales in the U.S., a percentage share (equal to our co-promotion interest) of operating profits from such product sales in the U.S.

Our agreement with Teva expires on the date of the expiration of all payment obligations to us under the agreement. Teva may terminate the agreement with 60 days advanced written notice to us after a pre-defined number of Phase 2 (or later stage) clinical trials have been completed or in the event that safety or efficacy issues arise in the development of the licensed products. Either party may terminate the agreement in the event of the other party's material breach which remains uncured for 90 business days. In certain termination circumstances we receive licenses to Teva intellectual property relating to XEN402 clinical development and regulatory filings. If patents within such Teva intellectual property cover the XEN402 product, then Teva is eligible to receive royalties from us based on a percentage of net product sales, within the low single-digit range.

Pursuant to the terms of our agreement, we have the right to require Teva, upon written notice, to purchase common shares issued in this offering if they have commenced a Phase 2b clinical trial of any licensed product under the agreement and if certain minimum price per common share and gross proceed thresholds are met in connection with this offering. The number of common shares Teva would be required to purchase in the offering upon receipt of such notice would equal the lesser of:

- \$20.0 million divided by the initial price to the public of our common shares in this offering, if this offering occurs on or after the date Teva commences a Phase 3 trial of any licensed product;
- \$10.0 million divided by the initial price to the public of our common shares in this offering, if this offering occurs prior to the date Teva commences a Phase 3 trial of any licensed product;
- 19% of our issued and outstanding shares after giving effect to the common shares issued in this offering; and
- a number of common shares that we specify in a notice to Teva.

We have not yet delivered the notice to Teva regarding the purchase of our common shares.

Agreement with Isis for XEN701

In November 2010, we entered into a collaboration and license agreement with Isis. We issued Isis a convertible, interest-bearing promissory note as payment of the \$1.5 million upfront fee required by the agreement. In June 2013, we made this payment to Isis, including accrued interest, pursuant to the terms of the convertible promissory note. Under the terms of this agreement we received an option to obtain from Isis worldwide exclusive licenses to develop and commercialize antisense products targeting hepcidin and/or hemojuvelin, each of which is a validated target for anemia of chronic disease. The option is exercisable until 30 days after the initiation of IND-enabling toxicology studies with a development candidate compound for the applicable target or November 2014, whichever is earliest. We collaborated with Isis on the research that led to the selection of XEN701 as the first drug to enter development under the collaboration. Each party bore its own expenses in conducting the research program under the Isis agreement.

In June 2013, we exercised our option and obtained an exclusive license to develop, manufacture and commercialize antisense products under the collaboration that target hepcidin. Under the terms of the agreement, we paid Isis an option exercise fee of \$2.0 million. Upon the achievement of specific development and regulatory events we are obligated to pay to Isis clinical milestone payments totaling up to \$13.0 million, regulatory-based milestone payments totaling up to \$75.0 million and sales-based milestone payments totaling up to \$60.0 million. In addition, Isis is eligible to receive royalties on net sales of licensed products by us and our affiliates, in the single-digit range. If we sublicense XEN701 to a third party for development or commercialization, then Isis is eligible to receive a percentage of our sublicensing revenue, including milestone payments and royalties we may receive from any sublicensee in lieu of some or all of the milestone payments and the royalties described above. The percentage Isis receives varies depending on the development or regulatory stage of XEN701 at the time such sublicense is granted.

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We may terminate this agreement upon 90 days notice to Isis, and either party may terminate in the event of material breach by the other party that is not cured within 60 days of receipt of notice thereof.

Agreement with Genentech for Selective Inhibitors of Nav1.7

In December 2011, we entered into a collaborative research and license agreement with Genentech and its affiliate, Roche, to discover and develop small and large molecules that selectively inhibit the Nav1.7 sodium channel and companion diagnostics for the potential treatment of pain. Pursuant to this agreement, we granted Genentech a worldwide exclusive license to develop and commercialize compounds directed to Nav1.7 and products incorporating such compounds for all uses. We also granted Genentech a worldwide non-exclusive license to diagnostic products for the purpose of developing or commercializing such compounds.

Under the terms of the agreement, Genentech paid us an upfront fee of \$10.0 million, and we have subsequently earned a \$5.0 million milestone payment for the selection of a product candidate for clinical development. Genentech is providing funding to us for certain of our FTEs performing the research collaboration plan. In addition, we are eligible to receive pre-commercial and commercial milestone payments with respect to the licensed products totaling up to an additional \$621.0 million, comprised of up to \$53.5 million in preclinical and clinical milestone payments, up to \$387.5 million in regulatory milestone payments, and up to \$180.0 million in sales-based milestone payments for multiple products and indications. In addition, we are eligible to receive royalties based on net sales of the licensed products, which range from a mid single-digit percentage to ten percent for small-molecule inhibitors for the timeframe that such products are covered by the licensed patents and a low single-digit percentage thereafter, plus a low single-digit percentage for large-molecule inhibitors of Nav1.7.

Our agreement with Genentech expires on the date of the expiration of all payment obligations to us under the agreement. Genentech may terminate the agreement with three months advance notice anytime on or after the third anniversary of the effective date of the agreement, and each party may terminate the agreement in the event of a material breach by the other party that remains uncured after 90 days. In the event that Genentech terminates the agreement due to our breach, Genentech retains its licenses and its payment obligations to us are reduced. In the event that we terminate the agreement due to Genentech's breach, the rights and licenses granted to Genentech revert back to Xenon, subject to certain rights to make and use certain large-molecule product candidates that are retained by Genentech, and Genentech is obligated to assign certain regulatory approvals and grant certain licenses to Xenon to enable it to develop and commercialize certain terminated products outside of the collaboration.

Agreement with Merck for Cardiovascular Disease

In June 2009, we entered into an exclusive collaborative research and option agreement with Merck, pursuant to which the parties conducted a research program to discover and develop novel small-molecule candidates for the potential treatment of cardiovascular disease. Merck provided payments to us for our FTEs who performed our activities pursuant to the research program conducted under the Merck agreement. The Merck collaborative research program ended in December 2012.

Under the terms of the agreement, Merck had the option to obtain an exclusive license under certain intellectual property controlled by us to develop and commercialize compounds and products directed to targets in the research program, which has now expired. In June 2012, Merck exercised its option to obtain such a worldwide exclusive license to develop and commercialize compound inhibitors of a target that was identified using our Extreme Genetics discovery platform. Through June 30, 2013, we have received milestone payments and an option fee totaling \$9.0 million, and we are eligible for further research, development and regulatory milestone payments of up to \$64.0 million, comprised of \$21.0 million in preclinical and clinical milestone payments and up to \$43.0 million in regulatory milestone payments for products directed to the licensed target, as well as royalties from the mid to high single-digit range.

We have an option to co-fund the Phase 1 and first Phase 2 clinical trials of product candidates licensed by Merck by paying Merck 50% of such development costs. Such co-funding option is available at the IND-filing stage for the applicable product candidate. If we exercise our co-funding option then the maximum eligible milestone amounts due to us increase to \$86.5 million and the royalties increase to the high single-digit to the sub-teen double-digit range.

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Our agreement with Merck expires on the date of the expiration of all royalty payment obligations to us under the agreement. Merck has the right to terminate the agreement upon providing certain notices to us. Each party may terminate the agreement in the event of a material breach by the other party that remains uncured for 90 days after notice of such breach. In the event that Merck terminates the agreement due to our breach, the licenses granted to Merck survive and becomes fully paid up. In the event that we terminate the agreement due to Merck's breach, the licenses granted to Merck terminate.

Intellectual Property

As part of our business strategy, we generally file patent applications disclosing and claiming the drug targets and their novel uses that we identified with the use of our Extreme Genetics discovery platform, novel compositions that modulate such targets, methods of making and using such compositions and various therapeutic formulations of such compositions that cover our product candidates. In some cases, we also file claims on screening assays as well as compositions and methods for use in diagnosing certain diseases. We generally file applications in the U.S., Canada, Europe and other commercially significant foreign jurisdictions. We also rely on trade secrets, internal know-how, technological innovations and agreements with third parties to develop, maintain and protect our competitive position. Our ability to be competitive will depend on the success of this strategy.

As of June 30, 2013, we owned, co-owned or licensed 61 issued U.S. patents and approximately 28 pending U.S. patent applications, including provisional and non-provisional filings. We also owned, co-owned or licensed an additional 687 pending and granted counterpart applications worldwide, including 151 country-specific validations of 13 European patents.

We have in-licensed from UBC patent applications and patents related to Glybera, and methods of making and using Glybera. These include European Patent No. 1,200,117, Japanese Patent No. 5,095,894, pending U.S. Patent Application No. 13/850,203, and pending Canadian Patent Application No. 2,370,081. European Patent No. 1,200,117 and Japanese Patent No. 5,095,894 are expected to expire in June 2020 (absent any extensions of term); U.S. Patent Application No. 13/850,203 and Canadian Patent Application No. 2,370,081, if issued, are expected to expire in 2020 (absent any extensions of term). In addition, U.S. Patent No. 6,814,962, related European Patent No. 763,116, and pending counterpart U.S. Patent Application No. 13/584,203 have composition claims directed to various recombinant viruses containing LPL coding sequences and methods of using such viruses to treat various pathologies, and various other related patents and applications claiming priority to PCT/FR1995/00669 are directed to the preparation of recombinant viruses and uses in gene therapy, all of which are expected to expire between 2014 and 2015 (absent any extensions of term).

As of June 30, 2013, we owned six issued U.S. patents and five pending U.S. patent applications related to XEN402, and methods of making and using this and certain related compounds. The issued patents are expected to expire between 2026 and 2030 (absent any extensions of term). In addition, we have 11 foreign issued patents (exclusive of European patent national validation) and filed 109 corresponding applications in various foreign jurisdictions relating to XEN402.

We have in-licensed from Isis patent applications and one patent related to XEN701, and the use of such compositions in treating hepcidin-mediated conditions. These include one issued U.S. patent with claims directed to methods of treating hepcidin-mediated conditions, as well as one pending U.S. patent application, and two pending counterpart European patent applications, directed to antisense compositions targeting hepcidin. The U.S. patent is expected to expire in 2028 (absent any extension of term), and any further allowances (worldwide) are expected to expire in 2027 (absent any extensions of term). In addition, a variety of core technology patents and patent applications have been in-licensed from Isis. These patents are generally directed to antisense compositions and methods of manufacture.

We may obtain patents on our novel compositions before we obtain marketing approval for product candidates containing such compositions. Because patents are only valid for a limited period, and the life of a particular patent may begin prior to the commercial sale of the related product, the commercial value of any patent is limited. However, in certain circumstances, we may be able to seek patent term extensions for patents in the U.S. and in a number of European countries, compensating in part for delays in obtaining marketing approval, but we cannot be certain we will obtain such extensions.

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Further, the existence of issued patents does not guarantee our right to practice the patented technology or commercialize any product candidate covered by such a patent. Third parties may have or obtain rights to other patents that could be used to prevent or attempt to prevent us from commercializing our product candidates. If these other parties are successful in obtaining valid and enforceable patents, and establishing our infringement of those patents, we could be prevented from commercializing our product candidates unless we were able to obtain a license under such patents, which may not be available on commercially reasonable terms or at all.

In the conduct of our business, we may infringe patents or other proprietary rights of third parties. If we do infringe such patents or other proprietary rights, we could be prevented from developing or selling products or from using the processes covered by those patents, could be required to pay substantial damages or could be required to obtain a license from the third party to allow us to use their technology, which may not be available on commercially reasonable terms or at all. If we are not able to obtain a required license or develop alternative technologies, we may be unable to develop or commercialize some or all of our products, and our business could be adversely affected.

Much of our scientific capabilities depend upon the knowledge, experience and skills of key scientific and technical personnel. To protect our rights to our proprietary know-how and technology, we require all our employees, consultants and advisors to enter into confidentiality agreements that require disclosure and assignment to us of ideas, developments, discoveries and inventions made by these employees, consultants and advisors in the course of their service to us.

We may be unable to obtain, maintain and protect the intellectual property rights necessary to conduct our business, and we may be subject to claims that we infringe or otherwise violate the intellectual property rights of others, which could materially harm our business. Although we believe our patents and patent applications provide us with a competitive advantage, the patent positions of biotechnology and pharmaceutical companies can be uncertain and involve complex legal and factual questions. We and our collaborators may not be able to develop patentable product candidates or processes or obtain patents from pending patent applications. Even if patent claims are allowed, the claims may not issue, or in the event of issuance, may not be sufficient to protect the technology owned by or licensed to us or to our collaborators. In certain cases where we have licensed rights to our intellectual property to our collaborators, such collaborators have assumed control of the prosecution and maintenance of the intellectual property portfolio related to such licensed rights. If our collaborators fail to adequately prosecute or maintain any portion of our licensed intellectual property, the competitive advantage and value of our intellectual property portfolio may be reduced. For more information, see "Risk Factors—Risks Related to Our Intellectual Property Rights."

We own a number of trademarks and intend to develop names for our product candidates and as appropriate seek to secure trademark protection for them, including domain name registration, in relevant jurisdictions.

Research and Development

We have committed, and expect to continue to commit, significant resources to developing new product candidates. We have assembled experienced research and development teams at our Burnaby, British Columbia location with scientific, clinical and regulatory personnel. As of June 30, 2013, we had 52 employees in research and development. Of these employees, 23 hold a Ph.D. degree or M.D. (or equivalent) degree. From time to time we engage individuals on a contractual basis for limited time periods. Our research and development expenses for the years ended December 31, 2010, 2011 and 2012 and the six months ended June 30, 2013 were \$17.6 million, \$12.2 million, \$10.4 million and \$6.9 million, respectively.

Manufacturing

We currently rely, and expect to continue to rely, on third parties and our collaborators for the manufacture of our product candidates for preclinical and clinical testing, as well as for commercial manufacture if our product candidates receive marketing approval. Accordingly, we have not internally developed any manufacturing facilities or hired related personnel.

To date, we have obtained materials for our product candidates from multiple third-party manufacturers. We believe that all of the materials required for the manufacture of our product candidates can be obtained from more than one

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source. However, the manufacturing processes for each of our product candidates, which include large and small-molecules and oligonucleotides, vary and sourcing adequate supplies may be made more difficult depending on the type of product candidate involved. For example, our small-molecule product candidates generally can be manufactured in reliable and reproducible synthetic processes from readily available starting materials. This chemistry generally is amenable to scale-up and does not require unusual equipment in the manufacturing process. In contrast, there are a limited number of companies that can produce oligonucleotides, like XEN701, with the quality and purity that we require for our development and future commercial efforts. Establishing relationships with alternative suppliers can be a lengthy process and might cause delays in our development efforts. 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.

Competition

The biotechnology and pharmaceutical industries are highly competitive and are characterized by rapidly advancing technologies and a strong emphasis on proprietary products. While we believe that our technology, development experience, scientific knowledge and drug discovery approach provide us with certain advantages, we face potential competition in target discovery and product development from many different approaches and sources, including pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions. Any product candidates or products that we or our collaborators successfully develop and commercialize will compete with existing products and new products that may become available in the future.

With respect to target discovery activities, competitors and other third parties, including academic and clinical researchers, may be able to access rare families and identify targets 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 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.

The key competitive factors affecting the success of all of our product candidates, if approved, are likely to be their efficacy, safety, convenience, price, the effectiveness of alternative products, the level of competition and the availability of coverage and adequate reimbursement from government and other third party payors.

Our commercial opportunity 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 in many cases by insurers or other third party payors seeking to encourage the use of generic products.

Aside from the product marketplace, our competitors also compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites, recruiting patients for clinical trials, and by acquiring technologies complementary to, or necessary for, our programs.

Our products and product candidates may compete with various therapies and drugs, both in the marketplace and currently under development.

Glybera (alipogene tiparvovec) Competition

There are no approved gene therapies currently on the market for LPLD. 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 LPL sequence containing the LPL^{S447X} genetic variant or otherwise.

XEN402 Competition

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

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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 for the treatment of pain, including Bioline Rx Ltd., Convergence Pharmaceuticals Limited, Dainippon Sumitomo Co., Ltd. and Pfizer, 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. We are not aware of any drugs or therapies currently approved specifically for treating primary EM.

XEN701 Competition

Our competitors currently market well-known drugs and treatments for anemia, including ESAs such as epogen, and intravenous iron therapy. We are aware of clinical-stage development programs at several major pharmaceutical and biotechnology companies targeting hepcidin for the treatment of cancer associated with anemia, including Eli Lilly and Company and NOXXON Pharma AG. Other companies' clinical-stage development programs do not directly target hepcidin such as prolyl hydroxylase inhibitors and soluble hemojuvelin for the treatment of CKD and ESRD, including Astellas Pharma Inc., AstraZeneca plc, FerruMax Pharmaceuticals, Inc., FibroGen, Inc. and GlaxoSmithKline plc. Another clinical-stage therapy aims to treat anemia by administering iron via dialysate. We are not aware of any drugs or therapies currently approved for treating anemia by inhibiting the production of human hepcidin at the transcriptional level.

Government Regulation

We are developing both small-molecule and large-molecule product candidates. Our small-molecule product candidates are regulated as drugs by the FDA. The gene therapy product, Glybera, and certain of our large-molecule product candidates, such as XEN701, are regulated by the FDA as biologics. Within the FDA, the Center for Drug Evaluation and Research, or CDER, regulates drugs and the Center for Biologics Evaluation and Research, or CBER, regulates biological products. Drugs and biological products are subject to regulation under the Federal Food, Drug, and Cosmetic Act, or FD&C Act, and other federal, provincial, state, local and foreign statutes and regulations. Biological products are also subject to regulation under the Public Health Service Act, or PHS Act. Both the FD&C Act and the PHS Act, as applicable, and their corresponding regulations govern, among other things, the testing, manufacturing, safety, efficacy, labeling, packaging, storage, record keeping, distribution, import, export, reporting, advertising and other promotional practices involving drugs and biological products. FDA approval must be obtained before clinical testing of drugs or biological products is initiated, and each clinical study protocol for such product candidates is reviewed by the FDA prior to initiation in the U.S. FDA approval also must be obtained before marketing of drugs and biological products in the U.S. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, provincial, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources and we may not be able to obtain the required regulatory approvals.

Federal and state agencies, congressional committees and foreign governments have expressed interest in further regulating biotechnology. In particular, ethical, social and legal concerns about genetic testing, genetic research and gene therapy could result in additional regulations restricting or prohibiting the processes we may use in discovering and developing our products candidates and in manufacturing and marketing Glybera and any other gene therapy products we or our collaborators may develop. More restrictive regulations or claims that our products are unsafe or pose a hazard could prevent us from commercializing any products. New government requirements may be established that could delay or prevent regulatory approval of our product candidates under development. It is impossible to predict whether legislative changes will be enacted, regulations, policies or guidance changed, or interpretations by agencies or courts changed, or what the impact of such changes, if any, may be.

U.S. Drug Development Process

The process required by the FDA before a drug or biological product may be marketed in the U.S. generally involves the following:

- ⁿ completion of nonclinical laboratory tests and animal studies according to good laboratory practices, or GLPs, and applicable requirements for the humane use of laboratory animals or other applicable regulations;

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- submission to the FDA of an application for an IND, which must become effective before human clinical studies may begin;
- performance of adequate and well-controlled human clinical studies according to the FDA's regulations commonly referred to as good clinical practices, or GCPs, and any additional requirements for the protection of human research subjects and their health information, to establish the safety and efficacy of the proposed product for its intended use;
- submission to the FDA of a NDA for drug products or a Biologic License Application, or BLA, for biological products for marketing approval that includes substantive evidence of safety, purity, and potency from results of nonclinical testing and clinical studies;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities where the product is produced to assess compliance with good manufacturing practices, or GMP, to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;
- potential FDA audit of the nonclinical and clinical study sites that generated the data in support of the NDA or BLA; and
- FDA review and approval of the NDA, or licensure of the BLA.

Before testing any drug or biological product candidate in humans, the product candidate enters the preclinical testing stage. Preclinical tests, also referred to as nonclinical studies, include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies to assess the potential safety and activity of the product candidate. The conduct of the preclinical tests must comply with federal regulations and requirements including GLPs.

The clinical study sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. Some preclinical testing may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA places the clinical study on a clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical study can begin. The FDA may also impose clinical holds on a product candidate at any time before or during clinical studies due to safety concerns or non-compliance. If the FDA imposes a clinical hold, studies may not recommence without FDA authorization and then only under terms authorized by the FDA. Accordingly, we cannot be sure that submission of an IND will result in the FDA allowing clinical studies to begin, or that, once begun, issues will not arise that suspend or terminate such studies.

Clinical studies involve the administration of the drug or biological product candidate to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the study sponsor's control. Clinical studies are conducted under protocols detailing, among other things, the objectives of the clinical study, dosing procedures, subject selection and exclusion criteria, and the parameters to be used to monitor subject safety, including stopping rules that assure a clinical study will be stopped if certain AEs should occur. Each protocol and any amendments to the protocol must be submitted to the FDA as part of the IND. Clinical studies must be conducted and monitored in accordance with the FDA's regulations comprising the GCP requirements, including the requirement that all research subjects provide informed consent. Further, each clinical study must be reviewed and approved by an independent institutional review board, or IRB, at or servicing each institution at which the clinical study will be conducted. An IRB is charged with protecting the welfare and rights of study participants and considers such items as whether the risks to individuals participating in the clinical studies are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the form and content of the informed consent that must be signed by each clinical study subject or his or her legal representative and must monitor the clinical study until completed.

Human clinical studies are typically conducted in three sequential phases that may overlap or be combined:

- *Phase 1.* The drug or biological product is initially introduced into healthy human subjects and tested for safety. In the case of some products for severe or life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.

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- *Phase 2.* The drug or biological product is evaluated in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance, optimal dosage and dosing schedule.
- *Phase 3.* Clinical studies are undertaken to further evaluate dosage, clinical efficacy, potency, and safety in an expanded patient population at geographically dispersed clinical study sites. These clinical studies are intended to establish the overall risk/benefit ratio of the product and provide an adequate basis for product labeling.

Post-approval clinical studies, sometimes referred to as Phase 4 clinical studies, may be conducted after initial marketing approval. These clinical studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication, particularly for long-term safety follow-up. The FDA recommends that sponsors observe subjects in studies of gene therapy products for potential gene therapy-related delayed AEs for a 15-year period, including a minimum of five years of annual examinations followed by 10 years of annual queries, either in person or by questionnaire, of study subjects. During all phases of clinical development, regulatory agencies require extensive monitoring and auditing of all clinical activities, clinical data, and clinical study investigators.

Concurrent with clinical studies, companies usually complete additional animal studies and must also develop additional information about the physical characteristics of the drug or biological product as well as finalize a process for manufacturing the product in commercial quantities in accordance with GMP requirements. To help reduce the risk of the introduction of adventitious agents with use of biological products, the PHS Act emphasizes the importance of manufacturing control for products whose attributes cannot be precisely defined. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the sponsor must develop methods for testing the identity, strength, quality, potency and purity of the final drug or biological product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug or biological product candidate does not undergo unacceptable deterioration over its shelf life.

Human gene therapy products are a new category of therapeutics, and studies of gene therapy products are subject to certain regulatory requirements in addition to those set forth above including certain requirements of the National Institutes of Health.

U.S. Review and Approval Processes

After the completion of clinical studies of a drug or biological product, FDA approval of an NDA or a BLA must be obtained before commercial marketing of the drug or biological product, respectively. The NDA or BLA must include results of product development, laboratory and animal studies, human studies, information on the manufacture and composition of the product, proposed labeling and other relevant information. In addition, under the Pediatric Research Equity Act, or PREA, an NDA or a BLA or supplement to an NDA or a BLA must contain data to assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers. Unless otherwise required by regulation, PREA does not apply to any drug or biological product for an indication for which orphan designation has been granted. The testing and approval processes require substantial time and effort and there can be no assurance that the FDA will accept the NDA or BLA for filing and, even if filed, that any approval will be granted on a timely basis, if at all.

Under the Prescription Drug User Fee Act, or PDUFA, as amended, each NDA or BLA must be accompanied by a substantial user fee. PDUFA also imposes an annual product fee for drugs and biologics and an annual establishment fee on facilities used to manufacture prescription drugs or biologics. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business. Additionally, no user fees are assessed on NDAs or BLAs for products designated as orphan drugs, unless the product also includes a non-orphan indication.

Within 60 days following submission of the application, the FDA reviews an NDA or BLA submitted to determine if it is substantially complete before the agency accepts it for filing. The FDA may refuse to file any marketing application that it deems incomplete or not properly reviewable at the time of submission and may request additional

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information. In this event, the NDA or BLA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review of the NDA or BLA. The FDA reviews the application to determine, among other things, whether the proposed product is safe and potent, or effective, for its intended use, and has an acceptable purity profile, and whether the product is being manufactured in accordance with GMP to assure and preserve the product's identity, safety, strength, quality, potency and purity. The FDA may refer applications for novel products or products that present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. During the product approval process, the FDA also will determine whether a Risk Evaluation and Mitigation Strategy, or REMS, is necessary to assure the safe use of the product. If the FDA concludes a REMS is needed, the sponsor of the NDA or BLA must submit a proposed REMS; the FDA will not approve the application without a REMS, if required.

Before approving an NDA or a BLA, the FDA will inspect the facilities at which the product is manufactured. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with GMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA or a BLA, the FDA will typically inspect one or more clinical sites to assure that the clinical studies were conducted in compliance with IND study requirements and GCP requirements. To assure GMP and GCP compliance, an applicant must incur significant expenditure of time, money and effort in the areas of training, record keeping, production, and quality control.

Notwithstanding the submission of relevant data and information, the FDA may ultimately decide that the NDA or BLA does not satisfy its regulatory criteria for approval and deny approval. Data obtained from clinical studies are not always conclusive and the FDA may interpret data differently than we interpret the same data. If the agency decides not to approve the marketing application, the FDA will issue a complete response letter that usually describes all of the specific deficiencies in the application identified by the FDA. The deficiencies identified may be minor, for example, requiring labeling changes, or major, for example, requiring additional clinical studies. Additionally, the complete response letter may include recommended actions that the applicant might take to place the application in a condition for approval. If a complete response letter is issued, the applicant may either resubmit the NDA or BLA, addressing all of the deficiencies identified in the letter, or withdraw the application.

If a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling. The FDA may impose restrictions and conditions on product distribution, prescribing, or dispensing in the form of a risk management plan, or otherwise limit the scope of any approval. In addition, the FDA may require post-approval clinical studies, sometimes referred to as Phase 4 clinical studies, designed to further assess a product's safety and effectiveness, and testing and surveillance programs to monitor the safety of approved products that have been commercialized.

One of the performance goals agreed to by the FDA under the PDUFA is to complete its review of 90% of standard NDAs and BLAs within 10 months from filing and 90% of priority NDAs and BLAs within six months from filing, whereupon a review decision is to be made. The FDA does not always meet its PDUFA goal dates and its review goals are subject to change from time to time. The review process and the PDUFA goal date may be extended by three months if the FDA requests or the application sponsor otherwise provides additional information or clarification regarding information already provided in the submission within the last three months before the PDUFA goal date.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biological product intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the U.S., or more than 200,000 individuals in the U.S. and for which there is no reasonable expectation that the cost of developing and making a drug or biological product available in the U.S. for this type of disease or condition will be recovered from sales of the product. Both Glybera and XEN402 have received orphan drug designation from the FDA. Orphan product designation must be requested before submitting an NDA or BLA. After the FDA grants

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orphan product designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has orphan designation subsequently receives the first FDA approval for such drug for the disease or condition for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug or biological product for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity. Competitors, however, may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity. Orphan product exclusivity also could block the approval of one of our products for seven years if a competitor obtains approval of the same product as defined by the FDA or if our product candidate is determined to be contained within the competitor's product for the same indication or disease. If a drug or biological product designated as an orphan product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan product exclusivity. Orphan drug status in the EU has similar, but not identical, benefits, including up to 10 years of exclusivity.

Post-Approval Requirements

Maintaining substantial compliance with applicable federal, provincial, state, and local statutes and regulations requires the expenditure of substantial time and financial resources. Rigorous and extensive FDA regulation of drug and biological products continues after approval, particularly with respect to GMP. We will rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of any products that we may commercialize. Manufacturers of our products are required to comply with applicable requirements in the GMP regulations, including quality control and quality assurance and maintenance of records and documentation. Other post-approval requirements applicable to drug and biological products, include reporting of GMP deviations that may affect the identity, potency, purity and overall safety of a distributed product, record-keeping requirements, reporting of adverse effects, reporting updated safety and efficacy information, and complying with electronic record and signature requirements. After an NDA or BLA is approved, the product also may be subject to official lot release. As part of the manufacturing process, the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. If the product is subject to official release by the FDA, the manufacturer submits samples of each lot of product to the FDA together with a release protocol showing a summary of the history of manufacture of the lot and the results of all of the manufacturer's tests performed on the lot. The FDA also may perform certain confirmatory tests on lots of some products before releasing the lots for distribution by the manufacturer. In addition, the FDA conducts laboratory research related to the regulatory standards on the safety, purity, potency, and effectiveness of drug and biological products.

We also must comply with the FDA's advertising and promotion requirements, such as those related to direct-to-consumer advertising, the prohibition on promoting products for uses or in patient populations that are not described in the product's approved labeling (known as "off-label use"), industry-sponsored scientific and educational activities, and promotional activities involving the internet. Discovery of previously unknown problems or the failure to comply with the applicable regulatory requirements may result in restrictions on the marketing of a product or withdrawal of the product from the market as well as possible civil or criminal sanctions. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant or manufacturer to administrative or judicial civil or criminal sanctions and adverse publicity. FDA sanctions could include refusal to approve pending applications, withdrawal of an approval, clinical hold, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, mandated corrective advertising or communications with doctors, debarment, restitution, disgorgement of profits, or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

Drug and biological product manufacturers and other entities involved in the manufacture and distribution of approved drug or biological products are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with GMPs and other laws. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain GMP compliance. Discovery of problems with a product

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after approval may result in restrictions on a product, manufacturer, or holder of an approved NDA or BLA, including withdrawal of the product from the market. In addition, changes to the manufacturing process or facility generally require prior FDA approval before being implemented and other types of changes to the approved product, such as adding new indications and additional labeling claims, are also subject to further FDA review and approval.

U.S. Patent Term Restoration and Marketing Exclusivity

Depending upon the timing, duration and specifics of the FDA approval of the use of our product candidates, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of an NDA or BLA plus the time between the submission date of an NDA or BLA and the approval of that application. Only one patent applicable to an approved product is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The U.S. Patent and Trademark Office, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration.

Under the Hatch-Waxman Amendments, a drug product containing a new chemical entity as its active ingredient is entitled to five years of market exclusivity, and a product for which the sponsor is required to generate new clinical data is entitled to three years of market exclusivity. A drug or biological product can also obtain pediatric market exclusivity in the U.S. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric study in accordance with an FDA-issued "Written Request" for such a study.

The Biologics Price Competition and Innovation Act of 2009 created an abbreviated approval pathway for biological products shown to be similar to, or interchangeable with, an FDA-licensed reference biological product. Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency, can be shown through analytical studies, animal studies, and a clinical study or studies. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product and, for products administered multiple times, the biologic and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic. However, complexities associated with the larger, and often more complex, structure of biological products, as well as the process by which such products are manufactured, pose significant hurdles to implementation that are still being worked out by the FDA.

A reference biologic is granted 12 years of exclusivity from the time of first licensure of the reference product. On April 10, 2013, President Obama released his proposed budget for fiscal year 2014 and proposed to cut this 12-year period of exclusivity down to seven years. He also proposed to prohibit additional periods of exclusivity for reference biologics due to minor changes in product formulations, a practice often referred to as "evergreening." The first biologic product submitted under the abbreviated approval pathway that is determined to be interchangeable with the reference product has exclusivity against other biologics submitted under the abbreviated approval pathway for the lesser of (i) one year after the first commercial marketing, (ii) 18 months after approval if there is no legal challenge, (iii) 18 months after the resolution in the applicant's favor of a lawsuit challenging the biologics' patents if an application has been submitted, or (iv) 42 months after the application has been approved if a lawsuit is ongoing within the 42-month period.

Additional Regulation

In addition to the foregoing, provincial, state and federal U.S. and Canadian laws regarding environmental protection and hazardous substances affect our business. These and other laws govern our use, handling and disposal of various biological, chemical and radioactive substances used in, and wastes generated by, our operations. If our operations result in contamination of the environment or expose individuals to hazardous substances, we could be liable for damages and governmental fines. We believe that we are in material compliance with applicable environmental laws

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and that continued compliance therewith will not have a material adverse effect on our business. We cannot predict, however, how changes in these laws may affect our future operations.

U.S. Foreign Corrupt Practices Act and Canadian Corruption of Public Officials Act

The U.S. Foreign Corrupt Practices Act and the Canadian Corruption of Public Officials Act, to which we are subject, prohibit corporations and individuals from engaging in certain activities to obtain or retain business or to influence a person working in an official capacity. It is illegal to pay, offer to pay or authorize the payment of anything of value to any foreign government official, government staff member, political party or political candidate in an attempt to obtain or retain business or to otherwise influence a person working in an official capacity.

Government Regulation Outside of the U.S.

In addition to regulations in the U.S., we will be subject to a variety of regulations in other jurisdictions governing, among other things, clinical studies and any commercial sales and distribution of our products.

Whether or not we obtain FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical studies or marketing of the product in those countries. Certain countries outside of the U.S. have a similar process that requires the submission of a clinical study application much like the IND prior to the commencement of human clinical studies. In the EU, for example, a clinical trial application, or CTA, must be submitted to each country's national health authority and an independent ethics committee, much like the FDA and the IRB, respectively. Once the CTA is approved in accordance with a country's requirements, clinical study development may proceed.

The requirements and process governing the conduct of clinical studies, product licensing, coverage, pricing and reimbursement vary from country to country. In all cases, the clinical studies are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

To obtain regulatory approval of an investigational drug or biological product under EU regulatory systems, we must submit a marketing authorization application, or MAA. The application used to file the NDA or BLA in the U.S. is similar to that required in the EU, with the exception of, among other things, country-specific document requirements. The EU also provides opportunities for market exclusivity. For example, in the EU, upon receiving marketing authorization, new chemical entities generally receive eight years of data exclusivity and an additional two years of market exclusivity. If granted, data exclusivity prevents regulatory authorities in the EU from referencing the innovator's data to assess a generic application. During the additional two-year period of market exclusivity, a generic marketing authorization can be submitted, and the innovator's data may be referenced, but no generic product can be marketed until the expiration of the market exclusivity. However, there is no guarantee that a product will be considered by the EU's regulatory authorities to be a new chemical entity, and products may not qualify for data exclusivity. Products receiving orphan designation in the EU can receive 10 years of market exclusivity, during which time no similar medicinal product for the same indication may be placed on the market. An orphan product can also obtain an additional two years of market exclusivity in the EU for pediatric studies. No extension to any supplementary protection certificate can be granted on the basis of pediatric studies for orphan indications.

The criteria for designating an "orphan medicinal product" in the EU are similar in principle to those in the U.S. Under Article 3 of Regulation (EC) 141/2000, a medicinal product may be designated as orphan if (1) it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (2) either (a) such condition affects no more than five in 10,000 persons in the EU when the application is made, or (b) the product, without the benefits derived from orphan status, would not generate sufficient return in the EU to justify investment; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the EU, or if such a method exists, the product will be of significant benefit to those affected by the condition, as defined in Regulation (EC) 847/2000. Orphan medicinal products are eligible for financial incentives such as reduction of fees or fee waivers and are, upon grant of a marketing authorization, entitled to 10 years of market exclusivity for the approved therapeutic indication. The application for orphan drug designation must be submitted before the application for marketing authorization. The applicant will receive a fee reduction for the marketing authorization application if the orphan drug designation has been granted, but not if the designation is still pending at the time the marketing authorization is submitted. Orphan drug designation does not

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convey any advantage in, or shorten the duration of, the regulatory review and approval process. Glybera has received orphan drug designation in the EU.

The 10-year market exclusivity may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan designation, for example, if the product is sufficiently profitable not to justify maintenance of market exclusivity. Additionally, marketing authorization may be granted to a similar product for the same indication at any time if:

- The second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior;
- The applicant consents to a second orphan medicinal product application; or
- The applicant cannot supply enough orphan medicinal product.

For other countries outside of the EU, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical studies, product licensing, coverage, pricing and reimbursement vary from country to country. In all cases, again, the clinical studies are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which we obtain regulatory approval. In the U.S. and markets in other countries, sales of any products for which we receive regulatory approval for commercial sale will depend, in part, on the availability of coverage and adequate reimbursement from third-party payors. Third-party payors include government programs such as Medicare or Medicaid, managed care plans, private health insurers, and other organizations. These third-party payors may deny coverage or reimbursement for a product or therapy in whole or in part if they determine that the product or therapy was not medically appropriate or necessary. Third-party payors may attempt to control costs by limiting coverage to specific drug products on an approved list, or formulary, which might not include all of the FDA-approved drug products for a particular indication, and by limiting the amount of reimbursement for particular procedures or drug treatments.

The cost of pharmaceuticals and devices continues to generate substantial governmental and third party payor interest. We expect that the pharmaceutical industry will experience pricing pressures due to the trend toward managed healthcare, the increasing influence of managed care organizations and additional legislative proposals. Third-party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain the FDA approvals. Our product candidates may not be considered medically necessary or cost-effective. A payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

Some third-party payors also require pre-approval of coverage for new or innovative devices or drug therapies before they will reimburse healthcare providers who use such therapies. While we cannot predict whether any proposed cost-containment measures will be adopted or otherwise implemented in the future, these requirements or any announcement or adoption of such proposals could have a material adverse effect on our ability to obtain adequate prices for our product candidates and to operate profitably.

In international markets, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. There can be no assurance that our products will be considered medically reasonable and necessary for a specific indication, that our products will be considered cost-effective by third-party payors, that coverage or an adequate level of reimbursement will be available

or that the third-party payors' reimbursement policies will not adversely affect our ability to sell our products profitably.

Healthcare Reform

In the U.S. and foreign jurisdictions, there have been a number of legislative and regulatory changes to the healthcare system that could affect our future results of operations. In particular, there have been and continue to be a number of initiatives at the U.S. federal and state levels that seek to reduce healthcare costs.

In the U.S., the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the Medicare Modernization Act, changed the way Medicare covers and pays for pharmaceutical products. The Medicare Modernization Act expanded Medicare coverage for drug purchases by the elderly by establishing Medicare Part D and introduced a new reimbursement methodology based on average sales prices for physician administered drugs under Medicare Part B. In addition, this legislation provided authority for limiting the number of drugs that will be covered in any therapeutic class under the new Medicare Part D program. Cost reduction initiatives and other provisions of this legislation could decrease the coverage and reimbursement rate that we receive for any of our approved products. While the Medicare Modernization Act applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the Medicare Modernization Act may result in a similar reduction in payments from private payors.

In March 2010, the President signed into law the Affordable Care Act, a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against healthcare fraud and abuse, add new transparency requirements for healthcare and health insurance industries, impose new taxes and fees on pharmaceutical and medical device manufacturers and impose additional health policy reforms. Among other things, the Affordable Care Act revises the definition of "average manufacturer price" for reporting purposes, which could increase the amount of Medicaid drug rebates to states. Further, the new law imposes a significant annual fee on companies that manufacture or import branded prescription drug products. Substantial new provisions affecting compliance have also been enacted, which may affect our business practices with healthcare practitioners and a significant number of provisions are not yet, or have only recently become, effective. Although it is too early to determine the full effect of the Affordable Care Act, the new law appears likely to continue the downward pressure on pharmaceutical pricing, especially under the Medicare program, and may also increase our regulatory burdens and operating costs.

In addition, other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. For example, on August 2, 2011, the President signed into law the Budget Control Act of 2011, which, among other things, created the Joint Select Committee on Deficit Reduction to recommend to Congress proposals in spending reductions. The Joint Select Committee on Deficit Reduction did not achieve a targeted deficit reduction of at least \$1.2 trillion for the years 2013 through 2021, triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, starting in 2013. On January 2, 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on our customers and accordingly, our financial operations.

We expect that the Affordable Care Act, as well as other healthcare reform measures that have been and may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product, and could seriously harm our future revenue. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our products.

In addition, different pricing and reimbursement schemes exist in other countries. In the European Community, governments influence the price of pharmaceutical products through their pricing and reimbursement rules and control of national healthcare systems that fund a large part of the cost of those products to consumers. Some

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jurisdictions operate positive and negative list systems under which products may be marketed only once a reimbursement price has been agreed upon. Some of these countries may require, as condition of obtaining reimbursement or pricing approval, the completion of clinical trials that compare the cost-effectiveness of a particular product candidate to currently available therapies. Other member states allow companies to fix their own prices for medicines, but monitor and control company profits. The downward pressure on healthcare costs in general, particularly prescription drugs, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert a commercial pressure on pricing within a country.

Other Healthcare Laws and Compliance Requirements

In the U.S., the research, manufacturing, distribution, sale and promotion of drug products and medical devices are potentially subject to regulation by various federal, provincial, state and local authorities in addition to the FDA, including the Centers for Medicare & Medicaid Services, other divisions of the U.S. Department of Health and Human Services (e.g., the Office of Inspector General), the U.S. Department of Justice, state Attorneys General, and other state and local government agencies. For example, sales, marketing and scientific/educational grant programs must comply with fraud and abuse laws such as the federal Anti-Kickback Statute, as amended, the federal False Claims Act, as amended, and similar state laws. Pricing and rebate programs must comply with the Medicaid Drug Rebate Program requirements of the Omnibus Budget Reconciliation Act of 1990, as amended, and the Veterans Health Care Act of 1992, as amended. If products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. All of these activities are also potentially subject to federal and state consumer protection and unfair competition laws.

The federal Anti-Kickback Statute prohibits any person, including a prescription drug manufacturer (or a party acting on its behalf), from knowingly and willfully soliciting, receiving, offering or providing remuneration, directly or indirectly, to induce or reward either the referral of an individual, or the furnishing, recommending, or arranging for a good or service, for which payment may be made under a federal healthcare program such as the Medicare and Medicaid programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand and prescribers, purchasers, and formulary managers on the other. The term "remuneration" is not defined in the federal Anti-Kickback Statute and has been broadly interpreted to include anything of value, including for example, gifts, discounts, the furnishing of supplies or equipment, credit arrangements, payments of cash, waivers of payments, ownership interests and providing anything at less than its fair market value. Although there are a number of statutory exemptions and regulatory safe harbors protecting certain business arrangements from prosecution, the exemptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exemption or safe harbor. Our practices may not in all cases meet all of the criteria for safe harbor protection from federal Anti-Kickback Statute liability. The reach of the Anti-Kickback Statute was broadened by the recently enacted Affordable Care Act, which, among other things, amends the intent requirement of the federal Anti-Kickback Statute such that a person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. In addition, the Affordable Care Act provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act (discussed below) or the civil monetary penalties statute, which imposes fines against any person who is determined to have presented or caused to be presented claims to a federal healthcare program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent. Additionally, many states have adopted laws similar to the federal Anti-Kickback Statute, and some of these state prohibitions apply to referral of patients for healthcare items or services reimbursed by any third-party payor, not only the Medicare and Medicaid programs in at least some cases, and do not contain safe harbors.

The federal False Claims Act imposes liability on any person or entity that, among other things, knowingly presents, or causes to be presented, a false or fraudulent claim for payment by a federal healthcare program. The qui tam provisions of the False Claims Act allow a private individual to bring civil actions on behalf of the federal government alleging that the defendant has submitted a false claim to the federal government, and to share in any monetary recovery. In recent years, the number of suits brought by private individuals has increased dramatically. In addition, various states have enacted false claims laws analogous to the False Claims Act. Many of these state laws apply

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where a claim is submitted to any third-party payor and not merely a federal healthcare program. There are many potential bases for liability under the False Claims Act. Liability arises, primarily, when an entity knowingly submits, or causes another to submit, a false claim for reimbursement to the federal government. The False Claims Act has been used to assert liability on the basis of inadequate care, kickbacks and other improper referrals, improperly reported government pricing metrics such as Best Price or Average Manufacturer Price, improper use of Medicare numbers when detailing the provider of services, improper promotion of off-label uses (i.e., uses not expressly approved by FDA in a drug's label), and allegations as to misrepresentations with respect to the services rendered. Our future activities relating to the reporting of discount and rebate information and other information affecting federal, provincial, state and third party reimbursement of our products, and the sale and marketing of our products and our service arrangements or data purchases, among other activities, may be subject to scrutiny under these laws. We are unable to predict whether we would be subject to actions under the False Claims Act or a similar state law, or the impact of such actions. However, the cost of defending such claims, as well as any sanctions imposed, could adversely affect our financial performance. Also, the Health Insurance Portability and Accountability Act of 1996, or HIPAA, created several new federal crimes, including healthcare fraud, and false statements relating to healthcare matters. The healthcare fraud statute prohibits knowingly and willfully executing a scheme to defraud any healthcare benefit program, including private third-party payors. The false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services.

In addition, we may be subject to, or our marketing activities may be limited by, data privacy and security regulation by both the federal government and the states in which we conduct our business. For example, HIPAA and its implementing regulations established uniform federal standards for certain "covered entities" (healthcare providers, health plans and healthcare clearinghouses) governing the conduct of certain electronic healthcare transactions and protecting the security and privacy of protected health information. The American Recovery and Reinvestment Act of 2009, commonly referred to as the economic stimulus package, included expansion of HIPAA's privacy and security standards called the Health Information Technology for Economic and Clinical Health Act, or HITECH, which became effective on February 17, 2010. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable to "business associates"—independent contractors or agents of covered entities that receive or obtain protected health information in connection with providing a service for or on behalf of a covered entity. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney's fees and costs associated with pursuing federal civil actions.

There are also an increasing number of state "sunshine" laws that require manufacturers to make reports to states on pricing and marketing information. Several states have enacted legislation requiring pharmaceutical companies to, among other things, establish marketing compliance programs, file periodic reports with the state, make periodic public disclosures on sales, marketing, pricing, clinical trials and other activities, and/or register their sales representatives, as well as to prohibit pharmacies and other healthcare entities from providing certain physician prescribing data to pharmaceutical companies for use in sales and marketing, and to prohibit certain other sales and marketing practices. In addition, beginning in 2013, a similar federal requirement will require manufacturers to track and report to the federal government certain payments and other transfers of value made to physicians and other healthcare professionals and teaching hospitals and ownership or investment interests held by physicians and their immediate family members. The federal government will disclose the reported information on a publicly available website beginning in 2014. These laws may affect our sales, marketing, and other promotional activities by imposing administrative and compliance burdens on us. If we fail to track and report as required by these laws or otherwise comply with these laws, we could be subject to the penalty provisions of the pertinent state and federal authorities.

Because of the breadth of these laws and the narrowness of available statutory and regulatory exemptions, it is possible that some of our business activities could be subject to challenge under one or more of such laws. If our operations are found to be in violation of any of the federal and state laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including criminal and significant civil monetary penalties, damages, fines, imprisonment, exclusion from participation in government healthcare programs,

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injunctions, recall or seizure of products, total or partial suspension of production, denial or withdrawal of pre-marketing product approvals, private “qui tam” actions brought by individual whistleblowers in the name of the government or refusal to allow us to enter into supply contracts, including government contracts, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. To the extent that any of our products are sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-approval requirements, including safety surveillance, anti-fraud and abuse laws, and implementation of corporate compliance programs and reporting of payments or transfers of value to healthcare professionals.

Legal Proceedings

From time to time, we may become involved in legal proceedings or be subject to claims arising in the ordinary course of our business. We are not presently a party to any legal proceedings that, in the opinion of our management would reasonably be expected to have a material adverse effect on our business, financial condition, operating results or cash flows if determined adversely to us. Regardless of the outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

Facilities

Our headquarters are located in Burnaby, British Columbia, where we occupy approximately 30,600 square feet of office and laboratory space. The term of the lease expires in March 2022. We currently pay an aggregate of approximately \$75,932 per month in base rent, property tax, common area maintenance fees and management fees, and the landlord holds a security deposit equal to approximately \$87,382. We believe that our existing facilities are adequate to meet our business requirements for the near-term and that additional space will be available on commercially reasonable terms, if required.

Environmental Matters

Our operations require the use of hazardous materials (including biological materials) which subject us to a variety of federal, provincial and local environmental and safety laws and regulations. Some of the regulations under the current regulatory structure provide for strict liability, holding a party potentially liable without regard to fault or negligence. We could be held liable for damages and fines as a result of our, or others', business operations should contamination of the environment or individual exposure to hazardous substances occur. We cannot predict how changes in laws or development of new regulations will affect our business operations or the cost of compliance.

Employees

As of June 30, 2013, we had 71 employees, consisting of 65 full-time employees. Of our employees, 52 were primarily engaged in research and development activities, 23 of whom had an M.D. (or equivalent) or Ph.D. degree. None of our employees is represented by a labor union. We have not experienced any work stoppages, and we consider our relations with our employees to be good.

MANAGEMENT**Executive Officers and Directors**

The following table sets forth information regarding our current executive officers and directors, and their ages as of June 30, 2013:

| <u>NAME</u> | <u>AGE</u> | <u>POSITION(S)</u> |
|---|------------|---|
| Executive Officers | | |
| Simon Pimstone, M.B. ChB., Ph.D. | 45 | President, Chief Executive Officer and Director |
| Gary Bridger, Ph.D. | 50 | Executive Vice President of Research and Development |
| Karen G. Corraini, J.D. | 58 | General Counsel and Corporate Secretary |
| Y. Paul Goldberg, M.B. ChB., Ph.D. | 53 | Vice President of Clinical Development |
| Robin Sherrington, Ph.D. | 52 | Senior Vice President of Business & Corporate Development |
| Non-Employee Directors | | |
| Michael Tarnow ⁽¹⁾⁽²⁾⁽³⁾ | 69 | Chair of the Board |
| Mohammad Azab, M.B. ChB. ⁽²⁾⁽³⁾ | 57 | Director |
| Johnston L. Evans ⁽¹⁾ | 65 | Director |
| Michael Hayden, M.B. ChB., Ph.D. | 61 | Director |
| Frank Holler ⁽¹⁾ | 56 | Director |
| Gary Patou, M.B. B.S., M.D. ⁽²⁾⁽³⁾ | 54 | Director |
| Evan A. Stein, M.B. ChB., Ph.D. | 66 | Director |

⁽¹⁾ Member of the audit committee.

⁽²⁾ Member of the compensation committee.

⁽³⁾ Member of the nominating and corporate governance committee.

Executive Officers

Simon Pimstone, M.B. ChB., Ph.D., FRCPC co-founded our company, has served as our President and Chief Executive Officer since January 2003, and has served on our board of directors, or Board, since our inception in November 1996. Prior to founding our company, Dr. Pimstone trained as a clinical research fellow with the Department of Medical Genetics at the University of British Columbia from 1994 until 1998, where he was responsible for managing a provincial lipid clinic outreach program providing lipid management to at risk patients in the province of British Columbia. Dr. Pimstone holds an M.B. ChB. from the University of Cape Town, a FRCPC. from the University of British Columbia, and a Ph.D. from the University of Amsterdam in cardiovascular genetics. Dr. Pimstone is a member and former chair of the board of directors of LifeSciences British Columbia, a non-profit industry association that supports the life science community, and is a member of the board of directors of Providence Health Care, a non-profit organization that provides health care services to British Columbia patients and residents. Dr. Pimstone also serves as director of the private biotechnology companies Enject Therapeutics Inc., Eupraxia Pharmaceuticals Inc. and Indel Therapeutics Inc. Our Board believes that Dr. Pimstone possesses specific attributes that qualify him to serve as a director, including his extensive executive leadership experience, many years of service on our Board and as our Chief Executive Officer and extensive knowledge of our company and industry.

Gary Bridger, Ph.D. has served as our Executive Vice President of Research and Development since January 2013. Prior to joining us, Dr. Bridger was a Venture Partner at Venture West Capital Management, a venture capital firm that invests in early stage technology companies, from June 2010 until June 2012. From January 2008 to May 2010, Dr. Bridger served as a consultant to various biotechnology companies. Prior to Venture West Capital Management, Dr. Bridger worked at Genzyme Corporation (subsequently acquired by Sanofi, S.A.), a global pharmaceutical company focused on rare diseases and multiple sclerosis, from November 2006 until December 2007. In this position he assisted with development, regulatory and commercial strategies for Mozobil. Prior to Genzyme, Dr. Bridger co-founded AnorMED Inc. a biopharmaceutical company, in June 1996 and was its Chief Scientific Officer from 2000 until its acquisition by Genzyme in November 2006. At AnorMED, he was responsible for research, development, and clinical programs. Dr. Bridger currently serves on the Scientific Advisory Board of

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Alectos Therapeutics Inc., a private company that discovers and develops novel small-molecule therapeutics. Dr. Bridger received his Ph.D. in Organic Chemistry from the University of Manchester Institute of Science and Technology (United Kingdom) and completed a post-doctoral fellowship at Boston College.

Karen G. Corraini, J.D. has served as our General Counsel and Corporate Secretary since February 2003, and has held various positions since joining us in June 2001. Prior to joining us, Ms. Corraini practiced law at McCarthy Tétrault LLP from January 2000 until June 2001. From 1996 to 1999, Ms. Corraini was Managing Director and Chief Executive Officer of the Canadian Bacterial Diseases Network, an organization focused on the discovery and commercialization of microbiology-related research from a Canada-wide consortium of researchers. Prior to that, Ms. Corraini practiced law at the Canadian law firms of Goldsmith and Harshorne and Ferguson Gifford. Ms. Corraini is a member of the board of the Cystic Fibrosis Technology Initiative and of the British Columbia Chapter of the Association of Corporate Counsel. She received her Medical Laboratory Technology Degree from SAIT and Foothills Hospital, and a J.D. from the University of Victoria.

Y. Paul Goldberg, M.B. ChB., Ph.D., FRCPC has served as our Vice President of Clinical Development since February 2010, as our Senior Director, Clinical Biology and Target Discovery from 2002 until February 2010, as our Senior Director, Scientific Programs from 2001 until 2002, and as our Director and Senior Scientist from 2000 until 2002. Since 2000 Dr. Goldberg has also worked at the University of British Columbia in the Department of Medical Genetics as a Medical Geneticist, Clinical Assistant Professor. Dr. Goldberg received his M.B. ChB. and Ph.D. from the University of Cape Town, and he obtained his specialization in clinical genetics, FRCPC from the University of British Columbia.

Robin Sherrington, Ph.D. has served as our Senior Vice President of Business & Corporate Development since February 2012, as our Vice President of Business & Corporate Development from January 2010 to February 2012, and has held various Senior Director positions in business development and other departments since joining us in March 2001. Prior to joining us, Dr. Sherrington worked at Pfizer, Inc., a global pharmaceutical company, as a neuroscientist from 1999 to 2001. Dr. Sherrington also previously served as Director of Neuroscience, from 1996 to 1999, at the biotechnology companies Axyx Pharmaceuticals and Sequana Therapeutics. Prior to 1996 Dr. Sherrington was a post-doctoral fellow at University of Toronto, received his Ph.D. from the University College London, and his B.Sc. with honors from University of Reading.

Directors

Michael Tarnow has served as chair of our Board since May 1999. Since 1995, Mr. Tarnow has been an advisor to and member of the boards of directors of private and public healthcare and biotechnology companies in the U.S., Canada and Europe, including Axcan Pharma, Creative Biomolecules, Inc, Caprion Pharmaceuticals Inc. and MediGene AG. He served as Chairman of EntreMed, Inc., or EntreMed, from February 2003 to February 2009, and served as Executive Chairman of EntreMed from February 2009 to January 2012. Mr. Tarnow holds a B.B.A. in Business Administration from Wayne State University and a J.D. from the University of Illinois, College of Law. Our Board believes that Mr. Tarnow is qualified to serve on our Board because of his senior management experience in the biopharmaceutical industry and his knowledge and perspective on our business.

Mohammad Azab, M.B. ChB. has served as a member of our Board since October 2003. Dr. Azab has been the Chief Medical Officer of Astex Pharmaceuticals, Inc., a pharmaceutical company focused on the discovery and development of drugs in oncology and other areas, since July 2009. Prior to joining Astex, he was with Intradigm Corporation, a developer of RNA interference (RNAi) therapeutics acquired by Silence Therapeutics PLC, where he served as President and Chief Executive Officer from July 2006 until November 2008 and as a director from July 2006 until January 2010. Prior to Intradigm Corporation, he served as Executive Vice President, of Research and Development and Chief Medical Officer for QLT Inc., and held several senior positions at AstraZeneca, and Sanofi. Dr. Azab holds an M.B.A. from the Richard Ivey School of Business, University of Western Ontario, and an M.B. ChB. from Cairo University. He received post-graduate training and degrees in oncology research from the University of Paris-Sud and biostatistics from the University of Pierre et Marie Curie in Paris, France. Our Board believes Dr. Azab is qualified to serve on the board of directors because of his extensive senior management experience in our industry.

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Johnston L. Evans, has served as a member of our Board since March 2008. Mr. Evans has been a General Partner at Invesco Private Capital, Inc., a venture capital firm, and its predecessor since 1995. He has served as a member of the board of directors of E2open, Inc., a publicly-traded software solutions provider, since June 2005. Mr. Evans holds a B.A. in Political Science from Boston University. Our Board believes that Mr. Evans' qualifications to serve on our Board include his extensive experience as a venture capital investor and a director of a public company.

Michael Hayden, M.B. ChB., Ph.D., FRCPC has served as a member of our Board since November 1996. Dr. Hayden previously served as our Chief Scientific Officer from January 1997 to September 2012. Since September 2012, Dr. Hayden has been Chief Scientific Officer and President of Global Research & Development of Teva Pharmaceutical Industries Ltd. Dr. Hayden has also been a professor of Medical Genetics at the University of British Columbia since August 1983 and Director of the Center for Molecular Medicine and Therapeutics since 1992. He is presently the Program Director of the Translational Laboratory in Genetic Medicine in Singapore. He received his Ph.D. and M.B. ChB. from the University of Cape Town and completed his post-doctoral fellowship and training at Harvard Medical School. Our Board believes Dr. Hayden is qualified to serve our Board because of his scientific background and his extensive knowledge and perspective on our company.

Frank Holler, has served as a member of our Board since February 1999 and previously served as our President and Chief Executive Officer from February 1999 until June 2003. Since March 2004, Mr. Holler has been the Chief Executive Officer at BC Advantage Funds (VCC) Ltd., a venture capital firm that invests in emerging life science, cleantech and information technology companies, where he served as Chairman since January 2010. Mr. Holler also served as President and Chief Executive Officer of ID Biomedical Corporation, a publicly-traded biotechnology company, from 1991 to 1998 and was a founding director of Angiotech Pharmaceuticals, a publicly-traded biotechnology company, from 1992 to 1997. Mr. Holler holds a B.A. in Economics and an M.B.A. from the University of British Columbia. Our Board believes Mr. Holler is qualified to serve on our Board because of his experience as a biotechnology entrepreneur and venture capitalist and his knowledge and perspective on our company.

Gary Patou, M.B. B.S., M.D. has served as a member of our Board since January 2004. Dr. Patou has been a managing director of MPM Capital, a venture capital fund, since May 2005. He has served as Chief Medical Officer of Pacira Pharmaceuticals, Inc., a specialty pharmaceutical company, since January 2009. Dr. Patou has previously served in various positions at private pharmaceutical companies, including as Chief Medical Officer for Peplin, Ltd. from June 2006 to April 2007, Chief Medical Officer at Cerimon Pharmaceuticals, Inc., from June 2005 to June 2006, and Chief Medical Officer at Oscient Pharmaceuticals, Inc. from February 2004 to April 2005. Dr. Patou has held a number of academic appointments at University College & Middlesex School of Medicine in London and holds an M.B. B.S. from University College Hospital, London and a B. Sc. in immunology from University College London. Our Board believes that Dr. Patou's qualifications to serve on our Board include his scientific background and extensive senior management experience in our industry.

Evan A. Stein, M.B. ChB., Ph.D., FRCPC, FCAP has served as a member of our board of directors since June 2011 and from June 2006 to June 2009. Dr. Stein previously served as Chief Scientific Officer and a member of the board of directors of Medpace LLC, a contract research organization servicing the pharmaceutical industry from January 2006 to December 2012. Medpace LLC was acquired by CCMP, a private equity firm, in 2011. Dr. Stein holds an M.B. ChB. and Ph.D. from the University of Witwatersrand Medical School in Johannesburg, South Africa. We believe that Dr. Stein's qualifications to serve on the board of directors include his senior management experience in our industry.

Board Composition and Risk Oversight

The board of directors is currently composed of eight members. _____ of our directors are independent within the meaning of the independent director guidelines of The NASDAQ Global Market, or NASDAQ. Dr. Stein and Mr. Evans were elected to the board of directors pursuant a nomination process set forth in a shareholders agreement that will terminate upon the completion of this offering. The articles of continuance and by-laws to be in effect upon the completion of this offering provide that the number of directors shall be at least one up to a maximum of 10 and will be fixed from time to time by resolution of the board of directors. Each of our directors is subject to election at each annual meeting of our shareholders. There are no family relationships among any of the directors or executive officers.

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During our 2012 fiscal year, the board of directors met five times.

The board of directors has an active role, as a whole and also at the committee level, in overseeing the management of our risks. The board of directors is responsible for general oversight of risks and regular review of information regarding our risks, including credit risks, liquidity risks and operational risks. The compensation committee is responsible for overseeing the management of risks relating to our executive compensation plans and arrangements. The audit committee is responsible for overseeing the management of risks relating to accounting matters, financial reporting and potential conflicts of interest. The nominating and corporate governance committee is responsible for overseeing the management of risks associated with the independence of the board of directors. While each committee is responsible for evaluating certain risks and overseeing the management of such risks, the entire board of directors is regularly informed through discussions with committee members about such risks. The board of directors believes its administration of its risk oversight function has not affected the board of directors' leadership structure.

Director Independence

Upon the completion of this offering, we anticipate that our common shares will be listed on NASDAQ. Under the NASDAQ rules, independent directors must comprise a majority of a listed company's board of directors within a specified period of the completion of this offering. In addition, NASDAQ rules require that, subject to specified exceptions, each member of a listed company's audit, compensation and nominating and governance committees be independent. Audit committee members must also satisfy the independence criteria set forth in Rule 10A-3 under the Securities Exchange Act of 1934, as amended. Under NASDAQ rules, a director will only qualify as an "independent director" if, in the opinion of that company's board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director.

To be considered independent for purposes of Rule 10A-3, a member of an audit committee of a listed company may not, other than in his capacity as a member of the audit committee, the board of directors or any other board committee: (1) accept, directly or indirectly, any consulting, advisory, or other compensatory fee from the listed company or any of its subsidiaries; or (2) be an affiliated person of the listed company or any of its subsidiaries.

In 2013, the board of directors undertook a review of its composition, the composition of its committees and the independence of directors and considered whether any director has a material relationship with us that could compromise his ability to exercise independent judgment in carrying out his responsibilities. Based upon information requested from and provided by each director concerning his background, employment and affiliations, including family relationships, the board of directors has determined that none of _____, representing _____ of our eight directors, has a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director and that each of these directors is "independent" as that term is defined under NASDAQ rules. The board of directors also determined that _____ (chair), _____ and _____, who comprise our audit committee, _____ (chair) and _____ and _____ who comprise our compensation committee, and _____ and _____ who comprise our nominating and corporate governance committee, satisfy the independence standards for those committees established by applicable SEC rules and NASDAQ rules.

In making this determination, the board of directors considered the relationships that each non-employee director has with us and all other facts and circumstances the board of directors deemed relevant in determining their independence, including the beneficial ownership of our shares by each non-employee director.

Board Committees

The board of directors has an audit committee, a compensation committee and a nominating and corporate governance committee, each of which has the composition and the responsibilities described below.

Audit Committee

Our audit committee oversees our corporate accounting and financial reporting process. Among other matters, the audit committee:

- approves the hiring, discharging and compensation of our independent auditors;
- oversees the work of our independent auditors;
- approves engagements of the independent auditors to render any audit or permissible non-audit services;
- reviews on a periodic basis, or as appropriate, our investment policy and recommends to our Board any changes to such policy;
- reviews company compliance with our investment policy;
- reviews the qualifications, independence and performance of the independent auditors;
- reviews financial statements, critical accounting policies and estimates;
- reviews the adequacy and effectiveness of our internal controls; and
- reviews and discusses with management and the independent auditors the results of our annual audit, our quarterly financial statements and our publicly filed reports.

The current members of our audit committee are _____ and _____ serves as the chair of the committee. All members of our audit committee meet the requirements for financial literacy under the applicable rules and regulations of the SEC and NASDAQ. Our audit committee chair, _____, is our audit committee financial expert, as that term is defined under the SEC rules implementing Section 407 of the Sarbanes-Oxley Act of 2002, and possesses financial sophistication, as defined under NASDAQ rules. Under the rules of the SEC and NASDAQ, members of the audit committee must also meet heightened independence standards. Our board has determined that each of _____ and _____ meet these heightened independence standards. Prior to the completion of this offering, the audit committee will operate under a written charter that satisfies the applicable standards of the SEC and NASDAQ.

During 2012, our audit committee met four times.

Compensation Committee

Our compensation committee oversees our compensation policies, plans and benefits programs. Among other matters, the compensation committee:

- reviews and recommends policies relating to compensation and benefits of our directors, officers and employees;
- reviews and approves corporate goals and objectives relevant to compensation of our chief executive officer and other senior officers;
- evaluates the performance of our officers in light of established goals and objectives;
- recommends compensation of our officers based on its evaluations; and
- administers the issuance of stock options and other awards under our stock plans.

The current members of our compensation committee are _____ and _____ serves as the chair of the committee. Each of the members of our compensation committee is an independent, outside and non-employee director under the applicable rules and regulations of the SEC, NASDAQ, the Internal Revenue Code of 1986, as amended, and the guidelines contained in National Instrument 58-201—Corporate Governance Guidelines, relating to compensation committee independence. Prior to the completion of this offering, the compensation committee will operate under a written charter that satisfies the applicable standards of the SEC and NASDAQ.

During 2012, our compensation committee met twice.

Nominating and Corporate Governance Committee

Our nominating and corporate governance committee oversees and assists the board of directors in reviewing and recommending nominees for election as directors. Among other matters, the nominating and corporate governance committee:

- evaluates and makes recommendations regarding the organization and governance of the board of directors and its committees;

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- assesses the performance of members of the board of directors and makes recommendations regarding committee and chair assignments;
- recommends desired qualifications for board of directors membership and conducts searches for potential members of the board of directors; and
- reviews and makes recommendations with regard to our corporate governance guidelines.

The current members of our nominating and corporate governance committee are _____, _____ and _____. Currently, no chair of the committee has been designated. Each of the members of our nominating and corporate governance committee is an independent director under the applicable rules and regulations of the SEC and NASDAQ relating to nominating and corporate governance committee independence. Prior to the completion of this offering, the nominating and corporate governance committee will operate under a written charter that satisfies the applicable standards of the SEC and NASDAQ.

During 2012, our nominating and corporate governance committee did not meet.

The board of directors may from time to time establish other committees.

Director Compensation

Pre-IPO Director Compensation Policies

In January 2012, the board of directors established a policy, or the 2012 director compensation policy, with respect to the compensation of directors, effective January 1, 2012.

For the purposes of the director compensation policy, the board of directors classified each director into one of the three following categories: (1) a "management director" is a director who is also an officer, or employed by us in a management role; (2) a "non-management director" is a director who is not an officer, and not employed by us in a management role; and (3) the chair of the board of directors.

Our 2012 director compensation policy provides that, effective January 1, 2012, we shall pay a combination of cash compensation and equity compensation to our non-management directors and the chair of the board of directors.

Our 2012 director compensation policy further provides that each of our non-management directors receives:

- (1) \$2,500 for each regular quarterly meeting of the full board of directors that a director attends for the full meeting either in person, or in part in person and in part by teleconference or videoconference, or \$1,250 for each regular quarterly meeting that a director attends for the full meeting by teleconference or videoconference, with such amounts payable within 30 days following the date of each board meeting;
- (2) upon commencement of service as our director, an option to purchase a number of our common shares determined by our board of directors up to a maximum of 25,000 shares; and
- (3) on an annual basis, to be granted on or about January 1 of each year, options as determined by our board of directors as follows:
 - (i) up to a maximum of 5,000 options for service as a director,
 - (ii) up to a maximum of 5,000 additional options for service on our audit committee and/or our compensation committee (or 10,000 additional options for service on both such committees),
 - (iii) up to a maximum of 5,000 additional options for service as chair of our audit committee or as chair of our compensation committee (or 10,000 additional options for service as chair on both such committees),
 - (iv) up to a maximum of 2,000 additional options for service as a member of our nominating and corporate governance committee and
 - (v) up to a maximum of 2,000 additional options for service as chair of our nominating and corporate governance committee.

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Our 2012 director compensation policy further provides that, effective January 1, 2012, the chair of our board of directors receives:

- (1) \$3,000 for each regular quarterly meeting of the full board of directors that the chair attends for the full meeting, in lieu of the amount the chair may otherwise receive for attendance as a non-management director, with such amount payable within 30 days following the date of each board meeting; and
- (2) upon commencement of service, or agreement to continue service as the chair of our board of directors for a six-month term, an option to purchase a number of our common shares determined by our board of directors up to a maximum of 10,000 shares, granted on or about January 1 and July 1.

Our 2012 director compensation policy further provides that in the event that a new chair is appointed before the completion of any six-month period noted above, our board of directors may, at its discretion, grant up to a maximum of 10,000 options to such newly-appointed chair on the date of appointment.

In January 2013, the board of directors amended our director compensation policy by increasing the cash compensation component while maintaining the stock option component of the 2012 director compensation policy.

Our revised director compensation policy, or 2013 director compensation policy, provides that, effective April 1, 2013, each of our non-management directors receives \$5,000 for each regular quarterly meeting of the full board of directors that a director attends for the full meeting in person, or \$2,000 for each regular quarterly meeting that a director attends for the full meeting either by teleconference or videoconference or in part in person and in part by teleconference or videoconference, with such amounts payable within 30 days following the date of each board meeting.

Our 2013 director compensation policy further provides that, effective January 1, 2013, the chair of our board of directors receives \$6,000 for each regular quarterly meeting of the full board of directors that the chair attends for the full meeting, in lieu of the amount the chair may otherwise receive for attendance as a non-management director, with such amount payable within 30 days following the date of each board meeting.

All of the above options will be granted under our then effective equity plan, and will vest pursuant to a three-year vesting schedule, with one-third vesting on the first year anniversary of the grant date, and the remaining two-thirds vesting monthly over the course of the next two years, in equal amounts, on the last day of each month subject to the recipient's continued service through each vesting date and the terms of our then effective equity plan as described in the section entitled "Management—Employee Benefit and Stock Plans."

The following table sets forth information concerning the compensation paid or accrued for services rendered to us by members of the board of directors for the year ended December 31, 2012. Dr. Pimstone, our president and chief executive officer, did not receive any additional compensation for service on the board of directors. Compensation paid or accrued for services rendered to us by Dr. Pimstone in his role as chief executive officer is included in our disclosures related to executive compensation in the section of this prospectus captioned "Executive Compensation."

| Name | FEES EARNED OR PAID IN CASH ⁽¹⁾ (\$) | OPTION AWARDS ⁽²⁾⁽³⁾ (\$) | ALL OTHER COMPENSATION ⁽¹⁾ (\$) | TOTAL ⁽¹⁾ (\$) |
|-------------------------------------|---|--|--|------------------------------|
| Mohammad Azab ⁽⁴⁾ | 10,000 | 7,065 | — | 17,065 |
| Johnston L. Evans ⁽⁴⁾ | 10,000 | — | — | 10,000 |
| Michael R. Hayden ⁽⁴⁾⁽⁵⁾ | 1,250 ⁽⁵⁾ | 35,889 ⁽⁷⁾ | 307,264 ⁽⁸⁾ | 344,403 |
| Frank A. Holler ⁽⁴⁾ | 10,000 | 18,841 | 25,000 ⁽⁹⁾ | 53,841 |
| Gary Patou ⁽⁴⁾ | 6,250 | 4,710 | — | 10,960 |
| Evan A. Stein ⁽⁴⁾ | 8,750 | 2,355 | — | 11,105 |
| Michael M. Tarnow ⁽⁴⁾⁽⁶⁾ | 12,000 | 18,806 | 36,789 ⁽¹⁰⁾ | 67,595 |

⁽¹⁾ Except as otherwise indicated, compensation amounts that were paid in Canadian dollars have been converted to U.S. dollars for purposes of the table. The U.S. dollar per Canadian dollar exchange rate used for such conversion is 1.0006.

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- (2) Represents the aggregate grant date fair value of stock option awards granted in 2012. These amounts have been computed in accordance with Financial Accounting Standards Board, or FASB, Accounting Standards Codification, or ASC, Topic 718, using the Black-Scholes option pricing model without regard to estimated forfeitures. For a discussion of valuation assumptions, see the notes to our financial statements included elsewhere in this prospectus. The exercise price for stock options was denominated in Canadian dollars on the date of grant. The amounts reflected in this column were converted to U.S. dollars using the U.S. dollar per Canadian dollar exchange rate on January 1, 2012 and July 1, 2012, the dates of grant, which is 0.9833 and 0.9813, respectively.
- (3) As of December 31, 2012, the below listed directors beneficially held outstanding options to purchase the number of common shares as follows: Dr. Azab (240,000 shares); Mr. Evans (zero shares); Dr. Hayden (550,000 shares, of which 252,500 shares are held by Dr. Hayden and 297,500 shares are held by Genworks Inc., Dr. Hayden's consulting company); Mr. Holler (502,000 shares); Dr. Patou (222,000 shares); Dr. Stein (40,000 shares); and Mr. Tarnow (427,000 shares).
- (4) Non-Management Director.
- (5) Dr. Hayden served as our Chief Scientific Officer until September 2012, and, accordingly, during that time period he did not receive compensation for attendance at meetings of the board of directors as a Non-Management Director.
- (6) Chair of Board of Directors.
- (7) Consists of (i) \$11,963 in stock option awards to Dr. Hayden and (ii) \$23,926 in stock option awards to Genworks Inc., Dr. Hayden's consulting company.
- (8) Represents consulting fees paid to Genworks Inc., Dr. Hayden's consulting company, for services rendered through August 31 during the year ended December 31, 2012.
- (9) Represents a \$25,000 bonus which was paid on a discretionary basis and was related to the successful negotiation and entry into our collaboration with Teva.
- (10) Consists of (i) a \$25,000 bonus which was paid on a discretionary basis and was related to the successful negotiation and entry into our collaboration with Teva and (ii) \$11,789 of reimbursable expenses in connection with attendance at meetings of the board of directors, including airfare, lodging, ground transportation, and meals.

Consulting Fees Paid to Genworks, Inc.

For the year ended December 31, 2012, we paid \$307,264 in consulting fees to Genworks Inc., or Genworks. Genworks is controlled by Dr. Michael Hayden, one of our directors. These consulting fees were paid to Genworks in consideration of certain scientific consulting services provided by Dr. Hayden during this period, as more fully described in the section entitled "Certain Relationships and Related Party Transactions—Consulting Services Provided by Genworks, Inc."

Discretionary Bonus

For 2012, Messrs. Holler and Tarnow were awarded a discretionary bonus by our board of directors in connection with their involvement with the successful negotiation and execution of our collaborative agreement with Teva.

For further information regarding the equity compensation of our directors, see the section "Executive Compensation—Employee Benefit and Stock Plans—Amended and Restated Stock Option Plan."

Post-IPO Director Compensation Policy

In August 2013, the board of directors approved a policy, or the post-IPO director compensation policy, with respect to the compensation of directors that will become effective following our initial public offering and replace our 2013 director compensation policy. For purposes of the policy, the board of directors maintained the categories of management director, non-management director and chair of the board of directors.

Non-management directors and the chair of the board of directors will receive compensation in the form of equity and cash under the post-IPO director compensation policy, as described below.

Equity Compensation

Upon joining our board of directors, each non-management director (including the chair of our board of directors) will receive an option to purchase 25,000 of our common shares. At the beginning of each fiscal year starting with 2014, each non-management director (including the chair of our board of directors) will be granted an option to purchase 15,000 of our common shares.

In addition to the annual grant, the chair of our board of directors will receive an option to purchase 5,000 of our common shares. This additional annual grant will be granted at the same time as and have the same terms and conditions as the annual grant made to each of our non-management directors.

The exercise price per share of the each of the above grants will be the fair market value of one of our common shares (determined pursuant to our then-effective equity plan) on the date of the grant.

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All of the above options granted to our non-management directors (including the chair of our board of directors) will be under our then-effective equity plan. The shares underlying the above initial and annual grants will vest as to one-third of the total shares subject to such award on the one year anniversary of the grant date, one-third of the total shares on the two year anniversary of the grant date and the balance of the total shares on the three year anniversary of the grant date. The shares underlying the additional annual grant made to the chair of our board of directors will vest as to all of the shares subject to such award on the one year anniversary of the grant date.

The vesting of each grant described above will be subject to the recipient's continued service as a director through each vesting date and the other terms and conditions of our then-effective equity plan and the applicable option agreement with that director.

Cash Compensation

For each fiscal year, each non-management director (including the chair of the board of directors) will receive an annual cash retainer of \$35,000 for serving on the board of directors. In addition to the annual retainer, the chair of the board of directors will receive an additional annual cash retainer of \$25,000.

The chairs of the three standing committees of the board of directors will be entitled to the following cash retainers for each fiscal year as follows:

| BOARD COMMITTEE | CHAIR RETAINER |
|---|---------------------------|
| Audit Committee | \$ 15,000 |
| Compensation Committee | \$ 10,000 |
| Nominating and Corporate Governance Committee | \$ 7,250 |

The non-chair members of the three standing committees of the board of directors will be entitled to the following cash retainers for each fiscal year as follows:

| BOARD COMMITTEE | MEMBER RETAINER |
|---|----------------------------|
| Audit Committee | \$ 7,500 |
| Compensation Committee | \$ 5,000 |
| Nominating and Corporate Governance Committee | \$ 3,750 |

All cash payments will be payable in four equal installments on the date of our annual meeting, and on the last day of the third month, sixth month and ninth month thereafter, during which such individual served as a director or chair of the board of directors or of the applicable committee (such payments to be prorated for service during a portion of such quarter).

All directors will be reimbursed for standard travel expenses incurred in their capacities as directors and/or committee members.

Compensation Committee Interlocks and Insider Participation

During the fiscal year ended December 31, 2012, Drs. Azab and Patou and Mr. Tarnow served as members of the compensation committee. No such person is currently, or has been at any time, one of our officers or employees. None of our executive officers currently serves, or has served during the last completed three fiscal years, as a member of the board of directors or compensation committee of any other entity that has or had one or more executive officers serving as a member of our board of directors or compensation committee.

Code of Business Conduct and Ethics

We intend to adopt a written code of business conduct and ethics that applies to all of our employees, officers and directors, including those officers responsible for financial reporting. Following the completion of this offering, the

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code of business conduct and ethics will be available on the investor section of our website at www.xenon-pharma.com. We intend to disclose on our website any amendment to, or waiver of, any provision of our code of business conduct and ethics applicable to our directors and executive officers required to be disclosed under the rules of the SEC and NASDAQ.

Indemnification Agreements and Directors' and Officers' Liability Insurance

We will enter into indemnification agreements with each of our directors and officers. For further information regarding the indemnification agreements with each of our directors and officers, see the section titled "Certain Relationships and Related Party Transactions—Indemnification Agreements and Directors' and Officers' Liability Insurance."

Under the Canada Business Corporations Act, or CBCA, we may indemnify our current or former directors or officers or any other individuals who act or have acted at our request as a director or officer, or an individual acting in a similar capacity, of another entity, against all costs, charges, and expenses, including an amount paid to settle an action or satisfy a judgment, reasonably incurred by the individual in respect of any civil, criminal, administrative, investigative or other proceeding in which the individual is involved because of his or her association with us or the other entity. The CBCA also provides that we may advance moneys to a director, officer or other individual for costs, charges and expenses reasonably incurred in connection with such a proceeding. The individual shall repay the moneys to us if indemnification of the individual is ultimately prohibited under the CBCA, as described below.

Indemnification is prohibited under the CBCA unless the individual:

- acted honestly and in good faith with a view to our best interests, or the best interests of the other entity for which the individual acted as director or officer or in a similar capacity at our request;
- in the case of a criminal or administrative action or proceeding that is enforced by a monetary penalty, the individual had reasonable grounds for believing that his or her conduct was lawful; and
- was not judged by the court or other competent authority to have committed any fault or omitted to do anything that the individual ought to have done.

Our by-laws require us to indemnify each of our directors, officers, former directors or officers or persons who act or acted at our request as a director or officer of a body corporate of which we are or were a direct or indirect shareholder or creditor except in respect of an action by or on behalf of us or such body corporate to procure a judgment in its favor in certain situations. We will indemnify such individual against all costs, charges and expenses, including an amount paid to settle an action or proceeding to which the individual is made a party by reason of being or having been a director or officer of us or such body corporate. Our by-laws also require us to, with the approval of a court, indemnify such individual referred to above, in respect of an action by or on behalf of us or such body corporate to procure a judgment in its favor, to which the individual is made a party by reason of being or having been a director or an officer of us or such body corporate, against all costs, charges and expenses reasonably incurred by him in connection with such action. However, we shall not indemnify such individual if the individual did not act honestly and in good faith with a view to our best interests or, in the case of a criminal or administrative action or proceeding that is enforced by a monetary penalty, the individual did not have reasonable grounds for believing that his or her conduct was lawful.

Our by-laws authorize us, with the approval of our board of directors, to purchase and maintain insurance for the benefit of each of our current or former directors or officers and each person who acts or acted at our request as a director or officer of another entity, against any liability incurred by him or her.

EXECUTIVE COMPENSATION

2012 Summary Compensation Table

The following table provides information regarding the compensation of our named executive officers during the year ended December 31, 2012.

| Name and Principal Position | YEAR | SALARY ⁽¹⁾ | BONUS ⁽¹⁾⁽²⁾ | OPTION AWARDS ⁽³⁾ | NON-EQUITY INCENTIVE PLAN ⁽¹⁾⁽⁴⁾ | ALL OTHER COMPENSATION ⁽¹⁾ | TOTAL ⁽¹⁾ |
|--|------|-----------------------|-------------------------|------------------------------|---|---------------------------------------|----------------------|
| Simon N. Pimstone President and Chief Executive Officer | 2012 | \$366,371 | \$100,060 | \$ 71,778 | \$183,185 | \$18,519 ⁽⁵⁾ | \$739,913 |
| Y. Paul Goldberg Vice President, Clinical Development | 2012 | 278,365 | 25,015 | 9,495 | 83,507 | 14,072 ⁽⁶⁾ | 410,454 |
| Tarek S. Mansour former Executive Vice President, Research & Development ⁽⁸⁾ | 2012 | 279,531 | — | 46,355 | 111,813 | 10,275 ⁽⁷⁾ | 447,974 |

- ⁽¹⁾ Except as otherwise indicated, compensation amounts were paid in Canadian dollars and have been converted to U.S. dollars for purposes of the table. The U.S. dollar per Canadian dollar exchange rate used for such conversion was 1.0006 which was the average Bank of Canada exchange rate for the 2012 fiscal year.
- ⁽²⁾ The amounts in the "Bonus" column represent bonus payments earned in 2012, which were paid on a discretionary basis and were related to the successful negotiation and entry into our collaboration with Teva. All such amounts were paid in February 2013.
- ⁽³⁾ Represents the aggregate grant date fair value of stock option awards granted in 2012. These amounts have been computed in accordance with Financial Accounting Standards Board, or FASB, Accounting Standards Codification, or ASC, Topic 718, using the Black-Scholes option pricing model without regard to estimated forfeitures. For a discussion of valuation assumptions, see the notes to our financial statements included elsewhere in this prospectus. The exercise price for stock options were denominated in Canadian dollars on the date of grant. The amounts reflected in this column were converted to U.S. dollars using the U.S. dollar per Canadian dollar exchange rate on January 1, 2012 and September 24, 2012, the dates of grant, which is 0.9833 and 1.0203, respectively.
- ⁽⁴⁾ The amount represents payments earned in 2012 under the 2012 Compensation Program Bonus Plan, which were paid in February 2013 as discussed under the section titled "Executive Compensation — 2012 Non-Equity Incentive Plan Payments".
- ⁽⁵⁾ Of the total amount, (i) \$616 represents life insurance premiums through our group extended benefit plan and (ii) \$17,903 represents contributions to our registered retirement savings plan.
- ⁽⁶⁾ Of the total amount, (i) \$616 represents life insurance premiums through our group extended benefit plan and (ii) \$13,456 represents contributions to our registered retirement savings plan.
- ⁽⁷⁾ Of the total amount, (i) \$1,863 represents life insurance premiums through our group extended benefit plan for coverage in both Canada and the U.S., (ii) \$525 relocation expenses and (iii) \$7,887 telecommuting expenses including hotel and airfare. The amounts representing relocation and telecommuting expenses were paid in U.S. dollars.
- ⁽⁸⁾ In January 2013, Dr. Mansour resigned as Executive Vice President, Research & Development of the Company.

Non-Equity Incentive Plan Compensation

2012 Non-Equity Incentive Plan Payments

For 2012, the target incentive amounts and the aggregate annual payments earned by our named executive officers under our 2012 Compensation Program Bonus Plan were the following:

| NAMED EXECUTIVE OFFICER | TARGET AWARD ⁽¹⁾ OPPORTUNITY | ACTUAL AWARD AMOUNT |
|-------------------------|---|---------------------|
| Simon N. Pimstone | \$ 183,185 | \$ 183,185 |
| Y. Paul Goldberg | \$ 83,507 | \$ 83,507 |
| Tarek S. Mansour | \$ 111,813 | \$ 111,813 |

- ⁽¹⁾ Except as otherwise indicated, compensation amounts were paid in Canadian dollars and have been converted to U.S. dollars for purposes of the table. The U.S. dollar per Canadian dollar exchange rate used for such conversion was 1.0006 which was the average Bank of Canada exchange rate for the 2012 fiscal year.

Annual Performance-Based Bonus Plan

Our 2012 Compensation Program Bonus Plan provides our named executive officers with an annual incentive compensation payments subject to our achievement of our corporate performance goals and individual achievement. For 2012, our corporate-level goals included establishing proof-of-concept for topical XEN402, declaring a new product candidate as a development track candidate, securing funding for at least 20 full-time employees, completing at least one new pharmaceutical collaboration and operating within our planned budget for the fiscal year. For 2012, we achieved all of our corporate-level goals at target levels. The individual goals for 2012 related generally to each named executive officer's overall contributions in his or her roles towards reaching our corporate goals. The following was our determination of individual goal attainment in 2012: Dr. Pimstone, 100%; Dr. Goldberg, 100%; and Dr. Mansour, 100%. The target bonus percentage for each of our named executive officers was determined through executive employment arrangements, set forth below. The annual incentive payments are calculated by weighing corporate goal attainment and individual goal attainment for each named executive officer at 75% corporate goal/25% individual goal for Drs. Goldberg and Mansour and 100% corporate goal for Dr. Pimstone.

Discretionary Bonus

Our board of directors may, in certain circumstances, authorize the payment of discretionary bonuses to our executive officers and other employees. For 2012, each of Drs. Pimstone and Goldberg were awarded a discretionary bonus by our board of directors in connection with their involvement with the successful negotiation and execution of our collaborative arrangement with Teva.

Executive Employment Arrangements

Dr. Simon N. Pimstone

We entered into an employment agreement on December 7, 2004 with Dr. Pimstone, our President and Chief Executive Officer. The employment agreement is for an indefinite term. Dr. Pimstone's current annual base salary is CAD\$380,779, and he is eligible for an annual incentive payment up to 50% of his base salary, subject to achievement of performance metrics. The employment agreement also provides for severance benefits if Dr. Pimstone is terminated without cause. We anticipate entering into an amended employment agreement with Dr. Pimstone prior to the completion of this offering, which we expect to provide enhanced severance and post-termination benefits. For details regarding our current obligations under such circumstances, please see "Termination Benefits" below.

Dr. Y. Paul Goldberg

We entered into an employment agreement on October 13, 2000 with Dr. Goldberg, our Vice President of Clinical Development. The employment agreement is for an indefinite term. Dr. Goldberg's current annual base salary is CAD\$289,312, and he is eligible for an annual incentive payment up to 30% of his base salary, subject to achievement of performance metrics. The employment agreement also provides for severance benefits if Dr. Goldberg is terminated without cause. We anticipate entering into an amended employment agreement with Dr. Goldberg prior to the completion of this offering, which we expect to provide enhanced severance and post-termination benefits. For details regarding our current obligations under such circumstances, please see "Termination Benefits" below.

Dr. Tarek S. Mansour

We entered into an employment agreement on April 14, 2010 with Dr. Mansour, our former Executive Vice President, Research & Development. The employment agreement was for an indefinite term. Dr. Mansour's 2012 annual base salary was CAD\$279,531, and he was eligible for an annual incentive payment up to 40% of his base salary, subject to achievement of performance metrics.

In January 2013, Dr. Mansour resigned as Executive Vice President, Research & Development of the Company.

Dr. Mansour's employment agreement provided that, for a period of one year following Dr. Mansour's termination of employment with us, he may not engage in certain activities in competition with our business activities or induce or attempt to influence, our employees from leaving us.

In addition, in connection with his departure, Dr. Mansour entered into a separation agreement and a consulting agreement. Pursuant to the terms of the separation agreement, Dr. Mansour received a lump sum cash payment of CAD\$31,000 and his options continued to vest through June 30, 2013, subject to Dr. Mansour providing consulting services through that date. The separation agreement also contained a customary mutual waiver and release of claims.

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Mr. Ian C. Mortimer

We entered into an employment agreement on August 1, 2013 with Mr. Mortimer. The employment agreement employs Mr. Mortimer for an initial three month term as a part-time Special Advisor to the Chief Executive Officer. At the end of that three month term, or earlier, as mutually agreed upon between Mr. Mortimer and us, Mr. Mortimer will commence full-time employment as our Chief Financial Officer, or CFO, for an indefinite term. Mr. Mortimer's annual base salary as our full-time CFO will be CAD\$305,000, and as CFO he will be eligible for an annual incentive payment up to 40% of his base salary, subject to achievement of performance metrics. The employment agreement also provides for severance benefits if Mr. Mortimer is terminated without cause. For details regarding our potential obligations to Mr. Mortimer under such circumstances, please see "Termination Benefits" below.

Ms. Karen Corraini

We entered into an employment agreement on May 15, 2001 with Ms. Corraini, our General Counsel and Corporate Secretary. The employment agreement is for an indefinite term. Ms. Corraini's current annual base salary is CAD\$251,301, and she is eligible for an annual incentive payment up to 35% of her base salary, subject to achievement of performance metrics. The employment agreement also provides for severance benefits if Ms. Corraini is terminated without cause. We anticipate entering into an amended employment agreement with Ms. Corraini prior to the completion of this offering. For details regarding our current obligations under such circumstances, please see "Termination Benefits" below.

Dr. Robin Sherrington

We entered into an employment agreement on February 12, 2001 with Dr. Sherrington, our Senior Vice President of Business and Corporate Development. The employment agreement is for an indefinite term. Dr. Sherrington's current annual base salary is CAD\$240,940, and he is eligible for an annual incentive payment up to 35% of his base salary, subject to achievement of performance metrics. The employment agreement also provides for severance benefits if Dr. Sherrington is terminated without cause. We anticipate entering into an amended employment agreement with Dr. Sherrington prior to the completion of this offering. For details regarding our current obligations under such circumstances, please see "Termination Benefits" below.

Termination Benefits

Dr. Pimstone's agreement provides that we may terminate his employment without cause, if we give him twelve months' written notice, or a payment equal to twelve months' base salary only, or any equivalent combination of working notice and base salary in lieu of notice. In addition, the board of directors will, in good faith, negotiate the vesting terms of Dr. Pimstone's then unvested share options.

Dr. Goldberg's agreement provides that we may terminate his employment without cause, if we pay him eight months' salary in lieu of notice.

Mr. Mortimer's agreement provides that we may terminate his employment without cause, if we give him twelve months' written notice, or a payment equal to twelve months' base salary only, or any equivalent combination of working notice and base salary in lieu of notice.

Ms. Corraini's agreement provides that we may terminate her employment without cause, if we pay her twelve months' money in lieu of notice.

Dr. Sherrington's agreement provides that we may terminate his employment without cause, if we pay him eight months' money in lieu of notice.

Prior to the completion of this offering, we expect to enter into amended employment agreements with each of Drs. Pimstone, Goldberg and Sherrington and Ms. Corraini.

Our named executive officers are not entitled to special benefits upon a change in control, except for the potential vesting acceleration of their stock options. For a description of such benefits, see below under "–Outstanding Equity Awards of Fiscal Year-End" and "Employee Benefit Plans."

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Outstanding Equity Awards at Fiscal Year-End

The following table presents information concerning equity awards held by our named executive officers at the end of 2012.

| NAME | VESTING COMMENCEMENT DATE | OPTION AWARDS | | OPTION EXERCISE PRICE (CAD\$) | OPTION EXPIRATION DATE |
|-------------------|---------------------------|---|------------------------|-------------------------------|------------------------|
| | | NUMBER OF SECURITIES UNDERLYING UNEXERCISED OPTIONS (#) | | | |
| | | EXERCISABLE | UNEXERCISABLE | | |
| Simon N. Pimstone | 1/1/2004 | 75,000 ⁽¹⁾ | — | 1.25 | 12/31/2013 |
| | 10/1/2004 | 25,000 ⁽¹⁾ | — | 1.25 | 9/30/2014 |
| | 1/11/2005 | 75,000 ⁽¹⁾ | — | 1.25 | 1/10/2015 |
| | 8/1/2006 | 60,000 ⁽¹⁾ | — | 0.77 | 7/31/2016 |
| | 1/1/2008 | 50,000 ⁽¹⁾ | — | 0.77 | 12/31/2017 |
| | 6/27/2008 | 175,000 ⁽³⁾ | — | 0.77 | 6/26/2018 |
| | 1/1/2009 | 45,000 ⁽¹⁾ | — | 0.77 | 12/31/2018 |
| | 9/1/2009 | 50,000 ⁽¹⁾ | 10,000 ⁽¹⁾ | 0.77 | 8/31/2019 |
| | 1/1/2010 | 22,500 ⁽¹⁾ | 7,500 ⁽¹⁾ | 0.77 | 12/31/2019 |
| | 1/1/2011 | 55,000 ⁽¹⁾ | 55,000 ⁽¹⁾ | 0.77 | 12/31/2020 |
| | 1/1/2012 | — ⁽¹⁾ | 100,000 ⁽¹⁾ | 0.77 | 12/31/2021 |
| | 1/1/2012 | — ⁽¹⁾ | 50,000 ⁽¹⁾ | 0.77 | 12/31/2021 |
| | Y. Paul Goldberg | 1/1/2004 | 6,000 ⁽¹⁾ | — | 1.25 |
| 10/1/2004 | | 5,000 ⁽¹⁾ | — | 1.25 | 9/30/2014 |
| 1/11/2005 | | 10,000 ⁽⁴⁾ | — | 1.25 | 1/10/2015 |
| 1/1/2006 | | 2,000 ⁽¹⁾ | — | 1.25 | 12/31/2015 |
| 1/1/2007 | | 10,000 ⁽¹⁾ | — | 0.77 | 12/31/2016 |
| 1/1/2008 | | 5,000 ⁽¹⁾ | — | 0.77 | 12/31/2017 |
| 1/1/2009 | | 25,000 ⁽¹⁾ | — | 0.77 | 12/31/2018 |
| 1/1/2010 | | 22,500 ⁽¹⁾ | 7,500 ⁽¹⁾ | 0.77 | 12/31/2019 |
| 7/2/2010 | | 13,500 ⁽²⁾ | 4,500 ⁽²⁾ | 0.77 | 7/1/2020 |
| 12/2/2010 | | 13,611 ⁽²⁾ | 6,389 ⁽²⁾ | 0.77 | 12/1/2020 |
| 1/1/2011 | | 60,000 ⁽¹⁾ | 60,000 ⁽¹⁾ | 0.77 | 12/31/2020 |
| 1/1/2011 | | 26,667 ⁽²⁾ | 13,333 ⁽²⁾ | 0.77 | 12/31/2020 |
| 1/1/2012 | | — ⁽²⁾ | 10,000 ⁽¹⁾ | 0.77 | 12/31/2021 |
| 1/1/2012 | 5,000 ⁽²⁾ | 5,000 ⁽²⁾ | 0.77 | 12/31/2021 | |
| Tarek S. Mansour | 5/17/2010 | 100,000 ⁽¹⁾ | 50,000 ⁽¹⁾ | 0.77 | 5/16/2020 |
| | 5/17/2010 | 35,000 ⁽⁵⁾ | — | 0.77 | 5/16/2020 |
| | 1/1/2011 | 10,000 ⁽¹⁾ | 10,000 ⁽¹⁾ | 0.77 | 12/31/2020 |
| | 1/1/2012 | — | 60,000 ⁽¹⁾ | 0.77 | 12/31/2021 |
| | 9/24/2012 | — | 50,000 ⁽¹⁾ | 0.55 | 9/23/2022 |

⁽¹⁾ Options vest over four years as follows: 25% of the shares vest one year following the vesting commencement date, with the remaining 75% vesting in equal monthly installments over the following three years. Notwithstanding the foregoing, if the named executive officer's employment is terminated other than for cause, because of death or disability or resigns for good reason, in each case, during the period beginning on, and ending 12 months after, a change in control, then 100% of the then-unvested shares vest.

⁽²⁾ Options vest over four years as follows: one-third of the shares vest on the vesting commencement date, with the remaining two-thirds vesting in equal monthly installments over the following four years. Notwithstanding the foregoing, if the named executive officer's employment is terminated other than for cause, because of death or disability, or resigns for good reason, in each case, during the period on, and 12 months after, a change in control, then 100% of the then-unvested shares vest.

⁽³⁾ Options vest over three years as follows: one-third of the shares vest on the vesting commencement date, with the remaining two-thirds vesting in equal monthly installments over the following two years. Notwithstanding the foregoing, if the named executive officer's employment is terminated other than for cause, because of death or disability, or resigns for good reason, in each case, during the period on, and 12 months after, a change in control, then 100% of the then-unvested shares vest.

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- (4) Options vest as follows: 25% of the shares vest on January 1, 2006, with the remaining 75% vesting in equal monthly installments over the following three years. Notwithstanding the foregoing, if the named executive officer's employment is terminated other than for cause, because of death or disability, or resigns for good reason, in each case, during the period on, and 12 months after, a change in control, then 100% of the then-unvested shares vest.
- (5) Options vest as follows: 100% of the shares vest on January 1, 2011. Notwithstanding the foregoing, if the named executive officer's employment is terminated other than for cause, because of death or disability, or resigns for good reason, in each case, during the period on, and 12 months after, a change in control, then 100% of the then-unvested shares vest.

Employee Benefit and Stock Plans

2013 Equity Incentive Plan

In August 2013, the board of directors adopted a 2013 Equity Incentive Plan, which we expect to be approved by our shareholders prior to the completion of this offering. The 2013 Equity Incentive Plan will be effective one business day prior to the effective date of the registration statement of which this prospectus forms a part. We do not expect to use the 2013 Equity Incentive Plan until after the completion of this offering. Our 2013 Equity Incentive Plan will provide for the grant of incentive share options, within the meaning of Section 422 of the Internal Revenue Code, to our employees and any parent and subsidiary corporations' employees, and for the grant of nonstatutory share options, restricted share, restricted share units, share appreciation rights, and performance shares to our employees, officers, directors and consultants and those of our parent and subsidiary corporations.

Our Plan permits the grant of share options or share awards of common shares to our directors, officers, employees and other persons as approved by our board of directors. The 2013 Equity Incentive Plan will continue in effect for a term of ten (10) years from the date adopted, unless terminated earlier as permitted under the 2013 Equity Incentive Plan's provisions.

Authorized Shares. We reserved a total of _____ common shares for issuance pursuant to the 2013 Equity Incentive plan of which no awards are issued and outstanding. In addition, the shares reserved under our 2013 Equity Incentive Plan will also include (1) those shares reserved but unissued under our Stock Plan and (2) shares that otherwise would return to the Stock Plan as the result of expiration or termination of awards (provided that the maximum number of shares that may be added to the 2013 Equity Incentive Plan pursuant to (1) and (2) is _____ common shares). The number of shares available for issuance under the 2013 Equity Incentive Plan will increase annually on the first day of each fiscal year beginning in 2014, equal to the least of:

- _____ common shares;
- _____ of the outstanding common shares on the last business day of the immediately preceding fiscal year; or
- _____ such other amount as the board of directors may determine.

Plan Administration. The board of directors, or one or more committees appointed by the board of directors, will administer the 2013 Equity Incentive Plan. Subject to the provisions of our 2013 Equity Incentive Plan, the administrator has the power to determine the eligible persons to whom awards may be granted, the number of common shares to be covered by each award, the exercise price (provided that such exercise price may not be less than the lowest permitted under all applicable law), the forms of award agreements for use under the 2013 Equity Incentive Plan, and terms and conditions of any award. In the case of awards intended to qualify as "performance-based compensation" within the meaning of Section 162(m) of the U.S. Internal Revenue Code, the committee will consist of two or more "outside directors" within the meaning of Section 162(m). In addition, if the board of directors determines it is desirable to qualify transactions under the 2013 Equity Incentive Plan as exempt under Rule 16b-3 of the Exchange Act, such transactions will be structured to satisfy the requirements for exemption under Rule 16b-3. Subject to the provisions of our 2013 Equity Incentive Plan, the administrator has the power to administer the plan, including but not limited to, the power to interpret the terms of the 2013 Equity Incentive Plan and awards granted under it, to create, amend and revoke rules relating to the 2013 Equity Incentive Plan, including creating sub-plans, and to determine the terms of the awards, including the exercise price, the number of shares subject to each such award, the exercisability of the awards, and the form of consideration, if any, payable upon exercise. The administrator also has the authority to amend existing awards to reduce or increase their exercise price, to allow participants the opportunity to transfer outstanding awards to a financial institution or other person or entity selected by the administrator, and to institute an exchange program by which outstanding awards may be surrendered in exchange for awards of the same type which may have a higher or lower exercise price or different terms, awards of a different type and/or cash.

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Share Options. We may grant share options under the 2013 Equity Incentive Plan. The exercise price of options granted under our 2013 Equity Incentive Plan must at least be equal to the fair market value of our common shares on the date of grant, provided that such price may not be less than the lowest exercise price permitted under applicable law. The term of an incentive share option may not exceed 10 years, except that with respect to any participant who owns more than 10% of the voting power of all classes of our outstanding shares, the term must not exceed five years and the exercise price must equal at least 110% of the fair market value on the grant date. The administrator will determine the methods of payment of the exercise price of an option, which may include cash, shares or other property acceptable to the administrator, as well as other types of consideration permitted by applicable law. After the termination of service of an employee, director or consultant, he or she may exercise his or her option for the period of time stated in his or her option agreement. Generally, if termination is due to death or disability, the option will remain exercisable for 365 days. In all other cases, the option will generally remain exercisable for 90 days following the termination of service. However, in no event may an option be exercised later than the expiration of its term except in certain circumstances where the expiration occurs during a blackout period as described more fully in the 2013 Equity Incentive Plan. Subject to the provisions of our 2013 Equity Incentive Plan, the administrator determines the other terms of options.

Share Appreciation Rights. We may grant share appreciation rights under our 2013 Equity Incentive Plan. Share appreciation rights allow the recipient to receive the appreciation in the fair market value of our common shares between the exercise date and the date of grant. Share appreciation rights may not have a term exceeding 10 years. After the termination of service of an employee, director or consultant, he or she may exercise his or her share appreciation right for the period of time stated in his or her agreement. However, in no event may a share appreciation right be exercised later than the expiration of its term. Subject to the provisions of our 2013 Equity Incentive Plan, the administrator determines the other terms of share appreciation rights, including when such rights become exercisable and whether to pay any increased appreciation in cash or with our common shares, or a combination thereof, except that the per share exercise price for the shares to be issued pursuant to the exercise of a share appreciation right will be no less than 100% of the fair market value per share on the date of grant.

Restricted Shares. We may grant restricted share awards under our 2013 Equity Incentive Plan. Restricted share awards are grants of common shares that vest in accordance with terms and conditions established by the administrator. The administrator will determine the number of restricted share awards granted to any employee, director or consultant and, subject to the provisions of our 2013 Equity Incentive Plan, will determine the terms and conditions of such awards. The administrator may impose whatever conditions to vesting it determines to be appropriate (for example, the administrator may set restrictions based on the achievement of specific performance goals or continued service to us); provided, however, that the administrator, in its sole discretion, may accelerate the time at which any restrictions will lapse or be removed. Recipients of restricted share awards generally will have voting and dividend rights with respect to such shares upon grant without regard to vesting, unless the administrator provides otherwise. Restricted share awards that do not vest are subject to our right of repurchase or forfeiture.

Restricted Share Units. We may grant restricted share units under our 2013 Equity Incentive Plan. Restricted share units are bookkeeping entries representing an amount equal to the fair market value of one of our common shares. Subject to the provisions of our 2013 Equity Incentive Plan, the administrator determines the terms and conditions of restricted share units, including the vesting criteria (which may include accomplishing specified performance criteria or continued service to us) and the form and timing of payment. Notwithstanding the foregoing, the administrator, in its sole discretion may accelerate the time at which any restrictions will lapse or be removed.

Performance Shares. We may grant performance shares under our 2013 Equity Incentive Plan. Performance shares are awards that will result in a payment to a participant only if performance goals established by the administrator are achieved or the awards otherwise vest. The administrator will establish organizational or individual performance goals or other vesting criteria in its discretion, which, depending on the extent to which they are met, will determine the number and/or the value of performance shares to be paid out to participants. After the grant of performance shares, the administrator, in its sole discretion, may reduce or waive any performance criteria or other vesting provisions for such performance shares. Performance shares shall have an initial value equal to the fair market value of our common shares on the grant date. The administrator, in its sole discretion, may pay earned performance shares in the form of cash, in shares or in some combination thereof.

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Outside Directors. Our 2013 Equity Incentive Plan provides that all outside directors will be eligible to receive all types of awards (except for incentive stock options) under the 2013 Equity Incentive Plan. In connection with this offering, we intend to implement a formal policy pursuant to which our outside directors will be eligible to receive equity awards under the 2013 Equity Incentive Plan. Our 2013 Equity Incentive Plan provides that in any given year an outside director will not receive (i) cash-settled awards having a grant date fair value greater than \$500,000, increased to \$1,000,000 in connection with his or her initial service; and (ii) share-settled awards having a grant date fair value greater than \$500,000, increased to \$1,000,000 in connection with his or her initial service, in each case, as determined under generally accepted accounting principles.

Non-Transferability of Awards. Unless the administrator provides otherwise, our 2013 Equity Incentive Plan generally will not allow for the transfer of awards and only the recipient of an award may exercise an award during his or her lifetime.

Certain Adjustments. In the event of certain changes in our capitalization, to prevent diminution or enlargement of the benefits or potential benefits available under the 2013 Equity Incentive Plan, the administrator will adjust the number and class of shares that may be delivered under the 2013 Equity Incentive Plan and/or the number, class, and price of shares covered by each outstanding award, and the numerical share limits set forth in the 2013 Equity Incentive Plan.

Merger or Change in Control. Our 2013 Equity Incentive Plan provides that in the event of a merger or change in control, as defined under the 2013 Equity Incentive Plan, each outstanding award will be treated as the administrator determines, except that if a successor corporation or its parent or subsidiary does not assume or substitute an equivalent award for any outstanding award, then such award will fully vest, all restrictions on such award will lapse, all performance goals or other vesting criteria applicable to such award will be deemed achieved at 100% of target levels and such award will become fully exercisable, if applicable, for a specified period prior to the transaction. The award will then terminate upon the expiration of the specified period of time. If the service of an outside director is terminated on or following a change of control, other than pursuant to a voluntary resignation, his or her options, restricted share units and share appreciation rights, if any, will vest fully and become immediately exercisable, all restrictions on his or her restricted shares will lapse, and all performance goals or other vesting requirements for his or her performance shares will be deemed achieved at 100% of target levels, and all other terms and conditions met.

Amendment, Termination. The administrator will have the authority to amend, suspend or terminate the 2013 Equity Incentive Plan provided such action does not impair the existing rights of any participant. Our 2013 Equity Incentive Plan will automatically terminate in 2023, unless we terminate it sooner.

Amended and Restated Stock Option Plan

Our Amended and Restated Stock Option Plan, or our Stock Plan, was initially adopted by our board of directors and shareholders in June 1999. Our Stock Plan permits the grant of stock options to our directors, officers and other Service Providers (as defined in the Stock Plan). Our Stock Plan was most recently amended and restated in January 2013. In connection with this offering, we expect to terminate our Stock Plan with respect to any future grant of options; however, our Stock Plan will continue to govern the terms and conditions of outstanding options granted thereunder.

Authorized Shares. The maximum aggregate number of our common shares reserved for issuance under the Stock Plan is 7,373,338 shares. Any shares for which an option had been exercised are not included in determining whether the maximum number of shares had been reached.

Plan Administration. Subject to the provisions of our Stock Plan, our board of directors has the power to determine the directors, officers and other Service Providers to whom options may be granted; to determine terms and conditions of options; and to extend the period of time following an optionee's termination of service within which the optionee's option may be exercised.

Stock Options. The per share exercise price of each option equals the market price of our common share on the date of grant, and each option has a term of up to 10 years, subject to earlier termination upon an optionee's termination

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of service. After an optionee's termination of service, the optionee may exercise his or her option, to the extent vested as of such date of termination, (i) until 5:00 p.m. Vancouver time on the date of termination if the optionee's service was terminated for cause (as determined by us in our sole discretion), (ii) for 365 days following a termination of the optionee's service due to death or disability, or (iii)(a) for optionees other than non-employee and non-consultant directors, 90 days following a termination of the optionee's service for any other reason and (b) for options of our directors other than those directors that are employees or consultants, 24 months following a termination of the optionee's service, each for any other reason. As of the date this registration statement becomes effective, the time periods in (iii)(a) and (iii)(b) of the previous sentence shall be changed to 30 days. In no event may an option be exercised later than the expiration of its term. Our board of directors determined the remaining terms and conditions of an option, as the board of directors, in its discretion, deemed to be consistent with the Stock Plan. The specific terms of any grant of stock options are set forth in an award agreement between us and the recipient.

Transferability. Optionees may not assign their options or their rights under the Stock Plan.

Certain Adjustments. In the event of certain changes in our capitalization, to prevent diminution or enlargement of the benefits or potential benefits available under the Stock Plan, our board of directors may make proportional adjustments to the number of common shares that may be delivered under the Stock Plan and/or the number and price of shares covered by each outstanding option.

Merger, Dissolution, Liquidation, or other Change of Control. Our Stock Plan provides that in the event of a dissolution, liquidation, sale of all or substantially all of our assets; merger, consolidation, amalgamation, arrangement or reorganization in which we are not the surviving corporation; reverse merger in which we are the surviving corporation but our common shares are converted into other property; or an acquisition by any person, entity or group within the meaning of Section 13(d) of the Exchange Act of our securities representing at least 35% of the combined voting power entitled to vote in an election of directors (collectively, a "Change of Control"), any successor corporation shall assume our obligations in respect of all outstanding options under our Stock Plan or shall substitute an equivalent option for all outstanding options under the Stock Plan. If a successor corporation does not assume or substitute for an outstanding option, then any options held by persons who are directors, officers, or Service Providers generally will fully vest and the time during which such option may be exercised shall be accelerated prior to the completion of the Change of Control. All options that are not assumed or are not substituted for will terminate unless exercised prior to the Change of Control. In the event of our merger into another corporation or other entity or any other Change of Control in which the options are assumed or substituted for by a successor corporation, the assumed options or the substitute options held by a director, officer or Service Provider will become fully vested and exercisable if, within 12 months following the Change of Control, either (i) the optionee's service is terminated by us or the successor corporation other than for Cause (as defined in the Stock Plan) or (ii) the optionee resigns for Good Reason (as defined in the Stock Plan).

Plan Amendment. Subject to any required regulatory approval, we may amend the Stock Plan at any time, provided that such amendment does not impair the existing rights of any optionee under any then-outstanding option.

Retirement and Pension Benefits

Our registered retirement savings plan, or RRSP Plan, provides Canadian resident employees with an opportunity to participate in a retirement savings plan. This type of retirement plan is a Canadian retirement plan with features similar to a 401(k) plan or an individual retirement account administered in the U.S. All of our named executive officers are eligible to participate in all or our employee benefit plans, in each case on the same basis as other employees. Under our current RRSP Plan, we match 100% of employee contributions by eligible employees up to a maximum of 5% of the employee's salary.

CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

The following is a description of transactions since January 1, 2010 to which we have been a party, in which the amount involved exceeds \$120,000, and in which any of our directors, executive officers, or holders of more than 5% of our shares, or an affiliate or immediate family member thereof, had or will have a direct or indirect material interest, other than compensation arrangements which are described under the sections of this prospectus captioned "Management—Director Compensation" and "Executive Compensation."

Related Person Transaction Policy

We intend to adopt a formal, written policy, which will become effective on the date of this prospectus, that our executive officers, directors (including director nominees), holders of more than 5% of any class of our voting securities, and any member of the immediate family of or any entities affiliated with any of the foregoing persons, are not permitted to enter into a related party transaction with us without the prior approval or, in the case of pending or ongoing related party transactions, ratification of our audit committee. For purposes of our policy, a related party transaction is a transaction, arrangement or relationship where we were, are or will be involved and in which a related party had, has or will have a direct or indirect material interest, other than transactions available to all of our employees.

Consulting Services Provided by Genworks, Inc.

During the fiscal years ended December 31, 2010, 2011 and 2012, we incurred consulting fees to Genworks Inc., or Genworks, in the amount of \$218,543, \$278,622 and \$307,264, respectively. These amounts were paid in Canadian dollars and have been converted to U.S. dollars based on the average annual U.S. dollar per Canadian dollar exchange rate for the applicable year in which the amounts were paid. The U.S. dollar per Canadian dollar exchange rate used for such conversions is 0.9713, 1.0117 and 1.0006, respectively. Genworks is controlled by Dr. Michael Hayden, one of our directors. These consulting fees were paid to Genworks in consideration of certain scientific consulting services provided by Dr. Hayden during this period.

Clinical and Regulatory Services Provided by Medpace, Inc.

During the fiscal years ended December 31, 2010, 2011 and 2012, we incurred contract research organization, or CRO, fees to Medpace, Inc., or Medpace, in the amount of \$2,295,354, \$876,474 and \$150,915, respectively. Dr. Evan A. Stein, one of our directors, is an equityholder and former director of Medpace. These CRO fees were paid to Medpace in consideration of certain clinical development services provided by Medpace during this period by individuals other than Dr. Stein. None of these fees were paid directly to Dr. Stein. We are not currently party to a consulting agreement with Medpace and we do not expect to engage Medpace for CRO services in the future. The fees paid to Medpace did not exceed five percent of the consolidated gross revenue of Medpace during any of these fiscal years.

Investor Rights Agreement

We have entered into an amended and restated investors' rights agreement, dated December 6, 2006, with certain holders of our preferred shares, including entities affiliated with Fidelity Investments, entities affiliated with InterWest Partners and entities affiliated with Lipotex, L.P., which provides these holders with, among other things, certain rights relating to the registration of our common shares. See the section of this prospectus captioned "Description of Share Capital—Registration Rights" for more information about the amended and restated investors' rights agreement.

Indemnification Agreements and Directors' and Officers' Liability Insurance

We will enter into indemnification agreements with each of our directors and officers. As provided by our by-laws, these agreements, among other things, will require us to indemnify each director and officer to the fullest extent

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permitted by Canadian law, including indemnification of all costs, charges and expenses reasonably incurred by such person in any action or proceeding, including any action or proceeding by or in right of us, arising out of the person's services as a director or officer.

Requirements under the Canada Business Corporations Act

Pursuant to the CBCA, directors and officers are required to act honestly and in good faith with a view to the best interests of the company. Under the CBCA, subject to certain limited exceptions, a director who holds a disclosable interest in a material contract or transaction into which we have entered or propose to enter shall not vote on any directors' resolution to approve the contract or transaction. A director or officer has a disclosable interest in a material contract or transaction if the director or officer is:

- ⁿ a party to the contract or transaction;
- ⁿ is a director or officer, or an individual acting in a similar capacity, of a party to the contract or transaction; or
- ⁿ has a material interest in a party to the contract or transaction.

Generally, as a matter of practice, directors or officers who have disclosed a material interest in any contract or transaction that our board of directors is considering will not take part in any board discussion respecting that contract or transaction. If such directors were to participate in the discussions, they would abstain from voting on any matters relating to matters in which they have disclosed a disclosable interest.

PRINCIPAL SHAREHOLDERS

The following table sets forth information relating to the beneficial ownership of our common shares as of June 30, 2013 as adjusted to reflect the sale of common shares offered by us in this offering, for:

- ⁿ each person, or group of affiliated persons, known by us to beneficially own more than 5% of our outstanding common shares;
- ⁿ each of our named executive officers;
- ⁿ each of our directors; and
- ⁿ all current executive officers and directors as a group.

The percentage of beneficial ownership prior to the offering shown in the table is based upon 39,586,986 common shares outstanding as of June 30, 2013. The percentage of beneficial ownership after this offering shown in the table is based on common shares outstanding after the closing of this offering, assuming no exercise of the underwriters' option to purchase additional common shares.

Information with respect to beneficial ownership has been furnished by each director, officer or beneficial owner of more than 5% of our common shares. We have determined beneficial ownership in accordance with the rules of the SEC. These rules generally attribute beneficial ownership of securities to persons who possess sole or shared voting power or investment power with respect to those securities. In addition, the rules take into account common shares issuable pursuant to the exercise of stock options or warrants that are either immediately exercisable or exercisable on or before the 60th day after June 30, 2013. Unless otherwise indicated, the persons or entities identified in this table have sole voting and investment power with respect to all shares shown as beneficially owned by them, subject to applicable community property laws.

Except as otherwise noted below, the address for each person or entity listed in the table is c/o Xenon Pharmaceuticals Inc., 200 – 3650 Gilmore Way, Burnaby, British Columbia V5G 4W8, Canada.

| NAME OF BENEFICIAL OWNER | NUMBER OF SHARES BENEFICIALLY OWNED | PERCENTAGE OF SHARES BENEFICIALLY OWNED | |
|--|--|--|----------------|
| | | BEFORE OFFERING | AFTER OFFERING |
| 5% and Greater Shareholders | | | |
| Entities affiliated with MX Associates, LLP ⁽¹⁾ | 5,972,378 | 15.1% | |
| Entities affiliated with Lipotex L.P. ⁽²⁾ | 4,207,811 | 10.6 | |
| Entities affiliated with InterWest Partners ⁽³⁾ | 3,734,882 | 9.4 | |
| FMR LLC ⁽⁴⁾ | 2,556,545 | 6.5 | |
| Named Executive Officers and Directors | | | |
| Simon N. Pimstone ⁽⁵⁾ | 1,735,657 | 4.3 | |
| Y. Paul Goldberg ⁽⁶⁾ | 261,750 | * | |
| Tarek Mansour ⁽⁷⁾ | 188,750 | * | |
| Michael M. Tarnow ⁽⁸⁾ | 629,615 | 1.6 | |
| Mohammad Azab ⁽⁹⁾ | 230,833 | * | |
| Gary Bridger | — | * | |
| Karen Corraini ⁽¹⁰⁾ | 258,076 | * | |
| Johnston L. Evans ⁽¹¹⁾ | 1,800,873 | 4.6 | |
| Michael Hayden ⁽¹²⁾ | 1,742,053 | 4.4 | |
| Frank A. Holler ⁽¹³⁾ | 1,298,302 | 3.2 | |
| Gary Patou ⁽¹⁴⁾ | 215,889 | * | |
| Robin Sherrington ⁽¹⁵⁾ | 227,069 | * | |
| Evan A. Stein ⁽¹⁶⁾ | 4,250,150 | 10.7 | |
| All current executive officers and directors as a group (13 persons) ⁽¹⁷⁾ | 12,839,017 | 29.9 | |

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* Indicates beneficial ownership of less than 1% of the total outstanding common shares.

- (1) Consists of 5,972,378 shares held by MX Associates, LLP. Dr. August Troendle, as the managing partner of MX Associates has sole voting and investment power with respect to the shares held by MX Associates, LLP. The address for this entity is 5375 Medpace Way, Cincinnati, Ohio 45227.
- (2) Consists of 4,207,811 shares held by Lipotex, Ltd. ("Lipotex"). Lipotex Holdings, LLC, the general partner of Lipotex, has sole voting and investment power with respect to the shares held by Lipotex. Dr. Stein, the managing partner of Lipotex Holdings, LLC has sole voting and investment power with respect to the shares held by Lipotex. The address for these entities is 25 E. Superior St., Chicago, Illinois 60611.
- (3) Consists of (i) 3,570,190 shares held by InterWest Partnership, LP ("IW7") and (ii) 289,835 shares held by InterWest Investors VII, LP ("II7"). InterWest Management Partners VII, LLC ("IMP7"), the general partner of IW7 and II7, has sole voting and investment power with respect to the shares held by IW7 and II7. Harvey B. Cash, Philip T. Gianos, W. Scott Hedrick, 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 shares held by IW7 and II7. IMP7 has delegated shared voting and investment power with respect to the shares held by IW7 and II7 to Nina Kjellson, one of our former directors. The address for these entities is c/o InterWest Partners, 2710 Sand Hill Road, Suite 200, Menlo Park, California 94025.
- (4) Consists of (i) 1,157,981 shares held by Fidelity Select Portfolios: Biotechnology Portfolio; (ii) 8,758 shares held by Fidelity Canadian Aggressive Fund; (iii) 700,955 shares held by Fidelity Canadian Growth Company Fund; and (iv) 688,851 shares by Fidelity Canadian Asset Allocation Fund. Fidelity Management & Research Company ("Fidelity"), 82 Devonshire Street, Boston, Massachusetts 02109, a wholly-owned subsidiary of FMR LLC and an investment adviser registered under Section 203 of the Investment Advisers Act of 1940, is the beneficial owner of 1,157,981 shares as a result of acting as investment adviser to various investment companies registered under Section 8 of the Investment Company Act of 1940. Edward C. Johnson 3d and FMR LLC, through its control of Fidelity, and the funds each has sole power to dispose of the 1,157,981 shares owned by the Funds. Members of the family of Edward C. Johnson 3d, Chairman of FMR LLC, are the predominant owners, directly or through trusts, of Series B voting common shares of FMR LLC, representing 49% of the voting power of FMR LLC. The Johnson family group and all other Series B shareholders have entered into a shareholders' voting agreement under which all Series B voting common shares will be voted in accordance with the majority vote of Series B voting common shares. Accordingly, through their ownership of voting common shares and the execution of the shareholders' voting agreement, members of the Johnson family may be deemed, under the Investment Company Act of 1940, to form a controlling group with respect to FMR LLC. Neither FMR LLC nor Edward C. Johnson 3d, Chairman of FMR LLC, has the sole power to vote or direct the voting of the shares owned directly by the Fidelity Funds, which power resides with the Funds' Boards of Trustees. Fidelity carries out the voting of the shares under written guidelines established by the Funds' Boards of Trustees. Pyramis Global Advisors Trust Company ("PGATC"), 900 Salem Street, Smithfield, Rhode Island, 02917, an indirect wholly-owned subsidiary of FMR LLC and a bank as defined in Section 3(a)(6) of the Securities Exchange Act of 1934, is the beneficial owner of 1,398,564 shares as a result of its serving as investment manager of institutional accounts owning such shares. Edward C. Johnson 3d and FMR LLC, through its control of PGATC, each has sole dispositive power over 1,398,564 shares and sole power to vote or to direct the voting of 1,398,564 shares owned by the institutional accounts managed by PGATC as reported above.
- (5) Consists of (i) 934,615 shares held by Dr. Pimstone; (ii) 80,000 shares held by Dr. Pimstone's spouse; and (iii) 721,042 shares issuable upon exercise of options exercisable within 60 days of June 30, 2013.
- (6) Consists of (i) 21,000 shares held by Dr. Goldberg and (ii) 240,750 shares issuable upon exercise of options exercisable within 60 days of June 30, 2013.
- (7) Consists of 188,750 shares issuable upon exercise of options exercisable within 60 days of June 30, 2013.
- (8) Consists of (i) 240,115 shares held by Mr. Tarnow and (ii) 389,500 shares issuable upon exercise of options exercisable within 60 days of June 30, 2013.
- (9) Consists of 230,833 shares issuable upon exercise of options exercisable within 60 days of June 30, 2013.
- (10) Consists of (i) 10,000 shares held by Ms. Corraini and (ii) 248,076 shares issuable upon exercise of options exercisable within 60 days of June 30, 2013.
- (11) Consists of (i) 1,070,619 shares held by Chancellor V, L.P. ("Chancellor V"); (ii) 561,513 shares held by Chancellor V-A, L.P. ("Chancellor V-A"); and (iii) 168,741 shares held by Citiventure 2000, L.P. ("Citiventure"). Invesco Private Capital, Inc. is the managing member of IPC Direct Associates V, LLC, which is a Managing Director of each of Chancellor V, Chancellor V-A and Citiventure (collectively referred to as the "Invesco Capital Entities"). Mr. Evans is the Head of Invesco Private Capital, Inc. and a member of the investment committee of IPC Direct Associates V, LLC. Accordingly, Mr. Evans shares voting and investment power of the shares held by the Invesco Capital Entities. Mr. Evans disclaims beneficial ownership of these shares except with respect to his pecuniary interest therein.
- (12) Consists of (i) 577,971 shares held by Dr. Hayden; (ii) 247,939 shares held by Dr. Hayden's spouse; (iii) 114,843 shares held by Sandra J. Hayden, in trust for Anna R. Hayden for which Dr. Hayden's spouse serves as trustee; (iv) 114,843 held by Sandra J. Hayden, in trust for Gideon R. Hayden for which Dr. Hayden's spouse serves as trustee; (v) 114,843 held by Sandra J. Hayden, in trust for Jessica R. Hayden for which Dr. Hayden's spouse serves as trustee; (vi) 114,843 held by Sandra J. Hayden, in trust for Sarah R. Hayden for which Dr. Hayden's spouse serves as trustee; (vii) 192,125 shares issuable upon exercise of options exercisable within 60 days of June 30, 2013 held by Dr. Hayden; and (viii) 263,646 shares issuable upon exercise of options exercisable within 60 days of June 30, 2013 held by Genworks Inc.
- (13) Consists of (i) 841,580 shares held by Mr. Holler and (ii) 456,722 shares issuable upon exercise of options exercisable within 60 days of June 30, 2013.

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- (14) Consists of 215,889 shares issuable upon exercise of options exercisable within 60 days of June 30, 2013.
- (15) Consists of (i) 10,000 shares held by Dr. Sherrington and (ii) 217,069 shares issuable upon exercise of options exercisable within 60 days of June 30, 2013.
- (16) Consists of (i) the shares listed in footnote (2) above, which are held by Lipotex L.P.; (ii) 4,700 shares held by the Stein Family LLC for which Dr. Stein serves as the managing member; and (iii) 37,639 shares issuable upon exercise of options exercisable within 60 days of June 30, 2013.
- (17) Consists of (i) 9,435,976 shares beneficially owned by our current executive officers and directors and (ii) 3,403,041 shares issuable upon exercise of options exercisable within 60 days of June 30, 2013.

DESCRIPTION OF SHARE CAPITAL

General

The following is a summary of the material rights of our common shares and new preferred shares, as contained in our articles and by-laws and any amendments thereto, that will be in effect upon completion of the offering. This summary is not a complete description of the share rights associated with our common shares and new preferred shares. For more detailed information, please see the forms of our articles and by-laws that will be in effect upon the closing of this offering, which are filed as exhibits to the registration statement of which this prospectus forms a part.

Upon or immediately prior to the closing of this offering:

- ⁿ we will cause all of our outstanding Series A preferred shares, Series B preferred shares, Series C preferred shares, Series D preferred shares and Series E preferred shares to convert into our common shares;
- ⁿ all of our outstanding subscription rights will automatically convert into our common shares; and
- ⁿ we will effect a -for- reverse share split of our common and preferred shares.

Share Capital

Outstanding Shares

As a result, upon closing of this offering, based on the common shares, preferred shares and subscription rights outstanding as of June 30, 2013, our authorized share capital will consist of an unlimited number of common shares, each without par value, of which will be issued and outstanding, and an unlimited number of new preferred shares, issuable in series, each without par value, none of which will be issued and outstanding.

As of June 30, 2013, we had 6,339,591 common shares issuable pursuant to outstanding options, and we had approximately 324 record holders of our common shares.

Voting Rights

Under our amended articles that will be in effect upon the closing of this offering, the holders of our common shares will be 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 to be in effect upon the completion of this offering 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 new 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. For more information, see the section titled "Dividend Policy."

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 new preferred shares.

Rights and Preferences

Our common shares contain no pre-emptive or conversion rights and 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 our common shares are subject to and may be adversely affected by, the rights of the holders of any series of new preferred shares that our board of directors may designate and we may issue in the future.

Fully Paid and Nonassessable

All of our outstanding common shares are, and the common shares to be issued pursuant to this offering, when paid for, will be fully paid and nonassessable.

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New preferred shares

Upon or immediately prior to the closing of this offering, our articles will be amended to delete all references to our Series A preferred shares, Series B preferred shares, Series C preferred shares, Series D preferred shares and Series E preferred shares. Under our amended articles that will be in effect upon the closing of this offering, our board of directors will have the authority to issue, without further action by our shareholders, an unlimited number of new preferred shares, issuable in one or more series, and subject to the provisions of the CBCA, and 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 and voting rights, may be superior to those of our common shares. The issuance of new 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 new 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.

Upon closing of this offering, no new preferred shares will be outstanding, and we have no present plan to issue any new preferred shares.

Subscription Rights

We entered into a research funding agreement with Genome B.C., which provides Genome B.C. with certain subscription rights upon certain funding payments. As of June 30, 2013, 69,356 common shares were issuable pursuant to these subscription rights, which rights will automatically convert into common shares immediately prior to the closing of this offering for no additional consideration.

Registration Rights

Under our amended and restated investors' rights agreement, the holders of approximately _____ 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. In connection with the current offering, _____ % of shareholders with registration rights have agreed not to sell or otherwise dispose of any securities without the prior written consent of the representatives of underwriters for a period of 180 days after the date of this prospectus, subject to certain terms and conditions. For more information regarding such terms and conditions, see "Shares Eligible for Future Sale—Lock-Up and Market Stand-off Agreements" and "Underwriting."

Demand Registration Rights

The holders of a majority of the 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, or \$4,756,500, as converted, 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

At any time after we are qualified to file a registration statement on Form S-3, each holder of 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 shares to be offered and sold under such registration statement on Form S-3 is at least CAD \$500,000, or \$475,650 as converted. 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.

Termination

The registration rights terminate upon the earliest of (1) the date that is four years after the closing of this offering and (2) as to a given holder of registration rights, if (a) we have completed our initial public offering and 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.

Right of First Refusal

Under our amended and restated investors' rights agreement, certain holders of our redeemable convertible preferred shares have rights of first refusal to purchase their pro rata share of equity securities that we may issue from time to time, with certain exceptions. Such rights of first refusal do not apply to the shares to be issued in this offering. On the effective date of a registration statement for an initial public offering that raises gross proceeds of \$40 million or more at a per share price of no less than \$4.42, subject to adjustment for any share split, these rights of first refusal will terminate.

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. Our by-laws require 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 day 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

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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 she does not intend to challenge the acquisition.

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 who is a World Trade Organization member country investor, including a U.S. investor, would be reviewable only if the value of our assets was equal to or greater than a specified amount. The specified amount for 2013 is CAD\$344.0 million. 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.

As a result of recent amendments to the Investment Canada Act substantial changes to the review threshold are pending. If and when these amendments come into force, the review threshold will increase to CAD\$600.0 million (and eventually to CAD\$1.0 billion) and will no longer be calculated on the basis of the book value of the Canadian business assets, but rather its "enterprise value".

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

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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 of Industry 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.

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 ²/₃% 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) in general, amending our articles or by-laws; (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. The notice must include information on the business the shareholder intends to bring before the meeting.

In addition, our amended articles that will be in effect upon the closing of this offering, 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 shareholder actions that are favored by the holders of a majority of our outstanding voting securities.

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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, as discussed below under “United States and Canadian Income Tax Considerations—Certain Canadian Federal Income Tax Information.”

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.

Listing

We intend to apply to have our common shares approved for listing on The NASDAQ Global Market under the symbol “XENE.”

Transfer Agent and Registrar

The transfer agent and registrar for our common shares is . The transfer agent and registrar’s address is .

MATERIAL DIFFERENCES BETWEEN THE CANADA BUSINESS CORPORATION ACT AND THE DELAWARE GENERAL CORPORATE LAW

Our corporate affairs are governed by our articles of continuance and by-laws and the provisions of the Canada Business Corporation Act, or CBCA. The CBCA differs from the various state laws applicable to U.S. corporations and their shareholders. The following table provides a summary of the material differences between the provisions of the CBCA and the Delaware General Corporation Law, or DGCL, taking into account certain specific provisions in our amended Articles that will be in effect upon the closing of this offering and our by-laws.

| | <u>CBCA</u> | <u>DGCL</u> |
|--|--|---|
| Authorized share capital | <p>Upon closing, under our amended Articles, as permitted by the CBCA, the authorized share capital will consist of (i) an unlimited number of common shares without par value and (ii) an unlimited number of new preferred shares without par value, issuable in series.</p> <p>Upon closing, under our amended Articles, our board of directors will have the authority to issue new preferred shares in one or more series, with such designations and special rights and restrictions as our board of directors may determine.</p> | <p>Under the DGCL, a corporation's certificate of incorporation must specify the number of shares of each class of stock and their par value, or include a statement that such shares are without par value. The certificate of incorporation must also set forth the designations, powers, preferences, rights, qualifications, limitations and restrictions of each class of shares, if any. Under the DGCL, a corporation's certificate of incorporation may give the board of directors the authority to issue preferred stock in one or more series, with such designations and special rights and restrictions as determined by the board of directors.</p> |
| Dividends | <p>Under the CBCA and our Articles, dividends may be declared at the discretion of our board of directors. Any dividends declared shall be subject to the rights, if any, of shareholders holding shares with special rights as to dividends. Our directors may declare dividends unless there are reasonable grounds for believing that we are insolvent or the payment of such dividends would render us insolvent.</p> | <p>The DGCL generally provides that, subject to certain restrictions, the directors of a corporation may declare and pay dividends upon the shares of its capital stock either out of the corporation's surplus or, if there is no such surplus, out of its net profits for the fiscal year in which the dividend is declared and/or the preceding fiscal year. Further, the holders of preferred or special stock of any class or series may be entitled to receive dividends at such rates, on such conditions and at such times as stated in the certificate of incorporation.</p> |
| Vote Required for Certain Transactions | <p>Under the CBCA, certain extraordinary corporate actions, such as continuances, certain amalgamations and sales, leases or exchanges of all, or substantially all, of the property of a corporation (other than in the ordinary course of business), and liquidations, dissolutions and certain arrangements, are required to be approved by special resolution of our shareholders.</p> <p>A special resolution is a resolution passed by not less than two-thirds of the votes cast by the shareholders who voted in respect of the resolution or signed by all shareholders entitled to vote on the resolution.</p> | <p>Under the DGCL, certain mergers, consolidation, sale, lease, exchange or other disposition of all, or substantially all, the property and assets of a corporation or dissolution of the corporation requires the approval of a majority of the outstanding voting stock of the corporation entitled to vote thereon.</p> |

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| Amendment of Organizing Documents | Under the CBCA, an amendment to our Articles generally requires approval by special resolution of holders of our voting shares. Specified amendments may also require the approval of other classes of our shares. In the event that an amendment to our Articles would prejudice or interfere with a right or special right attached to our issued shares of a class or series of our shares, such amendment must be approved separately by the holders of the class or series of shares being affected. | The DGCL provides that a corporation may amend its certificate of incorporation if its board of directors has adopted such amendment, followed by the affirmative vote of a majority of the outstanding voting stock and a majority of the outstanding shares of each class entitled to vote on the amendment as a class. In the event the amendment would alter the aggregate number of authorized shares of a class of stock, their par value, or the powers, preferences or special rights of the shares of a class so as to affect them adversely, the holders of the outstanding shares of the class are entitled to vote as a class upon a proposed amendment, whether or not entitled to vote thereon by the certificate of incorporation. |
| Amendment of By-laws | Under the CBCA, our board of directors may, by resolution, make, amend or repeal any by-law that regulates our business or affairs. Where our board of directors makes, amends or repeals a by-law, they are required under the CBCA to submit that action to our shareholders at the next meeting of shareholders and our shareholders may confirm, reject or amend that action by ordinary resolution. If the action is rejected by our shareholders, or our board of directors does not submit the action to our shareholders at the next meeting of shareholders, the action will cease to be effective and no subsequent resolution of our directors to make, amend or repeal a by-law having substantially the same purpose or effect will be effective until it is confirmed. | The DGCL provides that the stockholders entitled to vote have the power to adopt, amend or repeal bylaws. A corporation may also confer, in its certificate of incorporation, that power upon the board of directors. |
| Quorum of Shareholders | As permitted under the CBCA, our by-laws provide that quorum for meetings of shareholders is one person present or representing by proxy, shareholders holding no less than 10% of the issued shares entitled to be voted at the meeting. | Under the DGCL, unless otherwise provided in the certificate of incorporation, with respect to any matter, a quorum for a meeting of stockholders requires the holders of a majority of the shares entitled to vote are represented at the meeting in person or by proxy. |
| Annual Meetings of Shareholders | Under the CBCA, we must hold an annual 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 but no later than six months after the end of our preceding financial year. Our By-laws provide that a meeting of our shareholders may be held anywhere in Canada as our board of directors may determine. Under the CBCA, and our by-laws, we must provide notice of an annual general meeting to each shareholder entitled to vote thereat, to each director, and to our auditor at least 21 days in advance of the meeting. | Under the DGCL, a corporation must hold an annual meeting of stockholders in a place designated by the certificate of incorporation or bylaws, whether inside or outside of Delaware, or, if not so designated, as determined by the board of directors and on a date and at a time designated in the bylaws, except as otherwise provided by law. Written notice of every meeting of stockholders must be given to each stockholder of record not less than 10 not more than 60 days before the date of the meeting. |

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| Special Meetings of Shareholders | <p>Under the CBCA and our by-laws, our board of directors has the power at any time to call a special meeting of shareholders. Under the CBCA, the holders of not less than 5% of our issued shares that carry the right to vote at a meeting sought to be held can also requisition our directors to call a meeting of shareholders for the purposes stated in the requisition.</p> | <p>Under the DGCL, special meetings of stockholders may be called by the board of directors or by such person or persons as may be authorized by the certificate of incorporation or the bylaws.</p> |
| Anti-takeover Provisions and Interested Shareholder Transactions | <p>As permitted by the CBCA, our Articles provide that our board of directors may fix the number of preferred shares in, and determine the designation of the shares of, each series and create, define and attach rights and restrictions to the preferred shares without shareholder approval.</p> <p>Neither the CBCA nor our Articles restrict us from adopting a shareholder rights plan. The CBCA does not restrict related party transactions; however, in Canada takeovers and other related party transactions are addressed in provincial securities legislation and policies which may apply to us.</p> | <p>Under the DGCL, a certificate of incorporation may provide the board of directors with the ability to designate the terms of and issue a new class or series of preferred stock, and to issue a stockholder rights plan. Delaware corporations are subject to Delaware's "business combination" statute. In general, such statute prohibits a corporation from engaging in any business combination transactions with an interested stockholder for a period of three years after the time that the stockholder became an interested stockholder, unless approved by the board of directors beforehand or upon satisfaction of other criteria.</p> |
| Interested Director Transactions | <p>Under the CBCA, a director who holds a disclosable interest in a material contract or transaction into which we have entered or propose to enter may generally not vote on any directors' resolution to approve the contract or transaction. A director or officer has a disclosable interest in a material contract or transaction if the director or officer is:</p> <ul style="list-style-type: none">n a party to the contract or transaction;n is a director or officer, or an individual acting in a similar capacity, of a party to the contract or transaction; orn has a material interest in a party to the contract or transaction. <p>Under the CBCA, directors do not have to abstain from voting on matters related to director compensation.</p> | <p>Under the DGCL, a transaction in which a director of the corporation has a conflict of interest is not void or voidable solely because of the director's conflict, solely because the director is present at or participates in the meeting of the board of directors or committee which authorizes the transaction or solely because any such director's vote is counted for such purpose, if (a) the material facts of the conflict of interest are known to or disclosed to the board of directors or the committee and the board of directors or committee in good faith authorizes the transaction by a majority of the votes of the disinterested directors, (b) the material facts of the conflict of interest are known or disclosed to the stockholders of the corporation and the transaction is approved in good faith by the stockholders, or (c) the board of directors can demonstrate that the transaction is fair as to the corporation as of the time it is approved by the board of directors, committee or stockholders.</p> |
| Directors' and Officers'; Liability and Indemnification | <p>As permitted under the CBCA, our by-laws, subject to certain limitations, require us to indemnify our directors or former directors or persons acting, at our request, in such capacity of a body corporate of which we are or were a direct or indirect shareholder or creditor.</p> | <p>Under the DGCL, a corporation has the power to indemnify any person who was, is or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative, or any person who was, is or is threatened to be made a party to any threatened, pending or completed action or suit by or in the right of the corporation to</p> |

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| Dissent or Dissenters' Appraisal Rights | <p>Under the CBCA dissenters' rights are generally only available in connection with:</p> <ul style="list-style-type: none">n any amalgamation with another corporation (other than with certain affiliated corporations);n an amendment to our Articles to add, change or remove any provisions restricting or constraining the issue or transfer of shares of the class in respect of which a shareholder is dissenting;n an amendment to our Articles to add, change or remove any restriction upon the business or businesses that we may carry on;n a continuance under the laws of another jurisdiction;n a sale, lease or exchange of all, or substantially all, of our property other than in the ordinary course of business;n the carrying out of a going-private or a squeeze-out transaction;n a court order permitting a shareholder to dissent in connection with an application to the court for an order approving an arrangement proposed by us; andn certain amendments to our Articles which require a separate class or series vote by a holder of shares of any class or series. | <p>procure a judgment in its favor, in each case by reason of the fact that the person is or was a director, officer, employee or agent of the corporation, against expenses, judgments, fines and amounts paid in settlement actually and reasonably incurred by the person in connection with such action, suit or proceeding if the person acted in good faith and in a manner the person reasonably believed to be in or not opposed to the best interest of the corporation, and subject to certain other limitations.</p> <p>Under the DGCL, dissenters' rights are generally only available in connection with cash mergers or mergers where the target stockholders hold stock other than stock of a widely held corporation.</p> |
| Oppression Remedy | <p>The CBCA provides an oppression remedy that enables a court to make any order, whether interim or final, to rectify matters that are oppressive or unfairly prejudicial to or that unfairly disregard the interests of any of our securityholders, creditors, directors or officers if an application is made to a court by a "complainant".</p> | <p>The DGCL does not expressly provide for a similar remedy.</p> |

A "complainant" with respect to a corporation means any of the following:

- n a present or former registered holder or beneficial owner of securities of the corporation or any of its affiliates;
- n a present or former officer or director of the corporation or any of its affiliates;
- n the director responsible for the application of the CBCA; and
- n any other person who in the discretion of the court is a proper person to make the application.

The oppression remedy provides the court with very broad and flexible powers to intervene in corporate affairs to protect our shareholders and other complainants. While conduct that is in breach of fiduciary duties of directors or that is contrary to the legal right of a complainant will normally trigger the court's jurisdiction under the oppression remedy, the exercise of that jurisdiction does not depend on a finding of a breach of those legal and equitable rights.

Shareholder
Derivative Actions

Under the CBCA, a complainant may also apply to a Canadian court for leave to bring an action in the name of, and on behalf of us, or to intervene in an existing action to which we are a party, for the purpose of prosecuting, defending or discontinuing an action on our behalf. Under the CBCA, no action may be brought and no intervention in an action may be made unless a court is satisfied that:

- n the complainant has given the required notice to our board of directors of the shareholder's intention to apply to the court if our board of directors does not bring, diligently prosecute or defend or discontinue the action;
- n the complainant is acting in good faith; and
- n it appears to be in our interests or the interest of the relevant subsidiary that the action be brought, prosecuted, defended or discontinued.

Under the CBCA, the court in a derivative action may make any order it thinks fit.

Under the DGCL, stockholders may bring derivative actions on behalf of, and for the benefit of, the corporation. The plaintiff in a derivative action on behalf of the corporation either must be or have been a stockholder of the corporation at the time of the transaction or must be a stockholder who became a stockholder by operation of law.

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| Director Qualification | Generally, at least 25% of the directors of a CBCA corporation must be resident Canadians. Furthermore, under the CBCA, no business may be transacted at a meeting of our board of directors unless 25% of the directors present, or able to provide approval of the business transacted at the meeting in writing, by telephone or other means of communication, are resident Canadians. | The DGCL does not have director residency requirements although a corporation may prescribe qualifications for directors under its certificate of incorporation or bylaws. |
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SHARES ELIGIBLE FOR FUTURE SALE

Prior to this offering, there has been no public market for our common shares, and although we expect that our common shares will be approved for listing on The NASDAQ Global Market, we cannot assure investors that there will be an active public market for our common shares following this offering. We cannot predict what effect, if any, sales of our shares in the public market or the availability of shares for sale will have on the market price of our common shares. Future sales of substantial amounts of common shares in the public market, including shares issued upon exercise of outstanding options, or the perception that such sales may occur, however, could adversely affect the market price of our common shares and also could adversely affect our future ability to raise capital through the sale of our common shares or other equity-related securities of ours at times and prices we believe appropriate.

Upon completion of this offering, based on our shares outstanding as of June 30, 2013 and after giving effect to the conversion of all outstanding convertible preferred shares and the conversion of all subscription rights, _____ of our common shares will be outstanding, or _____ common shares if the underwriters exercise their option to purchase additional common shares in full. All of the common shares expected to be sold in this offering will be freely tradable without restriction or further registration under the Securities Act unless held by our "affiliates," as that term is defined in Rule 144 under the Securities Act. The remaining _____ outstanding common shares will be deemed "restricted securities" as that term is defined under Rule 144. Restricted securities may be sold in the public market only if their offer and sale is registered under the Securities Act or if the offer and sale of those securities qualify for an exemption from registration, including exemptions provided by Rules 144 and 701 under the Securities Act, which are summarized below.

As a result of the lock-up agreements and market stand-off provisions described below and the provisions of Rules 144 or 701 and no exercise of the underwriters' option to purchase additional common shares, the common shares that will be deemed "restricted securities" will be available for sale in the public market following the completion of this offering as follows:

- ⁿ _____ shares will be eligible for sale on the date of this prospectus; and
- ⁿ _____ shares will be eligible for sale upon expiration of the lock-up agreements and market stand-off provisions described below, beginning more than 180 days after the date of this prospectus.

We may issue common shares from time to time for a variety of corporate purposes, including in capital-raising activities through future public offerings or private placements, in connection with exercise of stock options, vesting of restricted stock units and other issuances relating to our employee benefit plans and as consideration for future acquisitions, investments or other purposes. The number of common shares that we may issue may be significant, depending on the events surrounding such issuances. In some cases, the shares we issue may be freely tradable without restriction or further registration under the Securities Act; in other cases, we may grant registration rights covering the shares issued in connection with these issuances, in which case the holders of the common shares will have the right, under certain circumstances, to cause us to register any resale of such shares to the public.

Lock-Up and Market Standoff Agreements

We, our directors and officers and substantially all of the holders of our equity securities have agreed, subject to certain exceptions, not to offer, sell or transfer any of our common shares or securities convertible into or exchangeable or exercisable for our common shares, for 180 days after the date of this prospectus without first obtaining the written consent of Jefferies LLC and Cowen and Company, LLC on behalf of the underwriters, after the date of this prospectus. These agreements are described in the section of this prospectus captioned "Underwriting."

Jefferies LLC and Cowen and Company, LLC have advised us that they have no present intent or arrangement to release any common shares subject to a lock-up, and will consider the release of any lock-up on a case-by-case basis. 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.

Following the lock-up periods set forth in the agreements described above, and assuming that the representatives of the underwriters do not release any parties from these agreements and that there is no extension of the lock-up

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period, all of the common shares that are restricted securities or are held by our affiliates as of the date of this prospectus will be eligible for sale in the public market in compliance with Rule 144 under the Securities Act.

In addition to the restrictions contained in the lock-up agreements described above, our amended and restated investors' rights agreement contains market stand-off provisions imposing restrictions on the ability of certain of our security holders to offer, sell or transfer our equity securities for a period of 180 days following the effective date of this registration statement.

Rule 144

In general, under Rule 144, as currently in effect, once we have been subject to the public company reporting requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act, for at least 90 days, a person (or persons whose common shares are required to be aggregated) who is not deemed to have been one of our "affiliates" for purposes of Rule 144 at any time during the three months preceding a sale, and who has beneficially owned restricted securities within the meaning of Rule 144 for at least six months, including the holding period of any prior owner other than one of our "affiliates," is entitled to sell those shares in the public market (subject to the lock-up agreement referred to above, if applicable) without complying with the manner of sale, volume limitations or notice provisions of Rule 144, but subject to compliance with the public information requirements of Rule 144. If such a person has beneficially owned the sales proposed to be sold for at least one year, including the holding period of any prior owner other than "affiliates," then such person is entitled to sell such shares in the public market without complying with any of the requirements of Rule 144 (subject to the lock-up agreement referred to above, if applicable). In general, under Rule 144, as currently in effect, once we have been subject to the public company reporting requirements of the Exchange Act for at least 90 days, our "affiliates," as defined in Rule 144, who have beneficially owned the common shares proposed to be sold for at least six months are entitled to sell in the public market, upon expiration of any applicable lock-up agreements and within any three-month period, a number of those common shares that does not exceed the greater of:

- 1% of the number of common shares then outstanding, which will equal approximately common shares immediately after this offering (calculated on the basis of the assumptions described above and assuming no exercise of the underwriter's option to purchase additional shares and no exercise of outstanding options or warrants); or
- the average weekly trading volume of our common shares on The NASDAQ Global Market during the four calendar weeks preceding the filing of a notice on Form 144 with respect to such sale.

Such sales under Rule 144 by our "affiliates" or persons selling shares on behalf of our "affiliates" are also subject to certain manner of sale provisions, notice requirements and to the availability of current public information about us. Notwithstanding the availability of Rule 144, the holders of substantially all of our restricted securities have entered into lock-up agreements as referenced above and their restricted securities will become eligible for sale (subject to the above limitations under Rule 144) upon the expiration of the restrictions set forth in those agreements.

Rule 701

In general, under Rule 701 as currently in effect, any of our employees, directors, officers, consultants or advisors who acquired common shares from us in connection with a written compensatory stock or option plan or other written agreement in compliance with Rule 701 under the Securities Act before the effective date of the registration statement of which this prospectus is a part (to the extent such common shares are not subject to a lock-up agreement) is entitled to rely on Rule 701 to resell such common shares beginning 90 days after we become subject to the public company reporting requirements of the Exchange Act in reliance on Rule 144, but without compliance with the holding period requirements contained in Rule 144. Accordingly, subject to any applicable lock-up agreements, beginning 90 days after we become subject to the public company reporting requirements of the Exchange Act, under Rule 701 persons who are not our "affiliates," as defined in Rule 144, may resell those common shares without complying with the minimum holding period or public information requirements of Rule 144, and persons who are our "affiliates" may resell those common shares without compliance with Rule 144's minimum holding period requirements (subject to the terms of the lock-up agreement referred to above, if applicable).

Equity Incentive Plans

We intend to file with the SEC a registration statement under the Securities Act covering the common shares that we may issue upon exercise of outstanding options under our Amended and Restated Stock Plan and the common shares that we may issue pursuant to future awards under our 2013 Equity Incentive Plan. Such registration statement is expected to be filed and become effective as soon as practicable after the completion of this offering. Accordingly, common shares registered under such registration statement will be available for sale in the open market following its effective date, subject to Rule 144 volume limitations and the lock-up agreements described above, if applicable.

Registration Rights

Upon completion of this offering, the holders of approximately _____ of our common shares will be eligible to exercise certain rights to cause us to register their common shares for resale under the Securities Act, subject to various conditions and limitations. These registration rights are described under the caption "Description of Share Capital— Registration Rights." Upon the effectiveness of a registration statement covering these common shares, the common shares would become freely tradable, and a large number of common shares may be sold into the public market. If that occurs, the market price of our common shares could be adversely affected.

UNITED STATES AND CANADIAN 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:

- ⁿ an individual citizen or resident of the U.S.;
- ⁿ 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;
- ⁿ an estate, the income of which is subject to U.S. federal income taxation regardless of its source; or
- ⁿ 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:

- ⁿ a dealer in securities or currencies;
- ⁿ a financial institution;
- ⁿ a regulated investment company;
- ⁿ a real estate investment trust;
- ⁿ an insurance company;
- ⁿ a tax-exempt organization;
- ⁿ a person holding our common shares as part of a hedging, integrated or conversion transaction, a constructive sale or a straddle;
- ⁿ a trader in securities that has elected the mark-to-market method of accounting for its securities;
- ⁿ a person liable for alternative minimum tax;
- ⁿ a person who owns, directly, indirectly or constructively, or is deemed to own 10% or more of our voting common shares;
- ⁿ a partnership or other pass-through entity for U.S. federal income tax purposes; or
- ⁿ 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 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.

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. 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 2012 and we do not expect to be a PFIC in 2013, although we could be a PFIC in one or more 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. Our U.S. counsel expresses no opinion with respect to our PFIC status and also expresses no opinion 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 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.

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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 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 shares. Gain realized from the sale of our 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 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.

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.

Medicare Tax

Certain U.S. Holders who are individuals, estates or trusts will be subject to a 3.8% 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 Medicare tax to any of their income or gains in respect of our common shares.

Information Reporting and Backup Withholding

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

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

Disclosure Requirements for Specified Foreign Financial Assets

Certain U.S. Holders (and to the extent provided in IRS guidance, certain non-U.S. Holders) who hold interests in "specified foreign financial assets" (as defined in Section 6038D of the Code) are generally required to file an IRS Form 8938 as part of their U.S. federal income tax returns with information relating to such assets for each taxable year in which the aggregate value of all such assets exceeds \$75,000 at any time during the taxable year or \$50,000 on the last day of the taxable year (or such higher dollar amount as prescribed by applicable IRS guidance). "Specified foreign financial assets" generally include, among other assets, financial accounts maintained by foreign financial institutions, and our common shares, unless the 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 the common shares pursuant to this offering 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. 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 has entered into, with respect to the common shares, a "synthetic disposition agreement" or a "derivative forward agreement" as those terms are defined in the Canadian Tax Proposals (as defined below) contained in the Notice of Ways and Means Motion that accompanied the federal budget tabled by the Minister of Finance (Canada) on March 21, 2013. 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.

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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 purchasing 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 residents of Canada, or Canadian Resident Holders.

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

Dividends on the Common Shares

Dividends received or deemed to be received on the common shares by a Canadian Resident Holder who is an individual (other than certain trusts) will be included in income and will be subject to the gross-up and dividend tax credit rules normally applicable under the Canadian Tax Act to taxable dividends received from taxable Canadian corporations. 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 33 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 tax will generally be refunded to a corporate Canadian Resident Holder at the rate of \$1 for every \$3 of taxable dividends paid while it is a private corporation.

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

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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 $6\frac{2}{3}\%$ on certain investment income, including taxable capital gains (as defined below), but excluding dividends or deemed dividends deductible in computing taxable income.

Taxation of Capital Gains and Capital Losses

Generally, one-half of any capital gain (a taxable capital gain) realized by a Canadian Resident Holder for a taxation year must be included in the Canadian Resident Holder’s income in the year. 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, are subject to a minimum tax. Generally, dividends received or deemed to be received on the common shares and capital gains realized on the disposition of common shares may result in a Canadian Resident Holder being liable for minimum tax. Canadian Resident Holders should consult with their own tax advisors with respect to the potential application of the minimum tax.

Non-Residents of Canada

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

Dividends on the Common Shares

Canadian withholding tax at a rate of 25% (subject to reduction under the provisions of any applicable income tax treaty or convention) will be payable on the gross amount of dividends on the common shares paid or credited, or deemed to be paid or credited, to a Non-Resident of Canada Holder. 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. Income 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 Holder of Canada who 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

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applicable income tax treaty or convention. As long as the common shares are then listed on a "designated stock exchange" (which currently includes the 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) 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) pursuant to certain Canadian Tax Proposals released on July 12, 2013, 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 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 the 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 Losses" will generally apply to the Non-Resident of Canada Holder but any such Holder should consult its own tax advisor in this regard.

Eligibility for Investment

Based on the provisions of the Canadian Tax Act in force on the date hereof and the Canadian Tax Proposals, the common shares will be qualified investments for the purposes of the Canadian Tax Act at the time of their acquisition for trusts governed by registered retirement savings plans, or RRSPs, registered retirement income funds, or RRIFs, deferred profit sharing plans, registered education savings plans, registered disability savings plans and tax-free savings accounts, or TFSAs, each as defined in the Canadian Tax Act, or collectively, the Deferred Plans, provided that at that time the common shares are listed on a designated stock exchange (which currently includes the NASDAQ), within the meaning of the Canadian Tax Act.

Notwithstanding the foregoing, if the common shares are "prohibited investments" for a trust governed by a TFSA, an RRSP or a RRIF, the holder of such TFSA or the annuitant of such RRSP or RRIF, may be subject to a penalty tax under the Canadian Tax Act. The common shares will generally not be a "prohibited investment" for a particular trust governed by a TFSA, RRSP or a RRIF, provided the holder or annuitant, as the case may be, (i) deals at arm's length with us for purposes of the Canadian Tax Act, and (ii) does not have a "significant interest," within the meaning of the Canadian Tax Act, in (A) us or (B) any corporation, partnership or trust with which we do not deal at arm's length for purposes of the Canadian Tax Act. Canadian Tax Proposals released on December 21, 2012 propose to delete the condition in (ii)(B) above. Prospective investors should consult their tax advisors for advice as to whether the common shares will be "prohibited investments" in their particular circumstances.

Prospective subscribers who intend to hold the common shares in Deferred Plans are advised to consult their tax advisors.

UNDERWRITING

Subject to the terms and conditions set forth in the underwriting agreement, dated _____, 2013, among us and Jefferies LLC and Cowen and Company, LLC, as the representatives of the underwriters named below and the joint book-running managers of this offering, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us, the respective number of common shares shown opposite its name below:

| UNDERWRITERS | NUMBER OF SHARES |
|-----------------------------|-------------------------|
| Jefferies LLC | |
| Cowen and Company, LLC | |
| Wells Fargo Securities, LLC | |
| RBC Capital Markets, LLC | |
| Total | |

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

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

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

Commission and Expenses

The underwriters have advised us that they propose to offer the common shares to the public at the initial public offering price set forth on the cover page of this prospectus 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 initial public offering price, concession and reallowance to dealers may be reduced by the representatives. No such reduction will change the amount of proceeds to be received by us as set forth on the cover page of this prospectus.

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

| | PER SHARE | | TOTAL | |
|---|--|---|--|---|
| | WITHOUT OPTION TO PURCHASE ADDITIONAL SHARES | WITH OPTION TO PURCHASE ADDITIONAL SHARES | WITHOUT OPTION TO PURCHASE ADDITIONAL SHARES | WITH OPTION TO PURCHASE ADDITIONAL SHARES |
| Public offering price | \$ | \$ | \$ | \$ |
| Underwriting discounts and commissions paid by us | \$ | \$ | \$ | \$ |
| Proceeds to us, before expenses | \$ | \$ | \$ | \$ |

We estimate expenses payable by us in connection with this offering, other than the underwriting discounts and commissions referred to above, will be approximately \$. We have also agreed to reimburse the underwriters for certain of their expenses in an amount up to \$ as set forth in the underwriting agreement.

Determination of Offering Price

Prior to this offering, there has not been a public market for our common shares. Consequently, the initial public offering price for our common shares will be determined by negotiations between us and the representatives. Among the factors to be considered in these negotiations will be prevailing market conditions, our financial information, market valuations of other companies that we and the underwriters believe to be comparable to us, estimates of our business potential, the present state of our development and other factors deemed relevant.

We offer no assurances that the initial public offering price will correspond to the price at which our common shares will trade in the public market subsequent to the offering or that an active trading market for our common shares will develop and continue after the offering.

Listing

We intend to apply to have our common shares approved for listing on The NASDAQ Global Market under the trading symbol "XENE".

Option to Purchase Additional Shares

We have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus, to purchase, from time to time, in whole or in part, up to an aggregate of common shares from us at the public offering price set forth on the cover page of this prospectus, 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 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.

No Sales of Similar Securities

We, all our officers and directors and holders of substantially all of our outstanding common shares and other securities have agreed, subject to specified exceptions, not to directly or indirectly:

- ⁿ sell, offer, contract or grant any option to sell (including any short sale), lend, pledge, transfer, establish or increase an open "put equivalent position" or liquidate or decrease a "call equivalent position" within the meaning of Rule 16a-1(h) and Rule 16a-1(b) under the Exchange Act, or
- ⁿ otherwise dispose of any common shares, options or warrants to acquire common shares, or securities exchangeable or exercisable for or convertible into common shares currently or hereafter owned either of record or beneficially, or

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- enter into any swap, hedge or similar arrangement or agreement that transfers, in whole or in part, the economic risk of ownership of common shares, or of options or warrants to acquire common shares, or securities or rights exchangeable or exercisable for or convertible into common shares, or
- make any demand for, or exercise any right with respect to, the registration under the Securities Act of the offer and sale of any common shares, or of options or warrants to acquire common shares, or securities or rights exchangeable or exercisable for or convertible into common shares, or cause to be filed a registration statement, prospectus or prospectus supplement (or an amendment or supplement thereto) with respect to any such registration, or
- publicly announce an intention to do any of the foregoing for a period of 180 days after the date of this prospectus without the prior written consent of the representatives.

The foregoing restriction terminates after the close of trading of our common shares on and including the 180th day after the date of this prospectus and shall not apply to our issuance during the 180-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.

The representatives may, in their sole discretion and at any time or from time to time before the termination of the 180-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 shares prior to the expiration of the lock-up period.

Stabilization

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

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

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

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

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

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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

A 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 the 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, has not been approved and/or endorsed by us or the underwriters and should not be relied upon by investors.

Other Activities and Relationships

The underwriters and certain of their respective affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. The underwriters and certain of their respective affiliates have, from time to time, performed, and may in the future perform, various commercial and investment banking and financial advisory services for us and our affiliates, for which they received or will receive customary fees and expenses.

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. In particular, an affiliate of RBC Capital Markets, LLC owns Series B preferred shares, Series E preferred shares and conversion rights for Series E preferred shares, which in the aggregate represent less than 5% of our common shares as adjusted to reflect the conversion of all outstanding preferred shares and subscription rights. The affiliate of RBC Capital Markets, LLC is not selling any shares in this offering, will not receive any of the net proceeds in this offering and is subject to the sale restrictions described above under "—No Sales of Similar Securities". 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

European Economic Area. In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a "Relevant Member State") an offer to the public of any shares which are the subject of the offering contemplated by this prospectus may not be made in that Relevant Member State except that an offer to the public in that Relevant Member State of any 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 legal entities which are authorized or regulated to operate in the financial markets or, if not so authorized or regulated, whose corporate purpose is solely to invest in securities;

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- (b) to any legal entity which has two or more of (1) an average of at least 250 employees during the last financial year; (2) a total balance sheet of more than €43,000,000 and (3) an annual net turnover of more than €50,000,000, as shown in its last annual or consolidated accounts;
- (c) to fewer than 100 natural or legal persons (other than qualified investors as defined in the Prospectus Directive) subject to obtaining the prior consent of the representatives for any such offer; or
- (d) in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of the shares shall result in a requirement for the publication by us or any underwriter of a prospectus pursuant to Article 3 of the Prospectus Directive.

Each person in a Relevant Member State who receives any communication in respect of, or who acquires any shares under, the offers contemplated in this prospectus will be deemed to have represented, warranted and agreed to and with each underwriter and us that:

- (a) it is a qualified investor within the meaning of the law in that Relevant Member State implementing Article 2(1)(e) of the Prospectus Directive; and
- (b) in the case of any shares acquired by it as a financial intermediary, as that term is used in Article 3(2) of the Prospectus Directive, (i) the shares acquired by it in the offer have not been acquired on behalf of, nor have they been acquired with a view to their offer or resale to, persons in any Relevant Member State, other than qualified investors, as that term is defined in the Prospectus Directive, or in circumstances in which the prior consent of the representatives has been given to the offer or resale; or (ii) where shares have been acquired by it on behalf of persons in any Relevant Member State other than qualified investors, the offer of those shares to it is not treated under the Prospectus Directive as having been made to such persons.

For the purposes of this provision, the expression an "offer to the public" in relation to any shares 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 any shares to be offered so as to enable an investor to decide to purchase any shares, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State and the expression "Prospectus Directive" means Directive 2003/71/EC and includes any relevant implementing measure in each Relevant Member State.

United Kingdom. Each underwriter has represented, warranted and agreed that:

- (a) it has only communicated or caused to be communicated and will only communicate or cause to be communicated any invitation or inducement to engage in investment activity (within the meaning of Section 21 of the Financial Services and Markets Act 2000, or the FSMA) to persons who are investment professionals falling within Article 19(5) of the FSMA (Financial Promotion) Order 2005 or in circumstances in which Section 21(1) of the FSMA does not apply to us; and
- (b) it has complied with and will comply with all applicable provisions of the FSMA with respect to anything done by it in relation to the shares in, from or otherwise involving the United Kingdom.

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 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, will act as Canadian counsel to the underwriters.

EXPERTS

The financial statements of Xenon Pharmaceuticals Inc. as of December 31, 2011 and 2012, and for the years then ended have been included herein in reliance on the report of KPMG LLP, independent registered public accounting firm, appearing elsewhere herein, and upon the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-1 under the Securities Act with respect to the common shares offered by this prospectus. This prospectus, which constitutes a part of the registration statement, does not contain all of the information set forth in the registration statement, some items of which are contained in exhibits to the registration statement as permitted by the rules and regulations of the SEC. For further information with respect to us and the common shares offered hereby, we refer you to the registration statement, including the exhibits filed as a part of the registration statement. Statements contained in this prospectus concerning the contents of any contract or document referred to are not necessarily complete. If a contract or document has been filed as an exhibit to the registration statement, please see the copy of the contract or document that has been filed. Each statement in this prospectus relating to a contract or document filed as an exhibit is qualified in all respects by the filed exhibit.

You may read and copy the registration statement, including the exhibits and schedules thereto, at the Public Reference Room of the SEC, 100 F Street, N.E., Washington, D.C. 20549. You may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. The SEC also maintains an Internet website that contains reports, proxy statements and other information about issuers, like us, that file electronically with the SEC. The address of that website is www.sec.gov.

Upon completion of this offering, we will become subject to the information and periodic reporting requirements of the Exchange Act and, in accordance therewith, will file periodic reports, proxy statements and other information with the SEC. Such periodic reports, proxy statements and other information will be available for inspection and copying at the public reference room and website of the SEC referred to above. We maintain a website at www.xenon-pharma.com. You may access our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act with the SEC free of charge at our website as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC. The reference to our website address does not constitute incorporation by reference of the information contained on our website, and you should not consider the contents of our website in making an investment decision with respect to our common shares.

XENON PHARMACEUTICALS INC.
INDEX TO FINANCIAL STATEMENTS

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and
Shareholders of Xenon Pharmaceuticals Inc.

We have audited the accompanying balance sheets of Xenon Pharmaceuticals Inc. (the "Company") as of December 31, 2011 and 2012, and the related statements of operations, comprehensive income (loss), changes in redeemable convertible preferred shares and shareholders' deficit, and cash flows for the years then ended. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Xenon Pharmaceuticals Inc. as of December 31, 2011 and 2012 and the results of its operations and its cash flows for the years then ended, in conformity with U.S. generally accepted accounting principles.

/s/ KPMG LLP
Chartered Accountants

August 14, 2013
Vancouver, Canada

XENON PHARMACEUTICALS INC.

Balance Sheets

(Expressed in thousands of U.S. dollars except share data)

| | DECEMBER 31, | | JUNE 30, 2013 | PRO FORMA JUNE 30, 2013 (unaudited) |
|--|--------------------|--------------------|--------------------|---|
| | 2011 | 2012 | | |
| Assets | | | | |
| Current assets: | | | | |
| Cash and cash equivalents | \$ 13,928 | \$ 60,162 | \$ 49,812 | \$ |
| Marketable securities | 996 | — | — | |
| Accounts receivable | 11,415 | 392 | 763 | |
| Prepaid expenses and other current assets | 305 | 149 | 710 | |
| Total current assets | 26,644 | 60,703 | 51,285 | |
| Property, plant and equipment, net | 3,821 | 2,602 | 2,173 | |
| Total assets | \$ 30,465 | \$ 63,305 | \$ 53,458 | \$ |
| Liabilities, Shareholders' Deficit and Redeemable Convertible Preferred Shares | | | | |
| Current liabilities: | | | | |
| Accounts payable | 394 | 557 | 378 | |
| Accrued expenses | 1,209 | 1,624 | 1,469 | |
| Deferred revenue | 4,505 | 17,015 | 16,105 | |
| Deferred tenant inducements | — | 1 | — | |
| Total current liabilities | 6,108 | 19,197 | 17,952 | |
| Deferred revenue, less current portion | 6,599 | 29,637 | 20,065 | |
| Deferred tenant inducements, less current portion | — | 183 | 148 | |
| Note payable | 1,586 | 1,665 | — | |
| Total liabilities | \$ 14,293 | \$ 50,682 | \$ 38,165 | \$ |
| Collaboration agreements (See Note 13) | | | | |
| Commitments and contingencies (See Note 14) | | | | |
| Redeemable convertible preferred shares: | | | | |
| Series A Convertible Preferred shares, without par value; 5,860,000 authorized and 5,596,330 issued and outstanding at each of December 31, 2011 and 2012, and June 30, 2013 (unaudited), respectively, and no shares issued and outstanding pro forma (unaudited) | 2,939 | 2,939 | 2,939 | — |
| Series B Convertible Preferred shares, without par value; 5,000,000 authorized and 4,835,177 issued and outstanding at each of December 31, 2011 and 2012, and June 30, 2013 (unaudited), respectively, and no shares issued and outstanding pro forma (unaudited) | 8,683 | 8,683 | 8,683 | — |
| Series E Convertible Preferred shares, without par value; 21,242,673 authorized and 21,005,767 issued and outstanding at each of December 31, 2011 and 2012, and June 30, 2013 (unaudited), respectively, and no shares issued and outstanding pro forma (unaudited) | 90,866 | 90,866 | 90,866 | — |
| | 102,488 | 102,488 | 102,488 | — |
| Shareholders' deficit: | | | | |
| Common shares, without par value; unlimited shares authorized; 6,436,055 and 6,467,510 and 6,488,141 issued and outstanding at December 31, 2011 and 2012, and June 30, 2013 (unaudited), respectively, and shares issued and outstanding pro forma (unaudited) | 5,986 | 6,008 | 6,035 | |
| Additional paid-in capital | 28,772 | 29,164 | 29,457 | |
| Accumulated deficit | (124,483) | (128,784) | (125,644) | |
| Accumulated comprehensive income | 3,409 | 3,747 | 2,957 | |
| Total shareholders' deficit | \$ (86,316) | \$ (89,865) | \$ (87,195) | \$ |
| Total liabilities, shareholders' deficit and redeemable convertible preferred shares | \$ 30,465 | \$ 63,305 | \$ 53,458 | \$ |

The accompanying notes are an integral part of these financial statements.

XENON PHARMACEUTICALS INC.**Statements of Operations**

(Expressed in thousands of U.S. dollars except share and per share data)

| | YEAR ENDED DECEMBER 31, | | SIX MONTHS ENDED JUNE 30, | |
|---|-------------------------|-------------------|---------------------------|-------------------|
| | 2011 | 2012 | 2012 | 2013 |
| | | | (unaudited) | |
| Revenue | | | | |
| Collaboration revenue | \$ 6,915 | \$ 14,300 | \$ 8,207 | \$ 10,985 |
| Royalties | 3 | 8 | 3 | — |
| | <u>6,918</u> | <u>14,308</u> | <u>8,210</u> | <u>10,985</u> |
| Operating expenses: | | | | |
| Research and development | 12,237 | 10,392 | 4,770 | 6,939 |
| General and administrative | 6,795 | 7,069 | 3,561 | 2,872 |
| Total operating expenses | <u>19,032</u> | <u>17,461</u> | <u>8,331</u> | <u>9,811</u> |
| Income (loss) from operations | (12,114) | (3,153) | (121) | 1,174 |
| Other income (expense): | | | | |
| Interest income | 153 | 144 | 56 | 76 |
| Interest expense | (91) | (93) | (46) | (41) |
| Foreign exchange gain (loss) | 60 | (169) | (143) | 1,920 |
| Gain (loss) on write-off and disposal of assets | — | (1,030) | (1,197) | 11 |
| Net income (loss) | <u>(11,992)</u> | <u>(4,301)</u> | <u>(1,451)</u> | <u>3,140</u> |
| Net income (loss) attributable to participating securities | — | — | — | (3,140) |
| Net income (loss) attributable to common shareholders | <u>\$ (11,992)</u> | <u>\$ (4,301)</u> | <u>\$ (1,451)</u> | <u>\$ —</u> |
| Net income (loss) per share attributable to common shareholders: | | | | |
| Basic | <u>\$ (1.86)</u> | <u>\$ (0.67)</u> | <u>\$ (0.23)</u> | <u>\$ 0.00</u> |
| Diluted | <u>\$ (1.86)</u> | <u>\$ (0.67)</u> | <u>\$ (0.23)</u> | <u>\$ 0.00</u> |
| Weighted-average shares outstanding: | | | | |
| Basic | <u>6,433,423</u> | <u>6,451,782</u> | <u>6,443,374</u> | <u>6,477,826</u> |
| Diluted | <u>6,433,423</u> | <u>6,451,782</u> | <u>6,443,374</u> | <u>6,477,826</u> |
| Pro forma net income (loss) per share attributable to common shareholders (unaudited): | | | | |
| Basic | | <u>\$ (0.11)</u> | | <u>\$ 0.08</u> |
| Diluted | | <u>\$ (0.11)</u> | | <u>\$ 0.07</u> |
| Pro forma weighted-average shares outstanding (unaudited): | | | | |
| Basic | | <u>39,535,661</u> | | <u>39,576,671</u> |
| Diluted | | <u>39,535,661</u> | | <u>41,948,921</u> |

The accompanying notes are an integral part of these financial statements.

XENON PHARMACEUTICALS INC.
Statements of Comprehensive Income (Loss)
(Expressed in thousands of U.S. dollars)

| | YEAR ENDED DECEMBER 31, | | SIX MONTHS ENDED JUNE 30, | |
|--|----------------------------|------------------|------------------------------|----------------|
| | 2011 | 2012 | 2012 (unaudited) | 2013 |
| Net income (loss) | \$(11,992) | \$(4,301) | \$(1,451) | \$3,140 |
| Other comprehensive income (loss): | | | | |
| Foreign currency translation adjustment | (293) | 342 | (6) | (790) |
| Unrealized gain (loss) on marketable securities measured at fair value | 4 | (4) | (4) | — |
| Comprehensive income (loss) | <u>\$(12,281)</u> | <u>\$(3,963)</u> | <u>\$(1,461)</u> | <u>\$2,350</u> |

The accompanying notes are an integral part of these financial statements.

XENON PHARMACEUTICALS INC.
Statements of Changes in Redeemable Convertible Preferred Shares and Shareholders' Deficit
(Expressed in thousands of U.S. dollars except per share data)

| | SERIES A CONVERTIBLE PREFERRED SHARES | | SERIES B CONVERTIBLE PREFERRED SHARES | | SERIES E CONVERTIBLE PREFERRED SHARES | | COMMON SHARES | | ADDITIONAL PAID-IN CAPITAL | ACCUMULATED DEFICIT | ACCUMULATED COMPREHENSIVE INCOME | TOTAL SHAREHOLDER'S DEFICIT |
|--|--|-----------------|--|-----------------|---|------------------|------------------|-----------------|----------------------------------|------------------------|--|-----------------------------------|
| | SHARES | AMOUNT | SHARES | AMOUNT | SHARES | AMOUNT | SHARES | AMOUNT | | | | |
| Balance as of January 1, 2011 | 5,596,330 | \$ 2,939 | 4,835,177 | \$ 8,683 | 21,005,767 | \$ 90,866 | 6,430,791 | \$ 5,980 | \$ 28,328 | \$ (112,491) | \$ 3,698 | \$ (74,485) |
| Net loss for the year | — | — | — | — | — | — | — | — | — | (11,992) | — | — |
| Unrealized gain on fair value of marketable securities | — | — | — | — | — | — | — | — | — | — | 4 | — |
| Cumulative translation adjustment | — | — | — | — | — | — | — | — | — | — | (293) | — |
| Stock option compensation expense | — | — | — | — | — | — | — | — | 435 | — | — | — |
| Subscription rights | — | — | — | — | — | — | — | — | 12 | — | — | — |
| Issuance of common shares on conversion of subscription rights | — | — | — | — | — | — | 3,140 | 2 | (2) | — | — | — |
| Issued pursuant to exercise of stock options | — | — | — | — | — | — | 2,124 | 4 | (1) | — | — | — |
| Balance as of December 31, 2011 | <u>5,596,330</u> | <u>\$ 2,939</u> | <u>4,835,177</u> | <u>\$ 8,683</u> | <u>21,005,767</u> | <u>\$ 90,866</u> | <u>6,436,055</u> | <u>\$ 5,986</u> | <u>\$ 28,772</u> | <u>\$ (124,483)</u> | <u>\$ 3,409</u> | <u>\$ (86,316)</u> |
| Net loss for the year | — | — | — | — | — | — | — | — | — | (4,301) | — | — |
| Unrealized loss on fair value of marketable securities | — | — | — | — | — | — | — | — | — | — | (4) | — |
| Cumulative translation adjustment | — | — | — | — | — | — | — | — | — | — | 342 | — |
| Stock option compensation expense | — | — | — | — | — | — | — | — | 406 | — | — | — |
| Subscription rights | — | — | — | — | — | — | — | — | 8 | — | — | — |
| Issuance of common shares on conversion of subscription rights | — | — | — | — | — | — | 31,455 | 22 | (22) | — | — | — |
| Balance as of December 31, 2012 | <u>5,596,330</u> | <u>\$ 2,939</u> | <u>4,835,177</u> | <u>\$ 8,683</u> | <u>21,005,767</u> | <u>\$ 90,866</u> | <u>6,467,510</u> | <u>\$ 6,008</u> | <u>29,164</u> | <u>\$ (128,784)</u> | <u>\$ 3,747</u> | <u>\$ (89,865)</u> |
| Net loss for the period (unaudited) | — | — | — | — | — | — | — | — | — | 3,140 | — | — |
| Cumulative translation adjustment (unaudited) | — | — | — | — | — | — | — | — | — | — | (790) | — |
| Stock option compensation expense (unaudited) | — | — | — | — | — | — | — | — | 273 | — | — | — |
| Subscription rights (unaudited) | — | — | — | — | — | — | — | — | 43 | — | — | — |
| Issuance of common shares on conversion of subscription rights (unaudited) | — | — | — | — | — | — | 15,631 | 23 | (23) | — | — | — |
| Issued pursuant to exercise of stock options rights (unaudited) | — | — | — | — | — | — | 5,000 | 4 | — | — | — | — |
| Balance as of June 30, 2013 (unaudited) | <u>5,596,330</u> | <u>\$ 2,939</u> | <u>4,835,177</u> | <u>\$ 8,683</u> | <u>21,005,767</u> | <u>\$ 90,866</u> | <u>6,488,141</u> | <u>\$ 6,035</u> | <u>\$ 29,457</u> | <u>\$ (125,644)</u> | <u>\$ 2,957</u> | <u>\$ (87,195)</u> |

The accompanying notes are an integral part of these financial statements.

XENON PHARMACEUTICALS INC.
Statements of Cash Flows
(Expressed in thousands of U.S. dollars)

| | YEAR ENDED DECEMBER 31, | | SIX MONTHS ENDED JUNE 30, | |
|--|----------------------------|-----------------|------------------------------|------------------|
| | 2011 | 2012 | 2012 | 2013 |
| | | | (unaudited) | |
| Operating activities: | | | | |
| Net income (loss) | \$(11,992) | \$ (4,301) | \$ (1,451) | \$ 3,140 |
| Adjustments to reconcile net income (loss) to net cash provided by (used in) operating activities: | | | | |
| Depreciation and amortization | 1,132 | 786 | 614 | 372 |
| Gain (loss) on write-off and disposal of assets | — | 1,030 | 1,197 | (11) |
| Stock-based compensation | 435 | 406 | 204 | 273 |
| Non-cash expense on issuance of subscription rights | 12 | 8 | 6 | 43 |
| Interest accrued on note payable | 78 | 77 | 40 | 35 |
| Deferred tenant inducements | — | 183 | — | (27) |
| Foreign exchange loss (gain) | (88) | (34) | (17) | 33 |
| Changes in operating assets and liabilities: | | | | |
| Accounts receivable | (11,008) | 11,230 | 8,852 | (423) |
| Prepaid expenses, and other current assets | (107) | 162 | 191 | (589) |
| Accounts payable and accrued expenses | (354) | 540 | (638) | (195) |
| Deferred revenue | 8,203 | 35,486 | (2,852) | (8,265) |
| Net cash provided by (used in) operating activities | <u>(13,689)</u> | <u>45,573</u> | <u>6,146</u> | <u>(5,614)</u> |
| Investing activities: | | | | |
| Purchases of property, plant and equipment, | (290) | (526) | (93) | (68) |
| Sale of property, plant and equipment | — | 7 | — | — |
| Proceeds from marketable securities | 14,179 | 1,010 | 1,003 | — |
| Net cash provided by (used in) investing activities | <u>13,889</u> | <u>491</u> | <u>910</u> | <u>(68)</u> |
| Financing activities: | | | | |
| Note payable | — | — | — | (1,701) |
| Proceeds from issuance of common shares | 2 | — | — | 4 |
| Net cash provided by (used in) financing activities | <u>2</u> | <u>—</u> | <u>—</u> | <u>(1,697)</u> |
| Effect of exchange rate changes on cash and cash equivalents | (314) | 170 | (122) | (2,971) |
| Increase (decrease) in cash and cash equivalents | (112) | 46,234 | 6,934 | (10,350) |
| Cash and cash equivalents, beginning of period | 14,040 | 13,928 | 13,928 | 60,162 |
| Cash and cash equivalents, end of period | <u>\$ 13,928</u> | <u>\$60,162</u> | <u>\$20,862</u> | <u>\$ 49,812</u> |
| Supplemental information: | | | | |
| Non-cash transactions: | | | | |
| Fair value of stock options transferred from additional paid-in capital to share capital on exercise | \$ 1 | — | — | — |
| Issuance of common shares on conversion of subscription rights | \$ 2 | \$ 22 | \$ 11 | \$ 2 |
| Interest paid | \$ (13) | \$ (16) | \$ (6) | \$ (207) |

The accompanying notes are an integral part of these financial statements.

XENON PHARMACEUTICALS INC.

Notes to Financial Statements

(Expressed in thousands of U.S. dollars except share and per share figures)

1. Nature of the Business and Basis of Presentation:

Description of business:

(a) Xenon Pharmaceuticals Inc. (the "Company"), incorporated in 1996 under the British Columbia Business Corporations Act and continued federally in 2000 under the Canada Business Corporation Act, is a biopharmaceutical company focused on the development of novel medicines through the application of the Company's proprietary discovery platform, which it refers to as Extreme Genetics.

Historically, the Company has funded operations primarily through payments received from its pharmaceutical collaborators and government funding as well as through the sale of redeemable convertible preferred shares in various financing transactions. The Company is seeking to complete an Initial Public Offering ("IPO") of its common shares in the United States. In the event that the Company does not complete an IPO, the Company may seek alternative funding, such as through existing or new collaboration agreements or through private financings.

The accompanying financial statements are prepared in accordance with accounting principles generally accepted in the United States of America ("U.S. GAAP").

These financial statements are presented in U.S. dollars.

(b) Unaudited interim financial information:

The accompanying balance sheet as of June 30, 2013, statements of operations, comprehensive income (loss) and of cash flows for the six months ended June 30, 2012 and 2013, and the statement of changes in redeemable convertible preferred shares and shareholders' deficit for the six months ended June 30, 2013 are unaudited. The interim unaudited financial statements have been prepared on the same basis as the annual audited financial statements and, in the opinion of management, reflect all adjustments, which include only normal recurring adjustments, necessary for the fair statement of the Company's financial position as of June 30, 2013 and the results of its operations, its comprehensive income (loss) and its cash flows for the six months ended June 30, 2012 and 2013. The financial data and other information disclosed in these notes related to the six months ended June 30, 2012 and 2013 are unaudited. The results for the six months ended June 30, 2013 are not necessarily indicative of results to be expected for the year ending December 31, 2013, any other interim periods, or any future year or period.

(c) Unaudited pro forma information:

On August 12, 2013, the Company's Board of Directors authorized the Company to submit a confidential draft registration statement to the Securities and Exchange Commission to sell its common shares to the public. Upon the closing of a qualified IPO satisfying certain threshold requirements, or approved by a combination of shareholder votes representing a majority of all preferred shares, along with a majority of the Series B shares and a majority of the Series E shares, all of the outstanding redeemable convertible preferred shares (see Note 9) will automatically convert into common shares. The accompanying unaudited pro forma balance sheet as of June 30, 2013 has been prepared to give effect to (i) the automatic conversion of all of the outstanding redeemable convertible preferred shares, plus additional applicable conversion rights, into 33,029,489 common shares, converted on a 1:1 basis and (ii) the exchange of all outstanding subscription rights into common shares as though the proposed IPO had occurred on June 30, 2013. Unaudited pro forma basic and diluted net income (loss) per share attributable to common shareholders for the year ended December 31, 2012 and the six months ended June 30, 2013 has been prepared to give effect to (i) the automatic conversion of all of the outstanding redeemable convertible preferred shares, plus additional applicable conversion rights, into 33,029,489 common shares, converted on a 1:1 basis and (ii) the exchange of all outstanding subscription rights into common shares as though the proposed IPO had occurred on January 1, 2012.

XENON PHARMACEUTICALS INC.**Notes to Financial Statements**

(Expressed in thousands of U.S. dollars except share and per share figures) (continued)

2. Significant Accounting Policies:**(a) Use of estimates:**

The preparation of financial statements in conformity with U.S. GAAP requires the Company to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenue and expenses during the reporting period. Significant areas of estimates include, but are not limited to, the valuation of accounts receivable, the estimated useful lives of property, plant and equipment, the recoverability of long-lived assets, the timing of revenue recognition, the determination of stock-based compensation and the assessment of contingent liabilities. Actual results could differ materially from those estimates. Estimates and assumptions are reviewed quarterly. All revisions to accounting estimates are recognized in the period in which the estimates are revised and in any future periods affected.

(b) Cash and cash equivalents:

Cash equivalents are highly liquid investments that are readily convertible into cash with terms to maturity of three months or less when acquired.

(c) Segment and geographic information:

Operating segments are defined as components of an enterprise about which separate discrete information is available for evaluation by the chief operating decision maker, or decision making group, in deciding how to allocate resources and in assessing performance. The Company views its operations and manages its business in one operating segment.

(d) Property, plant and equipment:

Property, plant and equipment is stated at historical cost less accumulated depreciation and/or accumulated impairment losses, if any. Subsequent costs are included in the asset's carrying amount or recognized as a separate asset, as appropriate, only when it is probable that future economic benefits associated with the item will flow to the Company and the cost of the item can be measured reliably. All other repairs and maintenance are charged to net loss during the financial period in which they are incurred.

Property, plant and equipment are recorded at cost and are amortized over their estimated useful lives using the straight-line method based on the following rates:

| <u>ASSET</u> | <u>RATE</u> |
|--------------------------------|--|
| Research equipment | 5 years |
| Office furniture and equipment | 5 years |
| Computer equipment | 3 years |
| Leasehold improvements | Over the lesser of lease term or estimated useful life |

(e) Impairment of long-lived assets:

The Company monitors its long-lived assets for indicators of impairment. If such indicators are present, the Company assesses the recoverability of affected assets by determining whether the carrying value of such assets is less than the sum of the undiscounted future cash flows of the assets. If such assets are found not to be recoverable, the Company measures the amount of such impairment by comparing the carrying value of the assets to the fair value of the assets, with the fair value generally determined based on the present value of the expected future cash flows associated with the assets. Although current and historical negative cash flows are indicators of impairment, the Company believes that the future cash flows it will receive from the long-lived assets and the potential success of the Company's research programs will exceed the assets' carrying value, and accordingly, the Company believes that no impairment of long-lived assets existed as of December 31, 2011 and 2012, and June 30, 2013 (unaudited).

XENON PHARMACEUTICALS INC.**Notes to Financial Statements**

(Expressed in thousands of U.S. dollars except share and per share figures) (continued)

2. Significant Accounting Policies (continued):

(f) Concentration of credit risk and of significant collaborators:

Financial instruments that potentially subject the Company to significant concentrations of credit risk consist primarily of cash and cash equivalents and accounts receivable. Cash and cash equivalents are invested through banks and other financial institutions in the U.S. and Canada. Such deposits may be in excess of insured limits. The Company maintains cash and cash equivalents with various high credit quality and capitalized financial institutions.

Accounts receivable are unsecured and primarily represent amounts due from our pharmaceutical collaborators. Accordingly, the Company may be exposed to credit risk generally associated with pharmaceutical companies or specific to the collaboration agreements with Teva, Genentech and Merck. To date the Company has not experienced any material losses related to its receivables.

Collaborators whose collaboration research and development revenue accounted for 10% or more of total revenue were as follows:

| | YEAR ENDED DECEMBER 31, | | SIX MONTHS ENDED |
|-----------|----------------------------|----------|------------------------------|
| | 2011 | 2012 | JUNE 30, 2013 (unaudited) |
| Genentech | — | \$ 6,948 | \$ 3,916 |
| Merck | \$ 6,389 | 5,562 | — |
| Teva | — | — | 6,901 |

(g) Financial instruments and fair value:

Marketable securities

Marketable securities are highly liquid investments with terms to maturity of greater than three months when acquired. Marketable securities have varying maturities of less than 12 months, are classified as available-for-sale investments and are measured at their fair values under Level 1 of the fair value hierarchy with unrealized holding gains or losses reported in other comprehensive income.

Fair value

U.S. GAAP establishes a fair value hierarchy for inputs to be used to measure fair value of financial assets and liabilities. This hierarchy prioritizes the inputs to valuation techniques used to measure fair value into three levels: Level 1 (highest priority), Level 2, and Level 3 (lowest priority).

- ⁿ *Level 1*—Unadjusted quoted prices in active markets for identical assets or liabilities that the Company has the ability to access at the balance sheet date.
- ⁿ *Level 2*—Inputs other than quoted prices included within Level 1 that are observable for the asset or liability, either directly or indirectly. Level 2 inputs include quoted prices for similar assets and liabilities in active markets, quoted prices for identical or similar assets or liabilities in markets that are not active, inputs other than quoted prices that are observable for the asset or liability (i.e., interest rates, yield curves, etc.), and inputs that are derived principally from or corroborated by observable market data by correlation or other means (market corroborated inputs).
- ⁿ *Level 3*—Inputs are unobservable and reflect the Company's assumptions as to what market participants would use in pricing the asset or liability. The Company develops these inputs based on the best information available.

XENON PHARMACEUTICALS INC.

Notes to Financial Statements

(Expressed in thousands of U.S. dollars except share and per share figures) (continued)

2. Significant Accounting Policies (continued):

Cash equivalents and marketable securities are reflected in the accompanying financial statements at fair value using Level 1. The carrying amount of accounts receivables, accounts payable and accrued expenses and note payable approximates fair value due to the nature and short-term of those instruments.

(h) Revenue recognition:

The Company recognizes revenue when all of the following criteria are met: (i) persuasive evidence of an arrangement exists; (ii) delivery has occurred or services have been rendered; (iii) the Company's price to the collaborator is fixed or determinable; and (iv) collectability is reasonably assured.

The Company generates revenue primarily through collaboration agreements.

Under these collaboration agreements, the Company is eligible to receive non-refundable upfront payments, funding for research and development services, milestone payments, other contingent payments and royalties. In assessing the appropriate revenue recognition related to a collaboration agreement, the Company first determines whether an arrangement includes multiple elements, such as the delivery of intellectual property rights and research and development services. Upfront payments are recorded as deferred revenue in the balance sheet and are recognized as collaboration revenue over the estimated period of research performance that is consistent with the terms of the research and development obligations contained in the collaboration agreement. The Company periodically reviews the estimated period of performance based on the progress made under each arrangement.

The Company recognizes funding related to full-time equivalent staffing funded through collaboration agreements as revenue on a gross basis as it performs or delivers such related services in accordance with the agreement terms, provided that it will receive payment for such services upon standard payment terms.

In January 2011, the Company adopted new authoritative guidance on revenue recognition for multiple element arrangements, Financial Accounting Standards Board ("FASB") Accounting Standards Update ("ASU") No. 2009-13, *Multiple-Deliverable Revenue Arrangements* ("ASU 2009-13"). This guidance, which applies to multiple element arrangements entered into or materially modified on or after January 1, 2011, amends the criteria for separating and allocating consideration in a multiple element arrangement by modifying the fair value requirements for revenue recognition and eliminating the use of the residual method. The estimated fair value of deliverables under the arrangement may be derived using a best estimate of selling price if vendor-specific objective evidence and third-party evidence are not available. Deliverables under the arrangement will be separate units of accounting provided that a delivered item has value to the customer on a stand-alone basis and if the arrangement does not include a general right of return relative to the delivered item and delivery or performance of the undelivered items is considered probably and substantially in the control of the vendor. The update also provided new guidance regarding how to apply the standard to arrangements that are materially modified following adoption of the update. The potential future impact of the adoption of this update will depend on the nature of any new agreements entered into or material modifications to existing arrangements.

In January 2011, the Company also adopted the guidance FASB ASU No. 2010-17, *Milestones Method of Revenue Recognition* ("ASU 2010-17") that permits the recognition of revenue contingent upon its achievement of a milestone in its entirety, in the period the milestone is achieved, only if the milestone meets certain criteria and is considered to be substantive.

The Company makes judgments which affect the periods over which the Company recognized revenue, including modifying such periods based on any amendments to its collaboration agreements.

(i) Research and development costs:

Research and development costs are expensed in the period in which they are incurred.

XENON PHARMACEUTICALS INC.

Notes to Financial Statements

(Expressed in thousands of U.S. dollars except share and per share figures) (continued)

2. Significant Accounting Policies (continued):

(j) Clinical trial expenses:

Clinical trial expenses are a component of research and development costs and include fees paid to contract research organizations, investigators and other vendors who conduct certain product development activities on behalf of the Company. The amount of clinical trial expenses recognized in a period related to service agreements is based on estimates of the work performed using an accrual basis of accounting. These estimates are based on patient enrollment, services provided and goods delivered, contractual terms and experience with similar contracts. The Company monitors these factors and adjusts the estimates accordingly. Prepaid expenses or accrued liabilities are adjusted if payments to service providers differ from estimates of the amount of service completed in a given period.

(k) Share-based compensation:

The Company grants stock options to employees, directors and consultants pursuant to a stock option plan described in Note 11. Compensation expense is recorded for stock options issued to employees and non-employees using the fair value method with a corresponding increase in additional paid-in capital. Any consideration received on exercise of stock options and the purchase of shares is credited to share capital.

Under the fair value based method, share-based payments to non-employees are measured at the fair value of the equity instruments issued, and the awards are periodically re-measured during the vesting period as the options are earned. Any changes therein are recognized over the period, and in the same manner as if the Company had paid cash instead of paying with or using equity instruments. The fair value of stock-based awards to employees is measured at the grant date and amortized over the vesting period.

Stock options issued to employees are recorded at the fair value of stock options determined at the date of the grant using the Black-Scholes option-pricing model and a single option award approach and are expensed on a straight-line basis over the vesting period of the options. In determining the expense, the Company deducts the number of options that are expected to be forfeited at the time of a grant and revises this estimate, if necessary, in subsequent years if actual forfeitures differ from those estimated. Any amounts paid by employees on exercise of the stock options and subsequent purchase of shares are credited to share capital.

(l) Net income (loss) per share:

The Company follows the two-class method when computing net income (loss) per share as the Company has issued shares that meet the definition of participating securities. The two-class method determines net income (loss) per share for each class of common and participating securities according to dividends declared or accumulated and participation rights in undistributed earnings. The two-class method requires income available to common shareholders for the period to be allocated between common and participating securities based upon their respective rights to receive dividends as if all income for the period had been distributed.

The Company's redeemable convertible preferred shares contractually entitle the holders of such shares to participate in dividends, but do not contractually require the holders of such shares to participate in losses of the Company. Accordingly, in periods in which the Company reports a net loss or a net loss attributable to common shareholders resulting from preferred share dividends or accretion, net losses are not allocated to participating securities. The Company reported a net loss attributable to common shareholders for each of the years ended December 31, 2011 and 2012 and for the six months ended June 30, 2012 (unaudited).

Basic net income (loss) per share attributable to common shareholders is computed by dividing the net income (loss) attributable to common shareholders by the weighted-average number of common shares outstanding for the period. Diluted net income (loss) attributable to common shareholders is computed by adjusting net income (loss) attributable to common shareholders to reallocate undistributed earnings based on the potential impact of dilutive securities, including outstanding stock options and outstanding subscription rights. Diluted net income (loss) per share attributable to common shareholders is computed by dividing the diluted net income (loss) attributable to

XENON PHARMACEUTICALS INC.

Notes to Financial Statements

(Expressed in thousands of U.S. dollars except share and per share figures) (continued)

2. Significant Accounting Policies (continued):

common shareholders by the weighted-average number of common shares outstanding for the period, including potential dilutive common shares assuming the dilutive effect of outstanding stock options and outstanding subscription rights. For periods in which the Company has reported net losses, diluted net loss per share attributable to common shareholders is the same as basic net loss per share attributable to common shareholders, since dilutive common shares are not assumed to have been issued if their effect is anti-dilutive. Diluted net loss per share attributable to common shareholders is the same as basic net loss per share attributable to common shareholders for each of the years ended December 31, 2011 and 2012 and for the six months ended June 30, 2012 (unaudited).

(m) Foreign currency translation:

The Company's functional currency is the Canadian dollar and the Company's reporting currency is the U.S. dollar. The Company initially records foreign currency transactions using the exchange rates prevailing at the dates of the transactions. At the balance sheet date, results of operations and cash flows are translated into the functional currency at average exchange rates during the period, and monetary assets and liabilities are translated at end of period exchange rates. Non-monetary assets and liabilities and equity transactions are translated at historical exchange rates. The effects of exchange rate fluctuations on translating foreign currency monetary assets and liabilities into Canadian dollars are included in the statement of operations as foreign exchange gain (loss).

At the balance sheet date, results of operations and cash flows are translated into the U.S. dollar reporting currency at average exchange rates during the period, and assets and liabilities are translated at end of period exchange rates, except for equity transactions, which are translated at historical exchange rates. The effects of exchange rate fluctuations on translating functional currency assets and liabilities into U.S. dollars are accumulated as a separate component in other accumulated comprehensive income (loss) as cumulative translation adjustment.

(n) Income taxes:

Deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases and net operating loss and credit carryforwards. Deferred tax assets and liabilities are measured at rates expected to apply to taxable income in the years in which those temporary differences and carryforwards are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in the statement of operations in the period that includes the enactment date. A valuation allowance is recorded when it is not more likely than not that all or a portion of the net deferred tax assets will be realized.

(o) Deferred tenant inducements:

Deferred tenant inducements, which include leasehold improvements paid for by the landlord and free rent, are recorded as liabilities on the balance sheet and recognized as a reduction of rent expense on a straight-line basis over the term of the lease.

3. Recent Accounting Pronouncements:

In May 2011, in an effort to assist in the convergence of U.S. GAAP and International Financial Reporting Standards ("IFRS"), the FASB issued an ASU related to "Fair Value Measurements: Amendments to Achieve Common Fair Value Measurements and Disclosure Requirements in U.S. GAAP and IFRSs." The standard expands existing disclosure requirements for fair value measurements and makes certain other amendments, including a requirement to categorize, by level in the fair value hierarchy, items that are required to be disclosed, but not measured, at fair value. The standard is effective for fiscal years, and interim periods within those years, beginning after December 15, 2011, and should be applied prospectively. The Company adopted this standard as of January 1, 2012 and its adoption did not have a material effect on the Company's financial statements for the year ended December 31, 2012.

XENON PHARMACEUTICALS INC.

Notes to Financial Statements

(Expressed in thousands of U.S. dollars except share and per share figures) (continued)

4. Fair Value of Financial Instruments:

In accordance with the fair value hierarchy described in Note 2(g), the following tables show the fair value of the Company's financial assets that are required to be measured at fair value:

| | FAIR VALUE MEASUREMENTS AT DECEMBER 31, 2011 | | | |
|---------------------------|--|------------------|----------|----------|
| | TOTAL | LEVEL 1 | LEVEL 2 | LEVEL 3 |
| Assets | | | | |
| Cash and cash equivalents | \$ 13,928 | \$ 13,928 | — | — |
| Marketable securities | 996 | 996 | — | — |
| Total | <u>\$ 14,924</u> | <u>\$ 14,924</u> | <u>—</u> | <u>—</u> |

| | FAIR VALUE MEASUREMENTS AT DECEMBER 31, 2012 | | | |
|---------------------------|--|------------------|----------|----------|
| | TOTAL | LEVEL 1 | LEVEL 2 | LEVEL 3 |
| Assets | | | | |
| Cash and cash equivalents | \$ 60,162 | \$ 60,162 | — | — |
| Total | <u>\$ 60,162</u> | <u>\$ 60,162</u> | <u>—</u> | <u>—</u> |

| | FAIR VALUE MEASUREMENTS AT JUNE 30, 2013 | | | |
|---------------------------|--|------------------|----------|-------------|
| | TOTAL | LEVEL 1 | LEVEL 2 | LEVEL 3 |
| | | | | |
| | | | | (unaudited) |
| Assets | | | | |
| Cash and cash equivalents | \$ 49,812 | \$ 49,812 | — | — |
| Total | <u>\$ 49,812</u> | <u>\$ 49,812</u> | <u>—</u> | <u>—</u> |

The Company's Level 1 assets include marketable securities with quoted prices in active markets.

The marketable securities are classified as available-for-sale investments with an amortization cost of \$992 and fair value of \$996 at December 31, 2011. The unrealized gain of \$4 is reported in other comprehensive income. The security matured on January 3, 2012 with final proceeds of \$996 received.

5. Accrued Expenses:

Accrued expenses consisted of the following:

| | DECEMBER 31, | | JUNE 30, |
|--|-----------------|-----------------|-----------------|
| | 2011 | 2012 | 2013 |
| | | | (unaudited) |
| Employee compensation, benefits and related accruals | \$ 699 | \$ 1,111 | \$ 359 |
| Consulting and contracted research | 210 | 236 | 420 |
| Professional fees | 291 | 233 | 634 |
| Other | 9 | 44 | 56 |
| Total | <u>\$ 1,209</u> | <u>\$ 1,624</u> | <u>\$ 1,469</u> |

XENON PHARMACEUTICALS INC.**Notes to Financial Statements**

(Expressed in thousands of U.S. dollars except share and per share figures) (continued)

6. Property, Plant and Equipment:

Property, plant and equipment consisted of the following:

| | DECEMBER 31, | | JUNE 30, |
|---|-----------------|-----------------|-----------------|
| | 2011 | 2012 | 2013 |
| Research equipment | \$ 6,872 | \$ 7,354 | \$ 7,027 |
| Office furniture and equipment | 1,619 | 1,144 | 1,083 |
| Computer equipment | 2,051 | 1,915 | 1,812 |
| Leasehold improvements | 10,538 | 7,296 | 6,905 |
| Less: accumulated depreciation and amortization | <u>(17,259)</u> | <u>(15,107)</u> | <u>(14,654)</u> |
| Total | <u>\$ 3,821</u> | <u>\$ 2,602</u> | <u>\$ 2,173</u> |

During the year ended December 31, 2012, the Company wrote off leasehold improvements with a net book value of \$1,030 in connection with a lease extension and modification agreement made effective April 1, 2012.

Depreciation expense was \$1,132 and \$786 for the years ended December 31, 2011 and 2012, respectively, and was \$614 and \$372 for the six months ended June 30, 2012 and 2013 (unaudited), respectively.

7. Deferred Revenue:

The Company receives upfront payments under various research and collaboration agreements. In assessing the appropriate revenue recognition related to a collaboration agreement, the Company first determines whether an arrangement includes multiple elements, such as the delivery of intellectual property rights and research and development services. Upfront payments are recorded as deferred revenue in the balance sheet and are recognized as collaboration revenue over the estimated period of the research commitment that is consistent with the terms of the research and development obligations contained in the collaboration agreement. The Company periodically reviews the estimated period of performance based on the progress made under each arrangement. The full amount as of December 31, 2012 of \$46,652 is expected to be realized as revenue as follows:

| YEAR ENDING DECEMBER 31, | |
|--------------------------|------------------|
| 2013 | \$ 17,015 |
| 2014 | 16,931 |
| 2015 | <u>12,706</u> |
| Deferred revenue | <u>\$ 46,652</u> |

8. Note Payable:

In November 2010, the Company entered into a collaboration and licensing agreement with Isis Pharmaceuticals, Inc. ("Isis") to discover, develop and commercialize antisense drugs that target the hepcidin-homojuvelin pathway. Upon signing the agreement, the Company issued a convertible promissory note to Isis as payment of an upfront fee of \$1,500. The note accrued interest at 5% per annum, compounded annually with interest payable at the time the note became due and payable. At the option of the Company, the note was convertible into equity securities upon occurrence of certain events specified in the note. As the number of equity securities that the note payable was potentially convertible into was variable until the time of conversion, the note was classified as a financial liability and measured at its amortized cost.

XENON PHARMACEUTICALS INC.

Notes to Financial Statements

(Expressed in thousands of U.S. dollars except share and per share figures) (continued)

8. Note Payable (continued):

At December 31, 2012, the note payable balance is comprised of the principal of \$1,500 (2011—\$1,500) and accrued interest of \$165 (2011—\$86).

In June 2013, the Company repaid the promissory note in full in cash (together with accrued interest) for \$1,701 in conjunction with the exercise of an option to exclusively license product rights under the collaboration with Isis (unaudited).

9. Redeemable Convertible Preferred Shares:

The rights and preferences of the shares of Series A, Series B and Series E convertible preferred shares (collectively, the "Redeemable Convertible Preferred Shares") are as follows:

Dividends—Holders of Series A, Series B and Series E preferred shares are entitled to receive non-cumulative cash dividends, in preference to any dividend payable on the common shares, at a rate of 8% per annum of the issue price of the preferred share when and as declared by the Board, but only if any dividends are declared on the common shares. In addition, holders of the Series A, Series B and Series E preferred shares will be entitled to receive, when and as declared by the Board, dividends in an amount equal to any dividend per common share declared by the Board on the common shares multiplied by the number of common shares that would be issued in exchange for the Series A, Series B and Series E preferred shares upon conversion.

Conversion—Each Series A, Series B, and Series E preferred share is convertible at any time at the option of the holder into common shares on a 1:1 basis, subject to certain adjustments for share splits, consolidations, stock dividends, and, as applicable, following certain capital reorganizations or mergers or acquisitions with another company as well as certain adjustments based on whether any common shares have been issued during certain specified time periods at a price per share which is lower than certain threshold amounts as set forth in the articles. Each of the Series A, Series B and Series E preferred shares will automatically convert into common shares in connection with an IPO satisfying certain threshold requirements.

As part of a financing of additional Series E preferred shares in 2006, those Series E preferred shares held by shareholders prior to the March 31, 2006 financing received additional conversion rights. Upon (1:1) conversion of such Series E preferred shares to common shares, these conversion rights operate to allow such shareholders to receive an additional number of common shares (such additional number which is equal to the number of conversion rights each holds). As of December 31, 2012, a total of 1,592,215 conversion rights are attached to the Company's Series E preferred shares.

Voting—At general meetings of the shareholders, each preferred shareholder is entitled to the number of votes that such shareholder would be entitled to if such preferred shares were converted to common shares. At meetings of the preferred class of shareholders or meetings of any series of the preferred class, each preferred shareholder is entitled to one vote.

Liquidation Preference—Upon the liquidation, dissolution, reorganization or winding-up of the Company, holders of preferred shares are entitled to receive, before any distribution or payment on the common shares, an amount equal to the amount such shareholder paid for such preferred shares, plus all declared, but unpaid, dividend (the "liquidation preference"). In cases where the liquidation preference applied, if there were insufficient funds to pay the full preference value to all holders, then, as a group, the holders of the preferred shares would be paid, ratably. To the extent there were excess assets to distribute, the holders of the preferred shares are entitled to a further distribution ratably along with the common shareholders. Dividends are payable only if and when declared. The Company has not declared any dividends through both December 31, 2012 and June 30, 2013 (unaudited).

Redemption—There are certain redemption rights afforded the Series A, Series B and Series E preferred shares. Such preferred shares have redemption rights in the event of a change of control event such as a merger, acquisition

XENON PHARMACEUTICALS INC.

Notes to Financial Statements

(Expressed in thousands of U.S. dollars except share and per share figures) (continued)

9. Redeemable Convertible Preferred Shares (continued):

or consolidation of the Company, or in the event of a sale, lease or other disposition of all or substantially all of the assets of the Company. Such events are not solely within the control of the Company, and therefore, the redeemable convertible preferred shares are classified outside of shareholders' deficit.

Retraction—The Company has the right to redeem Series A preferred shares at a redemption price equal to the greater of the fair market value of such Series A preferred share and the amount paid by such shareholder together with an amount equal to the cumulative annual yield calculated since the date of issuance of such shares at the rate of 8% per annum on the amount paid up thereon.

The Company has also authorized 4,620 Series C preferred shares and 9,376 Series D preferred shares. No Series C or D preferred shares are outstanding.

10. Subscription Rights:

At December 31, 2012, the Company had 54,390 (2011—74,055) subscription rights outstanding to Genome BC (See Note 13(a)). During the year ended December 31, 2012, 31,455 (2011—3,140) subscription rights were converted by Genome BC to an equal number of common shares.

During the six months ended June 30, 2013, 30,597 additional subscription rights were issued to Genome BC and 15,631 subscription rights were converted to an equal number of common shares, thus leaving 69,356 subscription rights outstanding to Genome BC as of June 30, 2013 (unaudited).

In exchange for research funding provided by Genome BC, the Company agreed to provide Genome BC with subscription rights on a quarterly basis (in arrears) equal to one-half of the Genome BC funding amount divided by the greatest of the following: (i) CAD\$10.64; (ii) the converted U.S. dollar share price; and (iii) the most recent issue price of common shares by the Company. The subscription rights are automatically exchangeable into common shares of the Company on a 1:1 basis on a date three years after the subscription right is issued without additional cash consideration being paid by Genome BC. In the event of an IPO, sale or liquidation of the Company, the remaining subscription rights would be automatically exchanged for common shares immediately prior to such event.

11. Stock Option Plan:

The Company has a stock option incentive plan (the "Plan") that provides for the Company to grant options for the purchase of common shares to directors, officers, employees and service providers, with vesting occurring on a graduated basis over a four-year period or less. Options may be exercised over a term of ten years.

As of both December 31, 2011 and 2012, the Company was authorized to grant up to 6,531,977 options under the Plan. In January 2013, the Plan was amended and restated to increase the maximum number of options under the Plan to 7,373,338 (unaudited). The Plan is administered by the Board and exercise prices, vesting and other restrictions are all determined at their discretion.

XENON PHARMACEUTICALS INC.

Notes to Financial Statements

(Expressed in thousands of U.S. dollars except share and per share figures) (continued)

11. Stock Option Plan (continued):

Summary of stock option activity is as follows:

| | NUMBER OF OPTIONS | WEIGHTED-AVERAGE EXERCISE PRICE | | WEIGHTED- AVERAGE REMAINING CONTRACTUAL LIFE (YEARS) | AGGREGATE INTRINSIC VALUE U.S.\$ |
|--|----------------------|------------------------------------|--------|---|---|
| | | CAD\$ | U.S.\$ | | |
| Outstanding, January 1, 2011 | 5,105,162 | 0.90 | 0.90 | | |
| Granted | 1,166,250 | 0.77 | 0.78 | | |
| Exercised | (2,124) | 0.74 | 0.75 | | |
| Forfeited and expired | (1,120,067) | 0.82 | 0.83 | | |
| Outstanding, December 31, 2011 | 5,149,221 | 0.88 | 0.87 | 6.07 | |
| Granted | 729,500 | 0.75 | 0.75 | | |
| Forfeited and expired | (394,515) | 1.08 | 1.08 | | |
| Outstanding, December 31, 2012 | 5,484,206 | 0.85 | 0.86 | 5.81 | |
| Granted | 1,214,150 | 0.55 | 0.53 | | |
| Exercised | (5,000) | 1.25 | 1.23 | | |
| Forfeited and expired | (353,765) | 1.00 | 0.98 | | |
| Outstanding, June 30, 2013 (unaudited) | <u>6,339,591</u> | 0.79 | 0.75 | 6.24 | 7,354 |

The following table summarizes the stock options outstanding and exercisable at December 31, 2011, 2012 and June 30, 2013 (unaudited):

| EXERCISE PRICES CAD\$ | OPTIONS OUTSTANDING | | | | OPTIONS EXERCISABLE | | |
|---------------------------|----------------------|--|------------------------------------|-------------|----------------------|------------------------------------|-------------|
| | NUMBER OF OPTIONS | WEIGHTED- AVERAGE REMAINING OPTION LIFE (YEARS) | WEIGHTED-AVERAGE EXERCISE PRICE | | NUMBER OF OPTIONS | WEIGHTED-AVERAGE EXERCISE PRICE | |
| | | | CAD\$ | U.S.\$ | | CAD\$ | U.S.\$ |
| December 31, 2011 | | | | | | | |
| 0.77 | 3,885,571 | 7.18 | 0.77 | 0.76 | 2,377,773 | 0.77 | 0.76 |
| 1.25 | 1,263,650 | 2.50 | 1.25 | 1.23 | 1,263,650 | 1.25 | 1.23 |
| | <u>5,149,221</u> | <u>6.07</u> | <u>0.88</u> | <u>0.87</u> | <u>3,641,423</u> | <u>0.94</u> | <u>0.92</u> |
| December 31, 2012 | | | | | | | |
| 0.55 | 68,250 | 9.76 | 0.55 | 0.55 | — | — | — |
| 0.77 | 4,404,056 | 6.76 | 0.77 | 0.77 | 3,128,294 | 0.77 | 0.77 |
| 1.25 | 1,011,900 | 1.45 | 1.25 | 1.26 | 1,011,900 | 1.25 | 1.26 |
| | <u>5,484,206</u> | <u>5.81</u> | <u>0.85</u> | <u>0.86</u> | <u>4,140,194</u> | <u>0.88</u> | <u>0.88</u> |
| June 30, 2013 (unaudited) | | | | | | | |
| 0.55 | 1,231,400 | 9.52 | 0.55 | 0.52 | 16,382 | 0.55 | 0.52 |
| 0.77 | 4,291,441 | 6.33 | 0.77 | 0.73 | 3,553,724 | 0.77 | 0.73 |
| 1.25 | 816,750 | 1.52 | 1.25 | 1.19 | 816,750 | 1.25 | 1.19 |
| | <u>6,339,591</u> | <u>6.24</u> | <u>0.79</u> | <u>0.75</u> | <u>4,386,856</u> | <u>0.86</u> | <u>0.82</u> |

XENON PHARMACEUTICALS INC.

Notes to Financial Statements

(Expressed in thousands of U.S. dollars except share and per share figures) (continued)

11. Stock Option Plan (continued):

The fair value of each option issued to employees and non-employees is estimated using the Black-Scholes option-pricing model with the following weighted-average assumptions:

| | YEARS ENDED DECEMBER 31, | | SIX MONTHS ENDED JUNE 30, | |
|--------------------------|--------------------------|-------|---------------------------|-------|
| | 2011 | 2012 | 2012 | 2013 |
| | | | (unaudited) | |
| Risk-free interest rate | 2.36% | 1.14% | 1.15% | 1.03% |
| Expected term (in years) | 6.2 | 6.2 | 6.2 | 6.2 |
| Expected volatility | 70% | 70% | 70% | 70% |
| Expected dividend yield | — | — | — | — |

The weighted-average fair value of options granted during the six months ended June 30, 2013 was, \$0.83 (unaudited), and the weighted-average fair value of options in 2012 was \$0.47 (2011—\$0.49) per option.

As of June 30, 2013, the unrecognized stock-based compensation cost related to the non-vested stock options was \$1,192 (unaudited) and December 31, 2012 and December 31, 2011 was \$633 and \$693 respectively, which is expected to be recognized over a weighted-average period of 2.8 years (2012—2.2 years; 2011—2.5 years).

The Company uses the “simplified method” to determine the expected term of options. Under this method, the expected term represents the average of the vesting period and the contractual term.

The expected volatility of share options was estimated based on a historical volatility analysis of peers that were similar to the Company with respect to industry, stage of life cycle, size, and financial leverage. The risk-free interest rate of the options is based on the U.S. Treasury yield curve in effect at the date of grant for a term similar to the expected term of the option.

Stock-based compensation expense is classified in the statements of operations as follows:

| | YEAR ENDED DECEMBER 31, | | SIX MONTHS ENDED JUNE 30, | |
|----------------------------|-------------------------|---------------|---------------------------|---------------|
| | 2011 | 2012 | 2012 | 2013 |
| | | | (unaudited) | |
| Research and development | \$ 145 | \$ 112 | \$ 58 | \$ 70 |
| General and administrative | 290 | 294 | 146 | 203 |
| Total | <u>\$ 435</u> | <u>\$ 406</u> | <u>\$ 204</u> | <u>\$ 273</u> |

12. Financial Risks:

(a) Foreign Currency Exchange Risk:

At December 31, 2012, the Company had U.S. dollar denominated cash and cash equivalents of \$51,100 (2011—\$8,100) and Canadian denominated cash and cash equivalents and marketable securities of CAD\$9,000 (2011—CAD\$6,900).

The Company faces foreign currency exchange rate risk in part, as a result of entering into transactions denominated in currencies other than Canadian dollars, particularly those denominated in U.S. dollars and Euros. The Company

XENON PHARMACEUTICALS INC.

Notes to Financial Statements

(Expressed in thousands of U.S. dollars except share and per share figures) (continued)

12. Financial Risks (continued):

also holds non-Canadian dollar denominated cash, accounts receivable and accounts payable, which are primarily denominated in U.S. dollars.

Changes in foreign currency exchange rates can create significant foreign exchange gains or losses to the Company. The Company's current foreign currency risk is primarily with the U.S. dollar as a majority of its non-Canadian dollar denominated expenses are denominated in U.S. dollars. To limit the Company's exposure to volatility in currency markets, the Company maintains a natural currency hedge against fluctuations in currency exchange rates by estimating its anticipated expenses that will be denominated in currencies other than the Canadian dollar and then purchasing a corresponding amount of the relevant foreign currency at the current spot rate. The Company does not otherwise hedge its exposure and thus assumes the risk of future gains or losses on the amounts of foreign currency held. The impact of an adverse change in foreign exchange rates may be offset in the event the Company receives a milestone payment from a foreign partner.

(b) Interest Rate Risk:

The Company had cash and cash equivalents of \$60.2 million as of December 31, 2012, which consisted of bank deposits. The goals of the Company's investment policy are liquidity and capital preservation; the Company does not enter into investments for trading or speculative purposes and has not used any derivative financial instruments to manage its interest rate exposure. The Company believes that it does not have any material exposure to changes in the fair value of these assets as a result of changes in interest rates due to the short term nature of the Company's cash and cash equivalents. Declines in interest rates, however, would reduce future investment income. Such interest-earning instruments carry a degree of interest rate risk; however, historical fluctuations in interest income have not been significant. The Company had no outstanding debt as of June 30, 2013 (unaudited).

13. Collaboration Agreements:

The Company has entered into a number of collaboration agreements with multiple deliverables under which it may have received non-refundable upfront payments. The Company generally recognizes revenue from upfront payments ratably over the term of its estimated period of performance of research under its collaboration agreements in the event that such arrangements represent a single unit of accounting.

The collaborations may also include contractual milestone payments, which relate to the achievement of pre-specified research, development, regulatory and commercialization events. The milestone events coincide with the progression of product candidates from research and development, to regulatory approval and through to commercialization. The process of successfully discovering a new product candidate, having it selected by the collaborator for development and having it approved and ultimately sold for a profit is highly uncertain. As such, the milestone payments that the Company may earn from its collaborators involve a significant degree of risk to achieve.

Research and development milestones in the Company's collaboration agreements may include the following types of events:

- completion of pre-clinical research and development work leading to selection of product candidates;
- initiation of Phase 1, Phase 2 or Phase 3 clinical trials; and
- achievement of certain other scientific or development events.

Regulatory milestone payments may include the following types of events:

- filing of regulatory applications for marketing approval in the U.S., Europe or Japan, including Investigational New Drug ("IND") applications and New Drug Applications ("NDA"); and
- marketing approval in a major market, such as the U.S., Europe or Japan.

XENON PHARMACEUTICALS INC.

Notes to Financial Statements

(Expressed in thousands of U.S. dollars except share and per share figures) (continued)

13. Collaboration Agreements (continued):

Commercialization milestone payments may include annual product sales that achieve pre-specified thresholds.

(a) Genome BC collaboration agreement:

In January 2009, the Company entered into a research funding agreement with Genome BC to co-fund IND-enabling studies for antisense products targeting hepcidin or hemojuvelin. The deliverables of the research activities are to identify development candidates for both hepcidin and hemojuvelin targets. Under the agreement with Genome BC the Company carried out certain research activities with partial funding that Genome BC provided on a quarterly basis over the term of the research program. This agreement will terminate in September 30, 2013.

Under the research funding agreement, the Company agreed to give to Genome BC at each quarter (and in connection with Genome BC delivering the agreed-upon research funding for that quarter) rights to be issued in the future a number of the Company's common shares without paying cash consideration, or subscription rights. The number of shares to which Genome BC is entitled under each quarter's subscription rights are proportional to their funding amount paid to the Company for that quarter, calculated by: the quotient of (a) one-half of the Genome BC funding amount to the Company for that quarter divided by (b) the greatest of: (i) CAD\$10.64; (ii) the converted U.S. dollar share price; and (iii) the most recent issue price of the Company's common shares. The subscription rights are automatically exchangeable into common shares of the Company on a 1:1 basis on a date three years after the subscription rights are issued without additional cash consideration being paid by Genome BC. However, in the event of a public offering, including an IPO or a sale or liquidation of the Company, Genome BC's remaining subscription rights would automatically convert to common shares immediately prior to such event.

As of December 31, 2012, Genome BC had subscription rights exchangeable for 54,390 common shares. As of June 30, 2013, 69,356 such subscription rights remain outstanding (unaudited). See Note 10 for further details.

In the event that a product arising from the research collaboration with Genome BC is the subject of a regulatory filing in any jurisdiction seeking marketing approval to sell such product, then one-half of the total research funding provided by Genome BC will become repayable by the Company within 60 days of such filing. As of June 30, 2013, Genome BC has provided \$2,359 in research funding to the Company, of which one-half (or \$1,179) could be subject to this contingent repayment condition. Given the uncertainty related to such an event and the early stage of development, the Company has determined that it would only be appropriate to recognize the contingent repayment to Genome BC when conditions suggest that such repayment is more likely than not to occur. As of June 30, 2013, the Company determined such an event continues to be unlikely (unaudited).

(b) Merck Sharp & Dohme GmbH (formerly known as Merck Sharp & Dohme Research Ltd.), an affiliate of Merck & Co., Inc. ("Merck"), exclusive collaborative research and option agreement:

In June 2009, the Company entered into an exclusive collaborative research and option agreement with Merck to conduct a research program to discover and develop novel small-molecule candidates for the potential treatment of cardiovascular disease. Merck provided payments to the Company for its FTEs who performed the Company's activities pursuant to the research program conducted under the Merck agreement. The Merck collaborative research program ended in December 2012.

In addition, the Company agreed to perform certain genome sequencing work in exchange for a milestone payment of \$5,000 payable upon successful conclusion of such work. This payment was made by Merck in February 2010. The Company has determined that this milestone payment was not substantive and should not be considered as a separate element. The Company identified several deliverables under the agreement with Merck, including options to obtain a license, a commitment to participate in a joint steering committee and research and development services to be performed by the Company on behalf of Merck. The Company concluded that the options to license did not have stand-alone value apart from the related research and development services to be delivered. In addition, the Company was unable to estimate a fair value for the undelivered items in the agreement with Merck. Accordingly, the Company has accounted for the deliverables under this agreement as a single unit of accounting.

XENON PHARMACEUTICALS INC.

Notes to Financial Statements

(Expressed in thousands of U.S. dollars except share and per share figures) (continued)

13. Collaboration Agreements (continued):

Under the terms of the agreement, Merck had the option to obtain an exclusive license under certain intellectual property controlled by the Company to develop and commercialize compounds and products directed to targets in the research program, which has now expired. In June 2012, Merck exercised its option and made a further payment to the Company of \$2,000. The option exercise was determined to be substantive and at risk at the inception of the agreement and, as such, was recognized in the period that the option was exercised by Merck.

Under the agreement with Merck, the Company is entitled to receive up to \$21,000 in preclinical and clinical milestone payments and up to \$43,000 in regulatory milestone payments for products directed to the licensed target, and also to receive royalties on future product sales at percentages between the mid to high single-digit range. The Company received a milestone payment of \$1,000 in 2010 and a milestone payment of \$1,000 in 2011 relating to research progress on two separate targets. Both research milestones were determined to be substantive and at risk at the inception of the agreement and, as such, were recognized in the respective period the milestones were achieved. The Company believes that future contingent consideration milestone payments are not considered substantive as the Company is not contributing effort to the achievement of such milestones now that the period of substantial involvement is complete, there are no undelivered elements and no continuing research obligations under this collaboration.

The Company has an option to co-fund Phase 1 and first Phase 2 clinical trials of product candidates licensed by Merck by paying Merck 50% of such development costs. Such co-funding option is available at the IND-filing stage for the applicable product candidate. If the Company exercises its co-funding option, the maximum eligible milestone payments due to the Company increase from \$64,000 to \$86,500, which would include \$28,500 in preclinical and clinical milestone payments and \$58,000 in regulatory milestone payments, and the royalties increase from the mid to high single-digit range to the high single-digit to sub-teen double-digit range. Through both December 31, 2012 and June 30, 2013 (unaudited), the Company has not yet exercised any such co-funding option.

Merck has the right to terminate the agreement upon providing notice to the Company. Each of Merck and the Company may terminate the agreement in the event of a material breach by the other that remains uncured for 90 days after notice of such breach. In the event that Merck terminates the agreement for a breach by the Company, then the licenses granted to Merck by the Company survive and become fully paid up. In the event that the Company terminates the agreement due to a breach by Merck, then the licenses previously granted to Merck terminate.

(c) Isis Pharmaceuticals, Inc. ("Isis") collaboration and licensing agreement:

In November 2010, the Company entered into a collaboration and license agreement with Isis to develop and commercialize antisense products targeting hepcidin and/or hemojuvelin. Upon signing of the agreement, the Company issued a convertible promissory note to Isis as payment of an upfront fee of \$1,500, which was accounted for as a research and development expense. The promissory note was paid in full in cash in June 2013 along with accrued interest. Under the terms of the agreement, Isis and the Company were responsible for their own costs related to the initial research program. Upon the identification of a development candidate and initiation of IND-enabling toxicology studies, the Company has the option to exclusively license the worldwide development and commercialization rights for these antisense products from Isis. In addition to license and option fees, Isis will be eligible to receive up to \$13,000 in clinical milestone payments, up to \$75,000 in regulatory-based milestone payments, sales-based milestone payments of up to \$60,000 and single-digit royalties on net sales of such antisense products licensed to the Company under the collaboration or of any sublicense revenue received by the Company. During the six months ended June 30, 2013, the Company exercised an option to an exclusive license to develop, manufacture and commercialize antisense products under the collaboration targeting hepcidin and paid Isis an option fee of \$2,000 which was accounted for as a research and development expense for the period (unaudited).

XENON PHARMACEUTICALS INC.

Notes to Financial Statements

(Expressed in thousands of U.S. dollars except share and per share figures) (continued)

13. Collaboration Agreements (continued):

The Company may terminate the agreement with Isis upon 90 days notice to Isis. Either party may terminate the agreement in the event of a material breach by the other party that remains uncured for 60 days.

(d) Genentech Inc. ("Genentech") collaborative research and license agreement:

In December 2011, the Company entered into a collaborative research and license agreement with Genentech and its affiliate, F. Hoffman-La Roche Ltd. ("Roche") to discover and develop small and large molecules for the potential treatment of pain. Under the terms of this agreement, Genentech has an exclusive license to compounds and a non-exclusive license to diagnostics from the Company for development and commercialization of such products.

The Company received an upfront payment of \$10,000 and Genentech is providing certain research funding to the Company for an initial term of three years ending December 2014. The Company identified several deliverables under the agreement with Genentech, including exclusive licenses to compounds and non-exclusive licenses to diagnostic products, a commitment to participate in a joint steering committee and research and development services to be performed by the Company on behalf of Genentech. The Company concluded that the licenses did not have stand-alone value to Genentech without the Company's technical expertise and joint steering committee participation during the initial three year period. Therefore, the Company has determined that the various deliverables should be considered as a single unit of accounting. As such the Company determined that the \$10,000 upfront payment should be recognized as revenue ratably over the expected period of performance, being the three-year period ending December 22, 2014.

The Company is eligible to receive up to \$58,500 in preclinical and clinical milestone payments, up to \$387,500 in regulatory milestone payments, and up to \$180,000 in sales-based milestone payments for multiple products and indications. In addition, the Company is eligible to receive royalties on sales of products resulting from the collaboration, which range from a mid single-digit percentage to ten percent for small-molecule inhibitors for the timeframe that such products are covered by the licensed patents and a low single-digit percentage thereafter, plus a low single-digit percentage for large-molecule inhibitors of Nav1.7. The Company believes that the potential milestone payments for preclinical, clinical and regulatory milestones under this agreement are substantive and at risk at inception of this agreement, and, as such, expects that these future milestone payments will be recognized as revenue in the period that each milestone is achieved. The Company believes that the potential sales-based milestone payments under this agreement are not substantive as the Company does not expect to contribute effort to their achievement and expects such sales-based milestones will generally be achieved after the period of substantial involvement under the collaboration. Therefore, the Company expects that future sales-based contingent consideration milestone payments will be recognized as revenue when such milestones are achieved, assuming all other revenue recognition criteria are met. As of both December 31, 2012 and June 30, 2013 (unaudited), no such milestone payments have been recognized.

The Company's agreement with Genentech expires on the date of the expiration of all payment obligations to the Company under the agreement. Genentech may terminate the agreement with three months notice anytime on or after the third anniversary of the agreement. Both Genentech and the Company may terminate the agreement in the event of a material breach by the other that remains uncured for 90 days. In the event that Genentech terminates the agreement for a breach by the Company, then Genentech retains its licenses granted under the agreement and the payment obligations of Genentech to the Company are reduced. In the event that the Company terminates the agreement for a breach by Genentech, previous licenses granted to Genentech will revert back to the Company except for certain rights to make and use certain large molecule product candidates which will be retained by Genentech.

(e) Teva Pharmaceutical Industries Ltd. ("Teva") collaborative development and license agreement:

In December 2012, the Company entered into a collaborative development and license agreement for with Teva, through its subsidiary, Ivax International GmbH, under which Teva was granted an exclusive license to develop and

XENON PHARMACEUTICALS INC.

Notes to Financial Statements

(Expressed in thousands of U.S. dollars except share and per share figures) (continued)

13. Collaboration Agreements (continued):

commercialize certain products, including XEN402, and a non-exclusive license to develop and commercialize companion diagnostics to those products.

Under the terms of the agreement, the Company received an upfront fee of \$41,000. Teva is responsible for all ongoing development costs with respect to developing XEN402 and other licensed products, including providing certain research funding to the Company over an initial term of three years ending December 2015. The Company identified several deliverables under the agreement with Teva, including exclusive licenses to compounds and non-exclusive licenses to companion diagnostic products, a commitment to participate in a joint steering committee and research and development services to be performed by the Company on behalf of Teva. The Company concluded that the licenses did not have stand-alone value to Teva without the Company's technical expertise and joint steering committee participation during the initial three-year period.

Therefore, the Company has determined that the various deliverables under this agreement should be considered as one single unit of accounting. As such the Company determined that the \$41,000 upfront payment should be recognized as revenue ratably over the expected period of performance, being the three year period ending December 31, 2015.

In addition, Teva is obligated to pay the Company up to \$20,000 in clinical milestone payments, up to \$285,000 in regulatory milestone payments, and up to \$30,000 in sales-based milestone payments. The Company is eligible to receive royalties in the low teens to low twenties on net sales of licensed products for the timeframe that such products are covered by the licensed patents and in certain other instances. The Company believes that potential milestone payments for development and regulatory milestones under this agreement are substantive and at risk at the inception of this agreement, and, as such, expects that these future milestone payments will be recognized as revenue in the period that each milestone is achieved. The Company believes that the potential sales-based milestone payments under this agreement are not substantive as the Company does not expect to contribute effort to their achievement and expects such sales-based milestones will generally be achieved after the period of substantial involvement under the collaboration. Therefore, the Company expects that future sales-based contingent consideration milestone payments will be recognized as revenue when such milestones are achieved, assuming all other revenue recognition criteria are met. As of June 30, 2013, no such milestone payments have been recognized (unaudited).

The Company has an option to a minority co-promotion interest for products incorporating XEN402 in the U.S. The Company's exercise of this option is subject to meeting objective financial conditions, staffing requirements and compliance standards to be determined in Teva's reasonable discretion in accordance with standard industry practice. The Company's co-promotion option is exercisable upon the filing of the first NDA for a XEN402 product with the FDA and the Company will be obligated to pay an opt-in fee to Teva, which is payable calculated based upon the applicable percentage of the Company's co-promotion interest and other factors relevant to certain pre-commercial development costs for such products, and is as a reduction to the milestone payments or the Company's share of operating profits that Teva would otherwise owe to the Company or a combination of the two. If the Company exercises this option, the Company will be eligible to receive, in lieu of royalties with respect to such product sales in the U.S., a share of operating profits from such product sales in the U.S. that is equal to the Company's percent interest of detailing activities and co-promotion expenses.

If the Company exercises this co-promotion option, the Company will be obligated to pay an opt-in fee to Teva that is calculated by multiplying the Company's co-promotion interest (as a percentage) by the amount of certain milestone payments paid or payable by Teva, to which is added certain past and future development costs on such product incurred by Teva with respect to the product for the U.S. The opt-in fee is payable as a reduction to the milestone payments or the Company's share of operating profits that Teva would otherwise owe to the Company, or a combination of the two.

XENON PHARMACEUTICALS INC.

Notes to Financial Statements

(Expressed in thousands of U.S. dollars except share and per share figures) (continued)

13. Collaboration Agreements (continued):

Under the agreement, the Company has the right to require Teva, upon written notice, to purchase the Company's common shares issued in an IPO if Teva has commenced a Phase 2b clinical trial of any licensed product under this agreement and if certain minimum price per share and gross proceed thresholds are met in connection with such offering. The number of shares that Teva would be required to purchase in an IPO upon receipt of such notice would equal to the lesser of:

- \$20,000 divided by the IPO price of common shares if the IPO occurs on or after the date Teva commences a Phase 3 clinical trial of any licensed product;
- \$10,000 divided by the IPO price of common shares if the IPO occurs prior to the date Teva commences a Phase 3 clinical trial of any licensed product;
- 19% of the Company's issued and outstanding shares, after giving effect to the common shares to be issued in an IPO; and
- a number of shares specified by the Company in a written notice to Teva.

Teva may terminate the agreement upon 60 days notice to the Company after a pre-defined number of Phase 2 (or later stage) clinical studies have been completed or in the event that safety or efficacy issues arise in the development of the licensed products. Either Teva or the Company may terminate the agreement in the event of the other's breach which remains uncured for 90 business days. Under certain circumstances, the Company receives licenses to Teva intellectual property relating to XEN402 development and regulatory filings in the event of termination.

(f) uniQure Biopharma B.V. ("uniQure") sublicense and research agreement:

Effective August 2000, the Company entered into a sublicense and research agreement with Amsterdam Molecular Therapeutics ("AMT") pursuant to which the Company granted to AMT an exclusive, worldwide sublicense under certain intellectual property. uniQure subsequently acquired certain assets of AMT including the rights to the intellectual property under this sublicense. Under the terms of the agreement, the Company is eligible to receive upfront fees and milestone payments of which CAD\$575 has been received and fully recognized as revenue as of June 30, 2013 (unaudited).

The Company is eligible to receive certain additional milestone payments, both for clinical and regulatory milestones, of less than CAD\$1,000 related to the first product developed under this sublicense, Glybera, and for each subsequent product developed under the sublicense. The Company believes that all potential milestone payments under this agreement are substantive and at risk at the inception of this agreement, and, as such, expects that future milestone payments will be recognized as revenue in the period that each milestone is achieved.

The Company is also eligible to receive mid single-digit royalties on net sales by uniQure and its affiliates, and other payments. The royalty rates are reduced to a low single-digit when the licensed patents expire. The Company, in turn, has certain payment obligations to its licensor, the University of British Columbia ("UBC"), based on amounts received from uniQure or otherwise based on the exploitation of the licensed intellectual property.

In July 2013, uniQure announced that it had granted a sublicense to commercialize Glybera to Chiesi Farmaceutici S.p.A. ("Chiesi") in certain countries. The Company is eligible to receive mid single-digit royalties on net sales of the licensed products, for sales made by uniQure and its affiliates. The royalty rates are reduced to a low single-digit for sales made by uniQure and its affiliates in countries where a licensed technology or a licensed product is not covered by a valid patent claim. With respect to uniQure's sublicense to Chiesi, the Company is eligible to receive a percentage in the low twenties of all non-royalty compensation that uniQure receives from Chiesi (for example upfront payments and milestone payments), a percentage in the low twenties of any royalties that uniQure receives from Chiesi based on sales of technology or products covered by the licensed patents, plus a mid single-digit percentage of certain further royalties that uniQure receives from Chiesi based on sales of our licensed technology or

XENON PHARMACEUTICALS INC.

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(Expressed in thousands of U.S. dollars except share and per share figures) (continued)

13. Collaboration Agreements (continued):

products after the expiration of all licensed patents covering the product. If uniQure grants a sublicense to a third party other than to Chiesi, then the Company is eligible to receive a percentage in the low twenties of all non-royalty compensation relating to the licensed technology or products that uniQure receives from such sublicensee (for example upfront payments and milestone payments) plus a percentage in the low twenties of any royalties that uniQure receives from such sublicensee based on sales of technology or products covered by the licensed patents.

Pursuant to the terms of the Company's agreement with UBC, the Company must pay to UBC a single-digit percentage of amounts the Company receives from sales of Glybera.

Also, pursuant to the terms of the Company's agreement with the Memorial University of Newfoundland, the Company must pay to the Memorial University of Newfoundland a single-digit percentage of net sales for products the Company sells directly and a single-digit percentage of royalties received for sales on products under the gene program or pain program.

The following table is a summary of the revenue recognized from the Company's collaborations for each of the years ended December 31, 2011 and 2012 and for each of the six months ended June 30, 2012 and 2013 (unaudited):

| | YEAR ENDED DECEMBER 31, | | SIX MONTHS ENDED JUNE 30, | |
|--|----------------------------|-----------------|------------------------------|-----------------|
| | 2011 | 2012 | 2012 | 2013 |
| | | | (unaudited) | |
| uniQure: | | | | |
| Milestone payment | — | \$ 198 | — | — |
| Teva: | | | | |
| Recognition of upfront payment | — | 927 | — | \$ 6,607 |
| Research funding | — | — | — | 294 |
| Genentech: | | | | |
| Recognition of upfront payment | \$ 94 | 3,431 | \$1,685 | 1,659 |
| Research funding | 93 | 3,517 | 1,647 | 2,257 |
| Merck: | | | | |
| Recognition of initial milestone payment | 2,145 | 1,060 | 1,054 | — |
| Option fee | — | 2,060 | 2,047 | — |
| Research funding | 3,206 | 2,442 | 1,688 | — |
| Milestone payment | 1,038 | — | — | — |
| Genome BC: | | | | |
| Research funding | 339 | 665 | 86 | 168 |
| Total collaboration revenue | <u>\$6,915</u> | <u>\$14,300</u> | <u>\$8,207</u> | <u>\$10,985</u> |

14. Commitments and Contingencies:

(a) Lease commitments:

The Company entered into an amended lease agreement for research laboratories and office space in Burnaby, British Columbia, Canada for a 120-month term from April 1, 2012 to March 31, 2022, which included an element of free rent and tenant inducement that will be amortized over the term of the lease.

Lease expense for the year ended December 31, 2012 was \$1,017 (2011—\$1,601). Lease expense for the six months ended June 30, 2013 was \$425 (2012—\$653) (unaudited).

XENON PHARMACEUTICALS INC.**Notes to Financial Statements**

(Expressed in thousands of U.S. dollars except share and per share figures) (continued)

14. Commitments and Contingencies (continued):

Future minimum annual lease payments under existing operating lease commitments are as follows:

| <u>YEAR ENDING DECEMBER 31,</u> | |
|---------------------------------|-----------------|
| 2013 | \$ 924 |
| 2014 | 930 |
| 2015 | 930 |
| 2016 | 930 |
| 2017 | 966 |
| 2018 and thereafter | 4,104 |
| Total | <u>\$ 8,784</u> |

(b) Guarantees and indemnifications:

The Company, as permitted under Canadian law and in accordance with its articles and by-laws, will enter into indemnification agreements with each of its officers and directors, and certain other Company employees, and will indemnify such persons for certain events or occurrences, subject to certain limits, while such person is or was serving at the Company's request in such capacity. The term of the indemnification period will last as long as such person may be subject to any proceeding arising out of acts or omissions of such person in such capacity.

The maximum amount of potential future indemnification is unlimited; however, the Company currently holds directors' and officers' liability insurance. This insurance limits the Company's exposure and may enable it to recover a portion of any future amounts paid. The Company believes that the fair value of these indemnification obligations is minimal. Accordingly, the Company has not recognized any liabilities relating to these obligations for any period presented.

15. Income Taxes:

Income tax expense (recovery) varies from the amounts that would be computed by applying the expected Canadian and provincial statutory income tax rate of 25% (2011 – 26.5%) to loss before income taxes as shown in the following table:

| | <u>2011</u> | <u>2012</u> |
|---|-------------|-------------|
| Computed taxes at Canadian federal and provincial tax rates | \$ (3,178) | \$ (1,075) |
| Change in valuation allowance | 1,910 | 2,710 |
| Investment tax credits earned | (1,804) | (1,418) |
| Tax attributes expired | 2,720 | (356) |
| Future tax rate reductions | 249 | — |
| Non-deductible expenditures | 113 | 107 |
| Other reconciling items | (10) | 32 |
| Income tax expense | <u>\$ —</u> | <u>\$ —</u> |

XENON PHARMACEUTICALS INC.**Notes to Financial Statements**

(Expressed in thousands of U.S. dollars except share and per share figures) (continued)

15. Income Taxes (continued):

Deferred income tax assets and liabilities result from the temporary differences between the amount of assets and liabilities recognized for financial statement and income tax purposes. The significant components of the net deferred income tax assets and liabilities are as follows:

| | 2011 | 2012 |
|---|-------------|-------------|
| Deferred income tax assets | | |
| Investment tax credits | \$ 21,025 | \$ 19,063 |
| Scientific research and experimental development pool | 16,508 | 17,873 |
| Deferred revenue | 2,776 | 11,663 |
| Non-capital losses | 7,070 | 2,122 |
| Property, plant and equipment | 1,728 | 2,112 |
| Other | 499 | 596 |
| Less—valuation allowance | (49,606) | (53,429) |
| Net deferred income tax assets | <u>\$ —</u> | <u>\$ —</u> |

The realization of deferred income tax assets is dependent upon the generation of sufficient taxable income during future periods in which the temporary differences are expected to reverse. The valuation allowance is reviewed on a quarterly basis and if the assessment of the “more likely than not” criteria changes, the valuation allowance is adjusted accordingly. The valuation allowance continues to be applied against deferred income tax assets where the Company has assessed that the realization of such assets does not meet the “more likely than not” criteria.

At December 31, 2012, the Company has unclaimed tax deductions for scientific research and experimental development expenditures of \$71,490 (2011—\$66,032) with no expiration date.

At December 31, 2012, the Company has \$16,180 (2011—\$17,163) of investment tax credits available to offset federal taxes payable and \$6,928 (2011—\$8,153) of provincial tax credits available to offset provincial taxes payable in the future.

At December 31, 2012, the Company has non-capital losses carried forward for tax purposes, which are available to reduce taxable income of future years of approximately \$8,489 (2011—\$28,223).

The investment tax credits and loss carry forwards expire over various years to 2032.

As of December 31, 2012, the total amount of the Company’s unrecognized tax benefits were \$6,400 (2011—\$1,300). If recognized in future periods, the unrecognized tax benefits would affect the Company’s effective tax rate.

The following table summarizes the activity related to the Company’s unrecognized tax benefits:

| | 2011 | 2012 |
|---|-----------------|-----------------|
| Balance as of January 1 | — | \$ 1,268 |
| Increases related to current year positions | \$ 1,268 | 5,082 |
| Balance as of December 31 | <u>\$ 1,268</u> | <u>\$ 6,350</u> |

The Company recognizes potential accrued interest and penalties related to unrecognized tax benefits within the income tax provision. Interest and penalties have not been accrued at December 31, 2012 as none would be owing on the unrecognized tax benefits due to the availability of non-capital losses to shelter any potential taxable income arising thereon.

XENON PHARMACEUTICALS INC.

Notes to Financial Statements

(Expressed in thousands of U.S. dollars except share and per share figures) (continued)

15. Income Taxes (continued):

The Company does not currently expect any significant increases or decreases to these unrecognized tax benefits within 12 months of the reporting date.

The Company currently files an income tax return in Canada, the jurisdiction in which it is subject to tax. In jurisdictions in which the Company does not believe it is subject to tax and therefore does not file income tax returns, the Company can provide no certainty that tax authorities in those jurisdictions will not subject one or more tax years (since the inception of the Company) to examination. Further, while the statute of limitations in each jurisdiction where an income tax return has been filed generally limits the examination period, as a result of loss carry-forwards, the limitation period for examination generally does not expire until several years after the loss carry-forwards are utilized. Other than routine audits by tax authorities for tax credits and tax refunds that the Company claims, the Company is not aware of any other material income tax examination currently in progress by any taxing jurisdiction.

16. Related Parties:

A director of the Company, is the president and principal beneficial shareholder of Genworks, Inc. ("Genworks"), a company that provides services to the Company pursuant to a consulting agreement.

The Company recorded consulting expenses for services provided by Genworks in the amount of \$279 for the year ended December 31, 2011, \$307 for the year ended December 31, 2012 and none for the six months ended June 30, 2013 (unaudited).

As of December 31, 2012, \$167 (2011—\$71) included in accrued expenses related to services provided by Genworks.

During the fiscal years ended December 31, 2011 and 2012, the Company incurred contract research organization fees to Medpace, Inc. ("Medpace") in the amount of \$876 and \$151, respectively. One of the Company's directors is an equityholder and former director of Medpace. These consulting fees were paid to Medpace in consideration of certain pre-clinical and non-clinical drug development services provided by Medpace during this period by individuals other than the Company's director. The Company is not currently party to a consulting agreement with Medpace.

17. Subsequent Events:

On August 1, 2013, the Company granted 207,000 stock options under its Plan pursuant to an employment agreement entered into with an individual who is scheduled to assume the position of chief financial officer by November 1, 2013. Each stock option entitles the holder the right to purchase one common share at an exercise price of \$1.91. The options vest in the amount of 25% on the one year anniversary date of the grant, then 75% vesting thereafter over the course of the following 4 years, in equal amounts, on the last day of each month.

Under the terms of the collaborative research and license agreement between the Company and Genentech, on August 7, 2013, the Company earned a \$5,000 milestone payment from Genentech following Genentech's internal approval of a program to begin IND-enabling toxicology studies.

Shares



Common Shares

PRELIMINARY PROSPECTUS

Joint Book-Running Managers

**Jefferies
Cowen and Company**

Co-Managers

**Wells Fargo Securities
RBC Capital Markets**

, 2013

PART II
INFORMATION NOT REQUIRED IN PROSPECTUS

Item 13. Other Expenses of Issuance and Distribution

Estimated expenses, other than underwriting discounts and commissions, payable by the registrant in connection with the sale of the common shares being registered under this registration statement are as follows.

| ITEM | AMOUNT TO BE PAID |
|---|------------------------------|
| SEC Registration Fee | \$ * |
| FINRA Filing Fee | * |
| The NASDAQ Global Market Listing Fee | * |
| Printing and Engraving Expenses | * |
| Legal Fees and Expenses | * |
| Accounting Fees and Expenses | * |
| Blue Sky, Qualification Fees and Expenses | * |
| Transfer Agent Fees and Expenses | * |
| Miscellaneous Expenses | * |
| Total | <u>\$ *</u> |

* To be completed by amendment.

Item 14. Indemnification of Directors and Officers

Under the Canada Business Corporations Act, or CBCA, we may indemnify our current or former directors or officers or any other individuals who act or have acted at our request as a director or officer, or an individual acting in a similar capacity, of another entity, against all costs, charges, and expenses, including an amount paid to settle an action or satisfy a judgment, reasonably incurred by the individual in respect of any civil, criminal, administrative, investigative or other proceeding in which the individual is involved because of his or her association with us or the other entity. The CBCA also provides that we may advance moneys to a director, officer or other individual for costs, charges and expenses reasonably incurred in connection with such a proceeding. The individual shall repay the moneys to us if indemnification of the individual is ultimately prohibited under the CBCA, as described below.

Indemnification is prohibited under the CBCA unless the individual:

- ⁿ acted honestly and in good faith with a view to our best interests, or the best interests of the other entity for which the individual acted as director or officer or in a similar capacity at our request;
- ⁿ in the case of a criminal or administrative action or proceeding that is enforced by a monetary penalty, the individual had reasonable grounds for believing that his or her conduct was lawful; and
- ⁿ was not judged by the court or other competent authority to have committed any fault or omitted to do anything that the individual ought to have done.

Our by-laws require us to indemnify each of our directors, officers, former directors or officers or persons who act or acted at our request as a director or officer of a body corporate of which we are or were a direct or indirect shareholder or creditor except in respect of an action by or on behalf of us or such body corporate to procure a judgment in its favor in certain situations. We will indemnify such individual against all costs, charges and expenses, including an amount paid to settle an action or proceeding to which the individual is made a party by reason of being or having been a director or officer of us or such body corporate. Our by-laws also require us to, with the approval of a court, indemnify such individual referred to above, in respect of an action by or on behalf of us or such body corporate to procure a judgment in its favor, to which the individual is made a party by reason of being or having been a director or an officer of us or such body corporate, against all costs, charges and expenses reasonably incurred by him in connection with such action. However, we shall not indemnify such individual if the individual did not act honestly and in good faith with a view to our best interests or, in the case of a criminal or administrative action or proceeding that is enforced by a monetary penalty, the individual did not have reasonable grounds for believing that his or her conduct was lawful.

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Our by-laws authorize us, with the approval of our board of directors, to purchase and maintain insurance for the benefit of each of our current or former directors or officers and each person who acts or acted at our request as a director or officer of another entity, against any liability incurred by him or her.

We will enter into indemnification agreements with each of our directors and certain officers. As provided by our by-laws, these agreements, among other things, will require us to indemnify each director and officer to the fullest extent permitted by Canadian law, including indemnification of all costs, charges and expenses reasonably incurred by such person in any action or proceeding, including any action or proceeding by or in right of us, arising out of the person's services as a director or officer; provided that, we will not indemnify such individual if, among other things, he or she did not act honestly and in good faith with a view to our best interests and, in the case of a criminal or penal action, the individual did not have reasonable grounds for believing that his or her conduct was lawful.

We expect to have an insurance policy in place prior to the closing of this offering that covers our directors and certain officers, substantially in line with that purchased by similarly situated companies.

Insofar as indemnification of liabilities arising under the Securities Act 1933, as amended, may be permitted to members of our board of directors, officers or persons controlling us pursuant to the foregoing provisions, we have been informed that, in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act 1933, as amended, and is therefore unenforceable.

We plan to enter into an underwriting agreement which provides that the underwriters are obligated, under certain circumstances, to indemnify our directors and officers against specified liabilities, including liabilities under the Securities Act 1933, as amended.

Item 15. Recent Sales of Unregistered Securities

The following list sets forth information regarding all unregistered securities sold by us since August 1, 2010, share numbers have not been adjusted for the reverse share split to be effective prior to the closing of this offering. No underwriters were involved in the sales.

- (a) From August 1, 2010 through September 25, 2013, we issued an aggregate of 63,915 common shares upon the exercise of stock options granted to certain of our directors, officers, employees and other service providers under our Amended and Restated Stock Option Plan, at exercise prices ranging from CAD\$0.50 to CAD\$1.25 per common share, for aggregate consideration of CAD\$48,096.
- (b) From August 1, 2010 through September 25, 2013, we issued an aggregate of 95,142 common shares pursuant to subscription rights issued under a research funding agreement and its predecessor agreement with Genome B.C.
- (c) From August 1, 2010 through September 25, 2013 we granted to certain of our directors and officers, stock options under the Amended and Restated Stock Option Plan to purchase an aggregate of 3,816,088 common shares at exercise prices ranging from CAD\$0.55 to CAD\$2.01 per common share.
- (d) From August 1, 2010 through September 25, 2013 we granted to certain of our non-officer employees and other service providers stock options under the Amended and Restated Stock Option Plan to purchase an aggregate of 313,400 common shares at exercise prices ranging from CAD\$0.55 to CAD\$0.77 per common share.
- (e) From August 1, 2010 through September 25, 2013, we issued to Genome B.C. 75,458 subscription rights, under a research funding agreement and its predecessor agreement, of which 70,162 subscription rights are outstanding. These outstanding subscription rights are automatically convertible into an aggregate of 70,162 common shares upon certain events, including the closing of this offering.

The securities described in Items 15(a) and 15(b) were offered, sold and issued pursuant to the Canadian prospectus exemption under section 2.42 of National Instrument 45-106—*Prospectus and Registration Exemptions*, or NI 45-106, as such securities were offered, sold and issued in accordance with the terms and conditions of securities that we had previously issued. The securities described in Items 15(c) and 15(d) were offered, sold and issued pursuant to the Canadian prospectus exemption under section 2.24 of NI 45-106 as such securities were offered, sold and issued by us to our directors, officers, employees and consultants. The securities described in Items 15(e) were issued pursuant to the Canadian prospectus exemption under section 2.3 of NI 45-106 as such securities were issued to an accredited investor, as such term is defined in NI 45-106.

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Any grant of our stock options and any issuance of our common shares upon the exercise of such stock options described Items 15(a), (c) and (d) above that was made to a resident of the U.S. was made pursuant to written compensatory plans or arrangements with our directors, officers, employees and service providers in reliance on the exemption provided by Rule 701 promulgated under Section 3(b) of the Securities Act. All recipients either received adequate information about us or had access, through employment or other relationships, to such information.

Item 16. Exhibits and Financial Statement Schedules

(a) Exhibits.

| EXHIBIT NUMBER | DESCRIPTION |
|----------------|---|
| 1.1* | Form of Underwriting Agreement. |
| 3.1* | Form of Articles of Amendment of the Company, to be effective upon completion of the offering. |
| 3.2* | Form of By-laws of the Company, to be effective upon completion of the offering. |
| 4.1* | Form of Common Share Certificate. |
| 4.2* | Amended and Restated Investor Rights Agreement, dated December 6, 2006, by and among the Company and the investors listed on Exhibit A and Exhibit B thereto. |
| 5.1* | Opinion of McCarthy Tétrault LLP. |
| 10.1†* | Collaboration and License Agreement, dated November 10, 2010, by and between the Company and Isis Pharmaceuticals, Inc. |
| 10.2†* | Exclusive Collaboration Research and Option Agreement, dated June 10, 2009, by and between the Company and Merck Sharp & Dohme Research Ltd, as amended. |
| 10.3†* | Sublicense and Research Agreement, dated June 18, 2001, by and between the Company and Amsterdam Molecular Therapeutics B.V., as amended by the Consent of the Company and the University of British Columbia to the uniQure-Chiesi Agreement, dated June 28, 2013. |
| 10.4†* | Collaborative Research and License Agreement, dated December 22, 2011, by and among the Company, Genentech, Inc. and F. Hoffmann-La Roche Ltd, as amended. |
| 10.5†* | Collaborative Development and License Agreement, dated December 7, 2012, by and between the Company and Ivax International GmbH, as amended. |
| 10.6†* | License Agreement, dated May 19, 2000, by and between the Company and the University of British Columbia, as amended. |
| 10.7 | Consulting Agreement, dated January 1, 2004, by and between the Company and Genworks Inc., as amended. |
| 10.8**# | Stock Option Plan, as amended, and form of option agreement thereunder. |
| 10.9*# | 2013 Equity Incentive Plan, and form of option agreement thereunder. |
| 10.10*# | Offer Letter, dated December 7, 2004, by and between the Company and Simon Pimstone. |
| 10.11*# | Offer Letter, dated October 13, 2000, by and between the Company and Paul Goldberg. |
| 10.12*# | Offer Letter, dated April 14, 2010, by and between the Company and Tarek Mansour. |
| 10.13*# | Offer Letter, dated August 1, 2013, by and between the Company and Ian Mortimer. |
| 10.14*# | Offer Letter, dated May 15, 2001, by and between the Company and Karen Corraini. |
| 10.15*# | Offer Letter, dated February 12, 2001, by and between the Company and Robin Sherrington. |
| 10.16** | Lease, dated as of 2001, by and between the Company and Discovery Parks Incorporated, as amended through July 18, 2013. |
| 21.1** | List of Subsidiaries of the Company. |
| 23.1* | Consent of KPMG LLP, Independent Registered Public Accounting Firm. |
| 23.2* | Consent of McCarthy Tétrault LLP (included in Exhibit 5.1). |
| 24.1* | Powers of Attorney (included in page II-5 to the original filing of this registration statement). |

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* To be filed by amendment.

** Previously filed.

† Confidential treatment has been requested with respect to certain portions of this exhibit. Omitted portions have been filed separately with the Securities and Exchange Commission.

Indicates management contract or compensatory plan.

(b) Financial Statement Schedules.

Schedules not listed above have been omitted because the information required to be set forth therein is not applicable or is shown in the financial statements or notes thereto.

Item 17. Undertakings

The undersigned registrant hereby undertakes to provide to the underwriters at the closing specified in the underwriting agreements, certificates in such denominations and registered in such names as required by the underwriters to permit prompt delivery to each purchaser.

Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act of 1933 and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act of 1933 and will be governed by the final adjudication of such issue.

The undersigned hereby undertakes that:

- (1) For purposes of determining any liability under the Securities Act of 1933, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this registration statement as of the time it was declared effective.
- (2) For the purpose of determining any liability under the Securities Act of 1933, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, the registrant has duly caused this amendment to this Registration Statement on Form S-1 to be signed on its behalf by the undersigned, thereunto duly authorized, in Burnaby, British Columbia, Canada, on _____, 2013.

XENON PHARMACEUTICALS INC.

By: _____
Simon Pimstone
President and Chief Executive Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Simon Pimstone and Karen Corraini as his or her true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for him or her and in his or her name, place and stead, in any and all capacities (including his or her capacity as a director and/or officer of Xenon Pharmaceuticals Inc.) to sign any or all amendments (including post-effective amendments) to this registration statement and any and all additional registration statements pursuant to Rule 462(b) of the Securities Act of 1933, and to file the same, with all exhibits thereto, and all other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as they, he or she might or could do in person, hereby ratifying and confirming all that said attorney-in-fact and agents or any of them, or their, his or her substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act, this Registration Statement has been signed by the following persons in the capacities and on the dates indicated.

| SIGNATURE | TITLE | DATE |
|-------------------------|---|-------------|
| _____ Simon Pimstone | President, Chief Executive Officer and Director (Principal Executive and Financial Officer) | _____, 2013 |
| _____ Sonia Graham | Controller (Acting Principal Accounting Officer) | _____, 2013 |
| _____ Michael Tarnow | Chair of the Board of Directors | _____, 2013 |
| _____ Mohammad Azab | Director | _____, 2013 |
| _____ Johnston Evans | Director | _____, 2013 |
| _____ Michael Hayden | Director | _____, 2013 |

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| SIGNATURE | TITLE | DATE |
|--------------|----------|--------|
| Frank Holler | Director | , 2013 |
| Gary Patou | Director | , 2013 |
| Evan Stein | Director | , 2013 |

EXHIBIT INDEX

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| 24.1* | Powers of Attorney (included in page II-5 to the original filing of this registration statement). |

* To be filed by amendment.

** Previously filed.

† Confidential treatment has been requested with respect to certain portions of this exhibit. Omitted portions have been filed separately with the Securities and Exchange Commission.

Indicates management contract or compensatory plan.

Consulting Agreement

This Agreement is made as of the 1st day of January, 2004 (the “**Effective Date**”),

BETWEEN:

XENON GENETICS INC., a Canadian corporation having its head office at 3650 Gilmore Way, Burnaby, BC, V5G 4W8; Phone: 604-484-3300; Fax: 604-484-3450

(the “**Company**”)

OF THE FIRST PART;

GENWORKS INC., a British Columbia corporation having its offices at 4484 West 7th Avenue, Vancouver, BC, V6R 1W9; Phone: 604-222-0236; Fax: 604-222-0241.

(the “**Consultant**”)

OF THE SECOND PART.

WHEREAS:

- A. The Company is carrying on business as a biotechnology company specializing in the discovery and validation of novel genes and drug targets and in the development of therapeutics and diagnostics for human disease (the “**Business**”); and
- B. The Company wishes to engage the Consultant to provide services to the Company in connection with the Business on the terms and conditions hereinafter set out.

NOW THEREFORE THIS AGREEMENT WITNESSES that in consideration of the premises and the covenants and agreements hereinafter contained (the receipt and sufficiency of which is hereby acknowledged), the Company and the Consultant hereby covenant and agree as follows:

1. ENGAGEMENT

- 1.1 Subject to the terms and conditions of this Agreement, the Company agrees to engage the Consultant to provide the Services (as described in Section 3.1 of this Agreement) during the term of this Agreement and the Consultant accepts such engagement from the Company.

2. TERM

- 2.1 Unless earlier terminated pursuant to Section 8.1, the term of the Consultant’s engagement pursuant to this Agreement (the “**Term**”) shall commence on the Effective Date and shall terminate on December 31st, 2004.

2.2 The Company and the Consultant may, at any time, extend or amend this Agreement, including the Term of this Agreement, by mutual written consent. Such amendments will be subject to approval by the Board of Directors of the Company.

3. SERVICES OF THE CONSULTANT

3.1 The Consultant agrees to faithfully, honestly and diligently provide the **Services** to the Company as described in **Schedule "A"**. The Consultant also represents, warrants and agrees that it can and will perform the Services required by this Agreement without disclosing or using any confidential information and/or proprietary information of a third Party.

4. NON-COMPETITION

4.1 The Consultant and the Company each acknowledge and agree that, during the term of this Agreement or any extension or renewal thereof, the Consultant may be retained as a consultant or employed by other persons, firms, or corporation engaged in the same or similar Business as that of the Company, provided however, that the provisions of this Agreement, particularly with regard to the Consultant's duties of non-use and non-disclosure of the Company's proprietary information, as provided below, shall be strictly observed by the Consultant with respect to such other persons, firms or corporations.

4.2 The Consultant warrants and represents to the Company that neither the Consultant nor its employees or agents have any agreement(s), either written or oral, to provide consulting or other services to any other person, firm or company in the Company's area of Business that would conflict with the Services the Consultant is providing to the Company hereunder. During the Term of this Agreement and for a period of one (1) year following said Term, the Consultant agrees that neither the Consultant nor its employees or agents will provide any consulting or other services to any other person, firm or company on matters relating to the Company's area of Business and/or the Services, unless the Consultant has first provided at least fifteen (15) days written notice to the Company prior to entering into any such other agreements.

5. CONFIDENTIAL INFORMATION AND NON-DISCLOSURE

5.1 For the purposes of this Agreement, "**Confidential Information**" means information, know-how and data (which may be oral, written, graphic, demonstrative, machine recognizable or otherwise) disclosed to the Consultant or developed by the Consultant as a consequence of or through the engagement of the Consultant by the Company pursuant to this Agreement, including without limitation the research, products, technology, ideas, inventions, methods, formulas, algorithms, computer programs, processes, designs, compositions, photographs, plans, product concepts, specifications, samples, reports, laboratory notebooks, services, business plans and strategies, business operations and systems, marketing techniques and pricing policies, financial information, information concerning employees, customers, licensors, licensees and/or vendors of the Company, all Company Inventions, and any Third Party Information. "**Third Party Information**" means any Confidential Information

(including those types of information enumerated in the definition of Confidential Information) owned by a third party and disclosed to the Consultant as a consequence of or through the engagement of the Consultant by the Company pursuant to this Agreement. Confidential Information shall not mean information, know how and data which:

- (a) was legally known to or in the possession of the Consultant as evidenced by written records at the time of disclosure to the Consultant by the disclosing party;
- (b) is or has become part of the public domain through no fault of the Consultant; or
- (c) has been disclosed to the Consultant by a third party without breaching any contractual, confidential, or fiduciary obligation to the Company.

5.2 With respect to Confidential Information that might be disclosed to the Consultant pursuant to this Agreement, the Consultant acknowledges and agrees as follows:

- (a) that all Confidential Information received by the Consultant is proprietary to the Company, or the third party in the case of the Third Party Information, has been designed, developed, accumulated at great expense and over lengthy periods and is secret and constitutes the exclusive property of the Company, or the third party in the case of Third Party Information; and
- (b) that, during the Term of this Agreement and for a period of five (5) years thereafter:
 - (i) the Consultant will hold and keep Confidential Information in the strictest confidence;
 - (ii) except as specifically authorized in writing by the Company, the Consultant shall not, directly or indirectly, (unless required to do so by applicable law), use, disseminate, disclose, lecture upon, publish, make copies of or otherwise summarize the Confidential Information; and
 - (iii) the Consultant will ensure that, in respect to Confidential Information, its employees and agents are under written confidentiality obligations of equivalent or greater stringency than those confidentiality obligations of the Consultant under this Agreement.

6. RIGHTS TO INTELLECTUAL PROPERTY

6.1 For the purpose of this Agreement, “**Company Inventions**” means any discoveries, concepts, inventions, improvements, ideas and developments, whether or not they may be patented, copyrighted or otherwise protected, including without limitation processes, methods, formulas, procedures, and techniques (including without limitation improvements and modifications thereto) developed or conceived by the Consultant, its employees or agents, whether alone or jointly with others, through the use of Confidential Information or through the use of information that was Confidential Information when it was first disclosed by the Company to the Consultant

6.2 With respect to Company Inventions made by the Consultant, its employees or agents, the Consultant agrees as follows:

- (a) Except as otherwise specifically provided by written agreement between the Company and the Consultant, the Consultant's employees or the Consultant's agents, the Company is the exclusive owner of any Company Invention made, conceived, developed or worked upon by the Consultant, during or after the Term, including all intellectual property rights in and to such Company Inventions;
- (b) The Consultant and/or the Consultant's employees or agents hereby assign to the Company all right, title and interest throughout the world he/she may have in any Company Inventions, including without limitation, all copyrights, patent rights, trade-marks, trade names, industrial designs, trade secrets and other intellectual property rights in and to each Company Invention, effective at the time each is created;
- (c) The Consultant and/or the Consultant's employees or agents shall fully and promptly disclose and deliver to the Company all Company Inventions, together with any documentation and materials that relate thereto and any explanations that may be necessary in connection with any registrations that may be made to obtain copyright, patent, trade-mark, trade name, industrial design or other protection relating to the Company Inventions;
- (d) To the extent a formal transfer or assignment of any "rights of the Consultant (or the Consultant's employees or agents) in any Company Invention is required, or the consent of the Consultant to the registration of any right in any Company Invention is required, the Consultant and the Consultant's employees and agents (as applicable) shall execute and deliver any further assignments, documentation and other instruments as may be reasonably required by the Company to effect the transfer, assignment or registration and
- (e) In the event that the Company makes or proposes to make any Canadian, United States or foreign patent applications relating the Company Invention, the Consultant and the Consultant's employees and agents shall cooperate fully with the Company and its patent counsel in preparing and prosecuting any such applications.

7. COMPENSATION

7.1 As full consideration for the Services and other covenants and agreements provided by the Consultant under this Agreement, the compensation payable by the Company to the Consultant shall be as follows:

- (a) for the period from January 1, 2004 to December 31, 2004: a consulting fee totaling One Hundred and Fifty Five Thousand Dollars (\$155,000.00), payable monthly in arrears; and
- (b) in addition to the above, on an annual basis, the Consultant is also eligible to receive a performance bonus, such bonus to be paid in an amount and in a manner to be

determined by the Board of Directors of the Company, in its sole discretion. The awarding of such bonus (if any) will be decided by the Board of Directors following the Board's assessment of the Consultant's contribution(s) to the Company's successful completion of its major corporate objectives including execution of a significant corporate partnership, an equity financing and a successful IND application for the Company's SCD1 program.

7.2 The Consultant will also receive reimbursement for the following expenses:

- (a) payments incurred by the Consultant in respect of disability insurance premiums, life insurance premiums, and/or health club memberships to which the employee(s) or agent(s) retained by the Consultant to perform the Services hereunder are the beneficiaries, provided that the total amount of such payments do not exceed more than 4.0% of the consulting fees to be paid to the Consultant over the Term of this Agreement (excluding performance bonus payments); and
- (b) all other reasonable and approved expenses incurred by the Consultant on behalf of the Company, including travel and other out-of-pocket expenses.

Such expenses shall be billed to the Company on a monthly basis and will be paid within thirty (30) days of the Company's receipt of the Consultant's invoice.

8. TERMINATION

8.1 The Company may terminate this Agreement at any time without cause by giving the Consultant written notice of such termination. In such event, the Consultant shall be entitled to receive the lesser of:

- (a) its consulting fee for a period of six months plus one additional month for each year of service to the Company up to a maximum of 12 months; or
- (b) all compensation due to the Consultant under this Agreement for the time remaining in the Term of this Agreement following the date on which the notice of termination occurred,

in each case due when such compensation would have otherwise been payable but for the termination of this Agreement. In such event(s), termination shall be effective immediately and the Company will have no further obligations to the Consultant under this Agreement.

8.2 The Company may also terminate this Agreement at any time for cause by giving the Consultant written notice of such termination. In the event of termination for cause, termination shall be effective immediately and the Company will have no further obligations to the Consultant under this Agreement. For purposes of this Agreement, cause includes but is not limited to, a failure by the Consultant to perform and discharge the Services hereunder, misconduct injurious to the Company, and/or personal dishonesty or conviction of a felony offence by the Consultant or by any of the Consultant's employees or agents that the Consultant has engaged in the course of its performance of Services under this Agreement.

- 8.3 The obligations set out in Sections 4, 5 and 6 herein shall survive any termination or expiration of this Agreement. Upon termination or expiration of this Agreement, the Consultant shall deliver to the Company all Confidential Information in its control or possession and shall promptly disclose any and all previously undisclosed Company Inventions.
- 8.4 The Company may terminate this Agreement immediately and further obligation to the Consultant if at any time the Consultant is unable or unwilling:
- (a) to perform the Services or is in breach of any material provision of this Agreement; or
 - (b) to engage an employee or agent that the Company views as acceptable and able, in the Company's sole discretion, to perform the Services under this Agreement.

9. MISCELLANEOUS

- 9.1 This Agreement, including all Schedules attached hereto, constitutes the whole agreement between the parties, there being no written or oral terms, conditions, covenants, agreements, representations or warranties except as expressly set out herein.
- 9.2 This Agreement shall be governed by and interpreted in accordance with the laws of the Province of British Columbia, and the laws of the Canada in force therein without regard to any conflict of law rules. Both parties agree that by executing this Agreement they have attorned to the jurisdiction of the Supreme Court of British Columbia, and the Supreme Court of British Columbia shall have non-exclusive jurisdiction over this Agreement.
- 9.3 The relationship between the Consultant and the Company is one of independent contractors, and neither party shall have the authority to bind or act as the agent for the other, nor shall be responsible for the actions, contracts, debts, or liabilities of the other by virtue of this Agreement. No partnership, joint venture or similar business arrangement will be created or will be deemed to be created by this Agreement or by any actions of the parties under this Agreement.
- 9.4 The Consultant shall be responsible for the management of its employees and without limiting the generality of the foregoing, shall be responsible for payment to the proper authorities of all income tax remittances, employment insurance premiums, Canada Pension Plan contributions, Workers' Compensation premiums and all other employment-related levies or expenses related to its employees.
- 9.5 Neither the Consultant nor its employees or agents will be entitled to receive, or receive, rights or privileges applicable to employees of the Company, including but not limited to liability insurance, group insurance, pension plans, holiday or vacation pay, or any other benefits which may be available to Company employees from time to time.
- 9.6 If at any time Canada Customs and Revenue Agency or any other competent authority determines that the Consultant or any employee or agent of the Consultant is an employee of the Company, then the Company will immediately commence to make all statutorily required withholding and remittances in respect of payments to the Consultant.

- 9.7 The Consultant represents and warrants that it is legally permitted to enter into this Agreement and perform the obligations thereof, and that such obligations are not inconsistent with any other obligation it may have. The Consultant further represents and warrants that it has entered into binding agreement(s) with each of its employees and agents that may be engaged by the Consultant to provide Services under this Agreement, and that said employees and agents have irrevocably agreed to any and all provisions of this Agreement, to the extent that such provisions may apply to them.
- 9.8 The Consultant may not assign or otherwise transfer any of its rights, duties or obligations under this Agreement without prior written consent of the Company.
- 9.9 All monetary amounts referred to herein are in Canadian currency.
- 9.10 In the event that any part, section, clause, paragraph or subparagraph of this Agreement shall be held to be indefinite, invalid, illegal or otherwise voidable or unenforceable, the entire Agreement shall not fail on the account thereof, and the balance of the Agreement shall continue in full force and effect.
- 9.11 This Agreement may be signed in counterparts, or facsimile counterparts, each of which when executed by any of the signatories hereto shall be deemed to be an original and such counterparts shall together constitute one and the same Agreement.

IN WITNESS WHEREOF duly-authorized signatories of the Company and the Consultant, each after having had the opportunity to discuss this Agreement with their respective legal advisors, have executed this Agreement on the date(s) indicated below but effective as of the Effective Date.

XENON GENETICS INC.

GENWORKS INC.

Per: /s/ Simon N. Pimstone
Simon N. Pimstone

Per: /s/ Michael R. Hayden
Michael R. Hayden

Date : 6 May, 2004

Date : 6 May, 2004

Schedule "A"- Services

Duties and Responsibilities of the Consultant

1. The Consultant shall ensure that all Services provided to the Company will be performed by Dr. Michael R. Hayden , and/or such other employee or agent of the Consultant that is approved in advance by the Company, in the Company's sole discretion.
2. The Consultant shall report to the President and CEO of the Company and shall devote sufficient working time and efforts to the clinical, scientific and business affairs of the Company as are necessary and consistent with the needs of the Company. The Services to be provided by the Consultant shall include the following:
 - a. Consults on all aspects of the Company's scientific research programs;
 - b. Chairs the Company's Scientific Advisory Board, consulting with individual members of the Board as necessary;
 - c. Consults on the recruitment of senior scientific staff;
 - d. Oversees development and implementation of the Company's R&D plans and participates in the development and execution of the Company's overall strategic plan;
 - e. Consults on the development and implementation of appropriate policies and procedures governing the Company's research activities;
 - f. Represents the Company in meetings with the pharmaceutical industry and the scientific and business community including attending conferences and meetings both within and outside of Canada;
 - g. Ensures that all scientific activities and operations are carried out in compliance with local, provincial, federal and governmental regulations and laws; and
 - h. Provide all such other services as the Board of Directors of the Company shall determine from time to time, in accordance with the policies and procedures established by the Company.
3. In addition to the above, at the option of the Company, the Consultant may from time to time perform services on behalf of affiliates of the Company and will accept a transfer of its Services to any such affiliate at the request of the Company.

BETWEEN:

XENON PHARMACEUTICALS INC. (formerly Xenon Genetics Inc.) having its head office at 3650 Gilmore Way, Burnaby, British Columbia, V5G 4W8

(the “**Company**”)

OF THE FIRST PART;

AND:

GENWORKS INC., a British Columbia corporation having its offices at 4484 West 7th Avenue, Vancouver, BC, V6R 1W9; Phone: 604-222-0236; Fax: 604-222-0241.

(the “**Consultant**”)

OF THE SECOND PART.

WHEREAS:

- A. The Company and the Consultant entered into a consulting agreement made as of January 1, 2004, (the “**Consulting Agreement**”); and
- B. The parties now wish to make certain amendments to the Consulting Agreement, as detailed here in this Agreement (the “**Amending Agreement**”).

NOW THEREFORE, for good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged by all parties hereto, the Company and the Consultant hereby covenant and agree as follows:

- 1. Capitalized terms used herein, which are not otherwise defined herein, shall have the meaning ascribed to such terms in the Consulting Agreement.
- 2. Section 2.1 of the Consulting Agreement is hereby amended by deleting it in its entirety and substituting therefor the following:
“Unless earlier terminated pursuant to Section 8.1, the term of the Consultant’s engagement pursuant to this Agreement (the “**Term**”) shall commence on the Effective Date and shall terminate on December 31, 2005.”

Section 7.1 is hereby amended by deleting it in its entirety and substituting the following:

“As full consideration for the Services and other covenants and agreements provided by the Consultant under this Agreement, the compensation payable by the Company to the Consultant shall be as follows:

- (a) for the period from January 1, 2004 to December 31, 2005: a consulting fee totaling One Hundred and Fifty Five Thousand Dollars (\$155,000.00) payable monthly in arrears; and
- (b) in addition to the above, on an annual basis, the Consultant is also eligible to receive a performance bonus, such bonus to be paid in an amount and in a manner to be determined by the Board of Directors of the Company, in its sole discretion. The awarding of such bonus (if any) will be decided by the Board of Directors following the Board’s assessment of the Consultant’s contribution(s) to the Company’s successful completion of its major corporate objectives including in-licensing (or acquisition) of a clinical compound or program, an equity financing and achievement of the IND filing milestone payment for the Company’s SCD1 program.”

4. Except as amended herein, the Consulting Agreement remains in full force and effect, unamended.

5. This Amending Agreement may be signed in counterparts, or facsimile counterparts, each of which when executed by any of the signatories hereto shall be deemed to be an original and such counterparts shall together constitute one and the same agreement.

IN WITNESS WHEREOF duly authorized signatories of the Company and the Consultant, each after having had the opportunity to discuss this Amending Agreement with their respective legal advisors, have executed this Amending Agreement on the date(s) indicated below but effective as of the Effective Date of the Consulting Agreement.

XENON PHARMACEUTICALS INC.

GENWORKS INC.

By: /s/ Simon N. Pimstone

By: /s/ Michael R. Hayden

SIMON N. PIMSTONE

MICHAEL R. HAYDEN

President & CEO

Date : 21 Jan/2005

Date : 20/1/05

BETWEEN:

XENON PHARMACEUTICALS INC. (formerly Xenon Genetics Inc.) having its head office at 3650 Gilmore Way, Burnaby, British Columbia, V5G 4W8
(the “**Company**”)

OF THE FIRST PART;

AND:

GENWORKS INC., a British Columbia corporation having its offices at 4484 West 7th Avenue, Vancouver, BC, V6R 1W9; Phone: 604-222-0236; Fax: 604-222-0241.
(the “**Consultant**”)

OF THE SECOND PART.

WHEREAS:

- A. The Company and the Consultant entered into a consulting agreement made as of January 1, 2004 and amended January 18, 2005, (the “**Consulting Agreement**”); and
- B. The parties now wish to make certain amendments to the Consulting Agreement, as detailed here in this Agreement (the “**Second Amending Agreement**”).

NOW THEREFORE, for good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged by all parties hereto, the Company and the Consultant hereby covenant and agree as follows:

- 1. Capitalized terms used herein, which are not otherwise defined herein, shall have the meaning ascribed to such terms in the Consulting Agreement.
- 2. Section 2.1 of the Consulting Agreement is hereby amended by deleting it in its entirety and substituting therefor the following:
“Unless earlier terminated pursuant to Section 8.1, the term of the Consultant’s engagement pursuant to this Agreement (the “**Term**”) shall commence on the Effective Date and shall terminate on December 31, 2006.”
- 3. Except as amended herein, the Consulting Agreement remains in full force and effect, unamended.

4. This Amending Agreement may be signed in counterparts, or facsimile counterparts, each of which when executed by any of the signatories hereto shall be deemed to be an original and such counterparts shall together constitute one and the same agreement.

IN WITNESS WHEREOF duly authorized signatories of the Company and the Consultant, each after having had the opportunity to discuss this Amending Agreement with their respective legal advisors, have executed this Amending Agreement on the date(s) indicated below but effective as of the Effective Date of the Consulting Agreement.

XENON PHARMACEUTICALS INC.

By: /s/ Simon N. Pimstone
SIMON N. PIMSTONE
President & CEO

Date : March 13/06

GENWORKS INC.

By: /s/ Michael R. Hayden
MICHAEL R. HAYDEN

Date : March 9, 2006

BETWEEN:

XENON PHARMACEUTICALS INC. (formerly Xenon Genetics Inc.) having its head office at 3650 Gilmore Way, Burnaby, British Columbia, V5G 4W8
(the “**Company**”)

OF THE FIRST PART;

AND:

GENWORKS INC., a British Columbia corporation having its offices at 4484 West 7th Avenue, Vancouver, BC, V6R 1W9; Phone: 604-222-0236; Fax: 604-222-0241.
(the “**Consultant**”)

OF THE SECOND PART.

WHEREAS:

A The Company and the Consultant entered into a consulting agreement made as of January 1, 2004, amended January 18, 2005, and further amended February 15, 2006 (the “**Consulting Agreement**”); and

B. The parties now wish to make certain amendments to the Consulting Agreement, as detailed here in this agreement (the “**Third Amending Agreement**”).

NOW THEREFORE, for good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged by all parties hereto, the Company and the Consultant hereby covenant and agree as follows:

1. Capitalized terms used herein, which are not otherwise defined herein, shall have the meaning ascribed to such terms in the Consulting Agreement.
2. Section 2.1 of the Consulting Agreement is hereby amended by deleting it in its entirety and substituting therefor the following:
“Unless earlier terminated pursuant to Section 8.1, the term of the Consultant’s engagement pursuant to this Agreement (the “**Term**”) shall commence on the Effective Date and shall terminate on December 31, 2008.”

3. Section 7.1 is hereby amended by deleting it in its entirety and substituting the following:
“As full consideration for the Services and other covenants and agreements provided by the Consultant under this Agreement, the compensation payable by the Company to the Consultant shall be as follows:
- (a) for the period from January 1, 2004 to December 31, 2006: a consulting fee totaling One Hundred and Fifty Five Thousand Dollars (\$155,000.00), payable monthly in arrears;
 - (b) for the period from January 1, 2007 to December 31, 2008: a consulting fee totaling One Hundred and Sixty Thousand Dollars (\$160,000.00), payable monthly in arrears; and
 - (c) in addition to the above, on an annual basis, the Consultant is also eligible to receive a performance bonus, such bonus to be paid in an amount and in a manner to be determined by the Board of Directors of the Company, in its sole discretion. The awarding of such bonus (if any) will be decided by the Board of Directors following the Board’s assessment of the Consultant’s contribution(s) to the Company’s successful completion of its major corporate objectives including in-licensing (or acquisition) of a clinical compound or program, a major pharmaceutical alliance, selection of a clinical candidate for topical administration and initiation of a phase Ha proof-of-concept trial.”
4. Except as amended herein, the Consulting Agreement remains in full force and effect, unamended.
5. This Third Amending Agreement may be signed in counterparts, and delivered personally or by courier, mail, facsimile or electronically, each of which counterparts when executed by any of the signatories hereto shall be deemed to be an original and such counterparts shall together constitute one and the same agreement

IN WITNESS WHEREOF duly authorized signatories of the Company and the Consultant, each after having had the opportunity to discuss this Third Amending Agreement with their respective legal advisors, have executed this Third Amending Agreement on the date(s) indicated below but effective as of the Effective Date of the Consulting Agreement.

XENON PHARMACEUTICALS INC.

GENWORKS INC.

By: /s/ Simon N. Pimstone
SIMON N. PIMSTONE
President & CEO

By: /s/ Michael R. Hayden
MICHAEL R. HAYDEN

Date : 20 Sept/07

Date : September 27, 2007

BETWEEN:

XENON PHARMACEUTICALS INC. (formerly Xenon Genetics Inc.) having its head office at 3650 Gilmore Way, Burnaby, British Columbia, V5G 4W8
(the “**Company**”)

OF THE FIRST PART;

AND:

GENWORKS INC., a British Columbia corporation having its offices at 4484 West 7th Avenue, Vancouver, BC, V6R 1W9; Phone: 604-222-0236; Fax: 604-222-0241.
(the “**Consultant**”)

OF THE SECOND PART.

WHEREAS

- A. The Company and the Consultant entered into a consulting agreement made as of January 1, 2004, which was subsequently amended and extended pursuant to Amending Agreements dated for reference January 18, 2005, February 15, 2006 and September 17, 2007 (the “**Consulting Agreement**”); and
- B. The parties now wish to make certain amendments to the Consulting Agreement, as detailed here in this agreement (the “**Fourth Amending Agreement**”).

NOW THEREFORE, for good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged by all parties hereto, the Company and the Consultant hereby covenant and agree as follows:

- 1. Capitalized terms used herein, which are not otherwise defined herein, shall have the meaning ascribed to such terms in the Consulting Agreement.
- 2. Section 2.1 of the Consulting Agreement is hereby amended by deleting it in its entirety and substituting therefor the following:
“Unless earlier terminated pursuant to Section 8.1, the term of the Consultant’s engagement pursuant to this Agreement (the “**Term**”) shall commence on the Effective Date and shall terminate on June 30, 2011.”

3. Section 7.1 is hereby amended by deleting it in its entirety and substituting the following:

“As full consideration for the Services and other covenants and agreements provided by the Consultant under this Agreement, the compensation payable by the Company to the Consultant shall be as follows:

- (a) for the period from January 1, 2004 to December 31, 2006: a consulting fee totaling One Hundred and Fifty Five Thousand Dollars (\$155,000.00), payable monthly in arrears;
- (b) for the period from January 1, 2007 to December 31, 2008: a consulting fee totaling One Hundred and Sixty Thousand Dollars (\$160,000.00), payable monthly in arrears;
- (c) for the period from January 1, 2009 to June 30, 2009: a consulting fee totaling Eighty-five Thousand Dollars (\$85,000.00), payable monthly in arrears;
- (d) for the period from July 1, 2009 to December 31, 2009: a consulting fee totaling One Hundred Thousand Dollars (\$100,000.00), payable monthly in arrears;
- (e) for the period from January 1, 2010 to December 31, 2010: a consulting fee totaling Two Hundred Thousand Dollars (\$200,000.00), payable monthly in arrears;
- (f) for the period from January 1, 2011 to June 30, 2011, a consulting fee totaling One Hundred Thousand Dollars (\$100,000.00), payable monthly in arrears; and
- (g) in addition to the above, on an annual basis, the Consultant is also eligible to receive a performance bonus, such bonus to be paid in an amount and in a manner to be determined by the Board of Directors of the Company, in its sole discretion. The awarding of such bonus (if any) will be decided by the Board of Directors following the Board’s assessment of the Consultant’s contribution(s) to the Company’s successful completion of its major corporate objectives.”

4. Subsection 8.1(b) is hereby amended by deleting it in its entirety and substituting the following:

“(b) all compensation due to the Consultant under this Agreement for the time remaining in the Term of this Agreement following the date on which the notice of termination occurred, *provided that* such compensation amount shall not be less than an amount equivalent to nine (9) months of the Consultant’s consulting fee then otherwise payable hereunder;”

5. Except as amended herein, the Consulting Agreement remains in full force and effect, unamended.

6. This Fourth Amending Agreement may be signed in counterparts, and delivered personally or by courier, mail, facsimile or electronically, each of which counterparts when executed by any of

the signatories hereto shall be deemed to be an original and such counterparts shall together constitute one and the same agreement,

IN WITNESS WHEREOF duly authorized signatories of the Company and the Consultant, each after having had the opportunity to discuss this Fourth Amending Agreement with their respective legal advisors, have executed this Fourth Amending Agreement as of the date first noted above

XENON PHARMACEUTICALS INC.

GENWORKS INC.

By: /s/ Simon N. Pimstone

By: /s/ Michael R. Hayden

SIMON N. PIMSTONE

MICHAEL R. HAYDEN

President & CEO

This **FIFTH AMENDING AGREEMENT** is dated and effective as of January 1, 2011.

BETWEEN:

XENON PHARMACEUTICALS INC. (formerly Xenon Genetics Inc.) having its head office at 3650 Gilmore Way, Burnaby, British Columbia, V5G 4W8
(the “**Company**”)

OF THE FIRST PART;

AND:

GENWORKS INC., A British Columbia corporation having its offices at 4484 West 7th Avenue, Vancouver, BC, V6R 1W9; Phone: 604-222-0236; Fax: 604-222-0241
(the “**Consultant**”)

OF THE SECOND PART.

WHEREAS:

A. The Company and the Consultant entered into a consulting agreement made as of January 1, 2004, which was subsequently amended and extended pursuant to Amending Agreements dated for reference January 18, 2005, February 15, 2006, September 17, 2007, and January 1, 2009 (collectively, the “**Consulting Agreement**”); and

B. The parties now wish to make certain amendments to the Consulting Agreement, as detailed here in this agreement (the “**Fifth Amending Agreement**”).

NOW THEREFORE, for good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged by all parties hereto, the Company and the Consultant hereby covenant and agree as follows;

1. Capitalized terms used herein, which are not otherwise defined herein, shall have the meaning ascribed to such terms in the Consulting Agreement.
2. Section 2.1 of the Consulting Agreement is hereby amended by deleting it in its entirety and substituting therefor the following:
“Unless earlier terminated pursuant to Section 8.1, the term of the Consultant’s engagement pursuant to this Agreement (the “**Term**”) shall commence on the Effective Date and shall terminate on December 31, 2011,”

3. Section 7.1 is hereby amended as follows:
- by deleting, in its entirety, subsection 7.1(f), as such is set out below:
“(f) for the period from January 1, 2011 to June 30, 2011, a consulting fee totaling One Hundred Thousand Dollars (\$100,000.00), payable monthly in arrears; and”
and
 - by substituting the above, with the following:
“(f) for the period from January 1, 2011 to December 31, 2011, a consulting fee totaling Two Hundred and Four Thousand Dollars (\$204,000.00), payable monthly in arrears; and”
4. Except as amended herein, the Consulting Agreement remains in full force and effect, unamended.
5. This Fifth Amending Agreement may be signed in counterparts, and delivered personally or by courier, mail, facsimile or electronically, each of which counterparts when executed by any of the signatories hereto shall be deemed to be an original and such counterparts shall together constitute one and the same agreement.

IN WITNESS WHEREOF duly authorized signatories of the Company and the Consultant, each after having had the opportunity to discuss this Fifth Amending Agreement with their respective legal advisors, have executed this Fifth Amending Agreement on the dates noted below, but effective as of the date first noted above.

XENON PHARMACEUTICALS INC.

GENWORKS INC.

By: /s/ Simon N. Pimstone
SIMON N. PIMSTONE
President & CEO

By: /s/ Michael R. Hayden
MICHAEL R. HAYDEN

Date : February 4, 2011

Date : February 8, 2011

This **SIXTH AMENDING AGREEMENT** is dated and effective as of January 1, 2012.

BETWEEN:

XENON PHARMACEUTICALS INC. (formerly Xenon Genetics Inc.) having its head office at 3650 Gilmore Way, Burnaby, British Columbia, V5G 4W8
(the “**Company**”)

OF THE FIRST PART;

AND:

GENWORKS INC., A British Columbia corporation having its offices at 4484 West 7th Avenue, Vancouver, BC, V6R 1W9; Phone: 604-222-0236; Fax: 604-222-0241.
(the “**Consultant**”)

OF THE SECOND PART.

WHEREAS:

- A. The Company and the Consultant entered into a consulting agreement made as of January 1, 2004, which was subsequently amended and extended pursuant to Amending Agreements dated for reference January 18, 2005, February 15, 2006, September 17, 2007, January 1, 2009, and January 1, 2011 (collectively, the “**Consulting Agreement**”); and
- B. The parties now wish to make certain amendments to the Consulting Agreement, as detailed here in this agreement (the “**Sixth Amending Agreement**”).

NOW THEREFORE, for good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged by all parties hereto, the Company and the Consultant hereby covenant and agree as follows;

- 1. Capitalized terms used herein, which are not otherwise defined herein, shall have the meaning ascribed to such terms in the Consulting Agreement.
- 2. Section 2.1 of the Consulting Agreement is hereby amended by deleting it in its entirety and substituting therefor the following:
“Unless earlier terminated pursuant to Section 8.1, the term of the Consultant’s engagement pursuant to this Agreement (the “**Term**”) shall commence on the Effective Date and shall terminate on December 31, 2012,”
- 3. Section 7.1 is hereby amended by inserting new subsection 7.1(g), as follows:

“(g) for the period from January 1, 2012 to December 31, 2012, a consulting fee totaling Two Hundred and Ten Thousand One Hundred and Twenty Dollars (\$210,120.00), payable monthly in arrears; and”

and by renumbering the subsequent subsection of Section 7.1 accordingly.

4. Except as amended herein, the Consulting Agreement remains in full force and effect, unamended.
5. This Sixth Amending Agreement may be signed in counterparts, and delivered personally or by courier, mail, facsimile or electronically, each of which counterparts when executed by any of the signatories hereto shall be deemed to be an original and such counterparts shall together constitute one and the same agreement.

IN WITNESS WHEREOF duly authorized signatories of the Company and the Consultant, each after having had the opportunity to discuss this Sixth Amending Agreement with their respective legal advisors, have executed this Sixth Amending Agreement on the dates noted below, but effective as of the date first noted above.

XENON PHARMACEUTICALS INC.

GENWORKS INC.

By: /s/ Simon N. Pimstone

SIMON N. PIMSTONE

President & CEO

By: /s/ Michael R. Hayden

MICHAEL R. HAYDEN

Date : 13 March/2012

Date : 08 - March - 2012

This SEVENTH AMENDING AGREEMENT is dated and effective as of September 1, 2012.

BETWEEN:

XENON PHARMACEUTICALS INC. (formerly Xenon Genetics Inc.) having its head office at 3650 Gilmore Way, Burnaby, British Columbia, V5G 4W8
(the “**Company**”)

OF THE FIRST PART;

AND:

GENWORKS INC., a British Columbia corporation having its offices at 4484 West 7th Avenue, Vancouver, BC, V6R 1W9; Phone: 604-222-0236; Fax: 604-222-0241.
(the “**Consultant**”)

OF THE SECOND PART.

WHEREAS:

- A. The Company and the Consultant entered into a consulting agreement made as of January 1, 2004, which was subsequently amended and extended pursuant to Amending Agreements dated for reference January 18, 2005, February 15, 2006, September 17, 2007, January 1, 2009, January 1, 2011, and January 1, 2012 (collectively, the “**Consulting Agreement**”); and
- B. The parties now wish to make certain amendments to the Consulting Agreement, as detailed here in this agreement (the “**Seventh Amending Agreement**”).

NOW THEREFORE, for good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged by all parties hereto, the Company and the Consultant hereby covenant and agree as follows:

- 1. Capitalized terms used herein, which are not otherwise defined herein, shall have the meaning ascribed to such terms in the Consulting Agreement.
- 2. Section 2.1 of the Consulting Agreement is hereby amended by deleting it in its entirety and substituting therefor the following:
“Unless earlier terminated pursuant to Section 8.1, the term of the Consultant’s engagement pursuant to this Agreement (the “**Term**”) shall commence on the Effective Date and shall terminate on August 31, 2013.”

3. Article 3 of the Consulting Agreement is hereby amended by adding new Subsection 3.2 as follows:
- “3.2 As requested by the Company and described in Schedule A attached hereto, the Consultant agrees to devote and dedicate, on average, up to eight (8) hours of time and effort per year, for each year of the Term beginning September 1, 2012, to providing Services to the Company.”
4. Article 7 of the Consulting Agreement is hereby amended by deleting it in its entirety and substituting therefor the following:
- “7.1 As full consideration for the Services and other covenants and agreements provided by the Consultant under this Agreement, the receipt and sufficiency of which is hereby specifically acknowledged by the Company and the Consultant, the compensation payable by the Company to the Consultant shall be as follows:
- (a) subject to the Company’s Stock Option Plan and any amendments thereto (collectively, the “**Plan**”), over the Term of this Agreement, the Company hereby confirms and agrees that the Consultant will be considered a “Service Provider” under Section 2.18 of the Plan;
 - (b) reimbursement for all reasonable out-of-pocket expenses incurred by the Consultant on behalf of the Company in the course of his provision of Services hereunder, provided that such expenses have received the prior approval of the Company; and
 - (c) the Consultant will invoice the Company on a monthly basis for expenses (as applicable), and provide relevant receipts. Such invoices will be paid by the Company within fifteen (15) days of receipt.
- 7.2 For avoidance of doubt, the Consultant and the Company hereby confirm and agree as follows:
- (a) that the consulting fee payable to the Consultant for the 8-month period from January 1, 2012 to August 31, 2012 shall total \$140,080 , such amount which is equivalent to 8/12th of the annual consulting fee referenced in the Sixth Amending Agreement to the Agreement;
 - (b) that, as set forth in the Fourth Amending Agreement to the Agreement, the Consultant remains eligible to receive a performance bonus respecting Services rendered by the Consultant for the 8-month period from January 1, 2012 to August 31, 2012, such bonus to be paid in an amount and in a manner to be determined by the Board of Directors of the Company, in its sole discretion. The awarding of such bonus (if any) will be decided by the Company’s Board of Directors following the Board’s assessment of the Consultant’s contribution(s) during said 8-month period

(c) from January 1, 2012 to August 31, 2012, to the Company's successful completion of its major corporate objectives for 2012; and except as specifically provided in Section 7.1(b) and Section 7.2(b) above, as of September 1, 2012 and for the duration of the Term of this Agreement, there shall be no consulting fees or performance bonuses or any other monetary fee(s) whatsoever payable by the Company to the Consultant."

5. Section 8.1 of the Consulting Agreement is hereby amended by deleting it in its entirety and substituting therefor the following:
"8.1 Except as provided under Section 8.2 below, either the Company or the Consultant can terminate this Agreement at any time by giving thirty (30) days written notice to other."
6. Schedule A of the Consulting Agreement is hereby amended by deleting it in its entirety and substituting therefore the Schedule A attached hereto.
7. Except as amended herein, the Consulting Agreement remains in full force and effect, unamended.
8. This Seventh Amending Agreement may be signed in counterparts, and delivered personally or by courier, mail, facsimile or electronically, each of which counterparts when executed by any of the signatories hereto shall be deemed to be an original and such counterparts shall together constitute one and the same agreement.

IN WITNESS WHEREOF duly authorized signatories of the Company and the Consultant, each after having had the opportunity to discuss this Seventh Amending Agreement with their respective legal advisors, have executed this Seventh Amending Agreement effective as of the date first noted above.

XENON PHARMACEUTICALS INC.

GENWORKS INC.

By: /s/ Simon N. Pimstone

By: /s/ Michael R. Hayden

SIMON N. PIMSTONE

MICHAEL R. HAYDEN

President & CEO

**Schedule "A"- Services
Duties and Responsibilities**

The Services to be provided by the Consultant shall include:

1. the Consultant shall ensure that all Services provided to the Company will be performed by Dr. Michael R. Hayden, and/or such other employee or agent of the Consultant that is approved in advance by the Company, in the Company's sole discretion;
2. the Consultant shall provide confidential information and advice to the Company, as requested by the Company's Board of Directors and/or the Company's Senior Management from time to time, regarding the following:
 - i. historical information regarding the Company's business, scientific and clinical affairs, including matters relating to the Company's partnerships with third parties and/or other Company matters, on which the Consultant may have knowledge of, as a result of the Consultant's employee's (Dr. Michael Hayden's) former and longstanding position as Chief Scientific Officer and Officer of the Company (such CSO and Officer position which, as of September 1, 2012, is no longer held by such employee of the Consultant), and
 - ii, advice and guidance, regarding the Company's ongoing or future strategic plans or financing plans or third party partnerships; and
3. the provision of such other advice and services as the Company may reasonably request from time to time.

BETWEEN:

XENON PHARMACEUTICALS INC. (formerly Xenon Genetics Inc.) having its head office at 3650 Gilmore Way, Burnaby, British Columbia, V5G 4W8
(the “**Company**”)

OF THE FIRST PART;

AND:

GENWORKS INC., a British Columbia corporation having its offices at 4484 West 7th Avenue, Vancouver, BC, V6R 1W9; Phone: 604-222-0236; Fax: 604-222-0241.
(the “**Consultant**”)

OF THE SECOND PART.

WHEREAS:

- A. The Company and the Consultant entered into a consulting agreement made as of January 1, 2004, which was subsequently amended and extended pursuant to Amending Agreements dated for reference January 18, 2005, February 15, 2006, September 17, 2007, January 1, 2009, January 1, 2011, January 1, 2012, and September 1, 2012 (collectively, the “**Consulting Agreement**”); and
- B. The parties now wish to make certain amendments to the Consulting Agreement, as detailed here in this agreement (the “**Eighth Amending Agreement**”).

NOW THEREFORE, for good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged by all parties hereto, the Company and the Consultant hereby covenant and agree as follows:

- 1. Capitalized terms used herein, which are not otherwise defined herein, shall have the meaning ascribed to such terms in the Consulting Agreement.
- 2. Section 2.1 of the Consulting Agreement is hereby amended by deleting it in its entirety and substituting therefor the following:
“Unless earlier terminated pursuant to Section 8.1, the term of the Consultant’s engagement pursuant to this Agreement (the “**Term**”) shall commence on the Effective Date and shall terminate on December 31, 2013.”

3. Article 7 of the Consulting Agreement is hereby amended by deleting subsection 7.2(c) in its entirety and substituting therefore the following:

“(c) other than reimbursement of expenses as specifically provided in Section 7.1(b) above, the Consultant and the Company confirm and agree that, as of September 1, 2012 and for the duration of the Term of this Agreement, there will be no consulting fees or other monetary amounts payable by the Company to the Consultant under this Agreement. Notwithstanding the foregoing, but at all times subject to the terms of the December 7, 2012 letter agreement between the Company, Teva Pharmaceuticals Industries Ltd. and Michael Hayden, the Consultant and the Company confirm and agree that, at the sole discretion of the Company’s Board of Directors, the Consultant may be eligible to receive a performance bonus from time to time, in the event that the Board of Directors in its sole discretion determines that the Consultant has in its provision of Services hereunder provided special and/or extraordinary value to the Company. Any such performance bonus would be paid in an amount and in a manner to be determined by the Company’s Board of Directors in its sole discretion at the relevant time.”
4. Except as amended herein, the Consulting Agreement remains in full force and effect, unamended.
5. This Eighth Amending Agreement may be signed in counterparts, and delivered personally or by courier, mail, facsimile or electronically, each of which counterparts when executed by any of the signatories hereto shall be deemed to be an original and such counterparts shall together constitute one and the same agreement.

IN WITNESS WHEREOF duly authorized signatories of the Company and the Consultant, each after having had the opportunity to discuss this Eighth Amending Agreement with their respective legal advisors, have executed this Eighth Amending Agreement effective as of the date first noted above.

XENON PHARMACEUTICALS INC.

GENWORKS INC.

By: /s/ Simon N. Pimstone
SIMON N. PIMSTONE
President & CEO

By: /s/ Michael R. Hayden
MICHAEL R. HAYDEN

Via EDGAR and Overnight Delivery

Securities and Exchange Commission
Division of Corporation Finance
100 F Street, N.E.
Washington, D.C. 20549-3720

Attention: Jeffrey P. Riedler, Assistant Director
Matthew Jones, Attorney Advisor
Joel Parker, Accounting Branch Chief
Tabatha Akins, Staff Accountant

**Re: Xenon Pharmaceuticals Inc.
Draft Registration Statement on Form S-1
Submitted August 16, 2013
CIK No. 0001582313**

Ladies and Gentlemen:

On behalf of Xenon Pharmaceuticals Inc. (the "**Company**"), we submit this letter in response to comments from the staff (the "**Staff**") of the Securities and Exchange Commission (the "**Commission**") received by letter dated September 12, 2013, relating to the Company's Confidential Draft Registration Statement on Form S-1 (CIK No. 0001582313) submitted to the Commission on August 16, 2013 (the "**Registration Statement**").

On behalf of the Company, we are concurrently submitting on a confidential basis via EDGAR an amended draft Registration Statement ("**Amendment No. 1**"), and for the convenience of the Staff, we are providing to the Staff by overnight delivery copies of this letter and marked copies of Amendment No. 1 (against the Confidential Draft Registration Statement submitted on August 16, 2013). Amendment No. 1, as confidentially submitted via EDGAR, is marked as specified in Item 310 of Regulation S-T.

In this letter, we have recited the comments from the Staff in italicized, bold type and have followed each comment with the Company's response. Except as otherwise specifically indicated, page references herein correspond to the page of Amendment No. 1, as applicable.

General

- 1. Please file all exhibits as soon as practicable. We may have further comments upon examination of these exhibits.***

The Company acknowledges the Staff's comment and will submit all exhibits as soon as practicable.

2. ***Prior to its use please provide us proofs of all graphic, visual or photographic information you will provide in the printed prospectus. Please note that we may have comments regarding this material.***

The Company acknowledges the Staff's comment and will submit proofs of all graphic, visual or photographic information it intends to provide in the printed prospectus as soon as practicable.

3. ***Please supplementally provide us with any written materials that you or anyone authorized to do so on your behalf provides in reliance on Section 5(d) of the Securities Act to potential investors that are qualified institutional buyers or institutional accredited investors. Similarly, please supplementally provide us with any research reports about you that are published or distributed in reliance upon Section 2(a)(3) of the Securities Act of 1933 added by Section 105(a) of the Jumpstart Our Business Startups Act by any broker or dealer that is participating or will participate in your offering.***

The Company acknowledges the Staff's comment and will provide the Staff with all written communications presented to potential investors, if any, in reliance on Section 5(d) of the Securities Act of 1933 (the "Securities Act") on a supplemental basis. The Company does not expect any research reports to be published or distributed in reliance on Section 2(a)(3) of the Securities Act by any broker or dealer that is participating or will participate in the Company's offering; however, should any such research reports be published or distributed, the Company will provide them to the Staff on a supplemental basis.

4. ***Comments to your application for confidential treatment will be delivered under separate cover.***

The Company acknowledges the Staff's comment.

Overview, page 1

5. ***We note that you state that you have three development-stage product candidates. Please identify the two development-stage product candidates that are pre-clinical.***

In response to the Staff's comment, the Company has revised the disclosure on page 1 of Amendment No. 1.

Our Programs, page 2

6. ***We note on page 2 that uniQure is preparing to apply for regulatory approval for Glybera in the U.S. Please expand your disclosure to discuss the timeline for applying for U.S. approval. If any regulatory issues or other factors have caused uniQure to delay filing an NDA with the FDA or an NDS with Health Canada, please provide appropriate disclosure.***

In response to the Staff's comment, the Company has revised the disclosure on page 2 of Amendment No. 1. The Company supplementally advises the Staff that it is not aware of any regulatory issues or other factors that have caused uniQure to delay regulatory filings with the FDA or Health Canada.

7. The first time you refer to the terms “antisense oligonucleotide” and “hepcidin,” please explain how each functions in the human body.

In response to the Staff’s comment, the Company has revised the disclosure on pages 2 and 3 of Amendment No. 1.

Our Extreme Genetics Discovery Platform, page 3

8. Please expand your disclosure on page 3 and 84 to discuss the differences between your Extreme Genetics discovery platform and the methods commonly used by other pharmaceutical companies that are developing products based upon isolating genes or portions of the human genome.

In response to the Staff’s comment, the Company has revised the disclosure on pages 3 and 87 of Amendment No. 1.

Implications of Being an Emerging Growth Company, page 6

9. Please disclose your election under Section 107(b) of the Jobs Act:

- ***If you have elected to opt out of the extended transition period for complying with new or revised accounting standards pursuant to Section 107(b) of the Jobs Act, include a statement that the election is irrevocable; or***
- ***If you have elected to use the extended transition period for complying with new or revised accounting standards under Section 102(b) of the Jobs Act, provide a risk factor explaining that this election allows you to delay the adoption of new or revised accounting standards that have different effective dates for public and private companies until those standards apply to private companies. Please state in your risk factor that, as a result of this election, your financial statements may not be comparable to companies that comply with public company effective dates. Include a similar statement in your critical accounting policy disclosures in MD&A.***

The Company acknowledges the Staff’s comment and, once such an election has been made, will include the appropriate disclosure in a future submission.

“Recent patent reform legislation and court decisions could increase . . .,” page 38

10. Please explain specifically how the Leahy-Smith Act increases uncertainty as to any of your licensed or owned patents. Additionally, please identify any of your licensed or owned patents that may be vacated or adversely affected by the U.S. Supreme Court decision in *Association for Molecular Pathology v. Myriad Genetics, Inc.*

In response to the first sentence of the Staff’s comment, the Company submits that the Leahy-Smith Act increases uncertainty with respect to all patents in the U.S., including the Company’s licensed and owned patents, because this new statute and implementing regulations represent the most far-reaching revision of the U.S. patent laws since 1952. Until the statute and implementing regulations have been subject to judicial review and clarification in the process of litigation, certain aspects of the law, and their significance for all biotechnology and pharmaceutical companies, including the Company, will remain unclear.

In response to the second sentence of the Staff's comment, the Company does not believe that the decision of the U.S. Supreme Court in *Association for Molecular Pathology v. Myriad Genetics, Inc.* will have a material impact on any patents currently owned by or licensed to the Company that relate to the Company's products and product candidates. The Company's products and product candidates are not naturally occurring isolated genes or compounds, but rather novel compositions of matter made by the Company and its collaborators and, accordingly, the Company's patents do not cover naturally occurring isolated genes or compounds like those that were at issue in the *Myriad* decision.

"We or the third parties upon whom we depend may be adversely affected . . .," page 42

11. Please clarify whether your business interruption insurance applies in the event of an earthquake.

In response to the Staff's comment, the Company has revised the disclosure on page 43 of Amendment No. 1.

Cautionary Note Regarding Forward-Looking Statements, page 49

12. Please remove your statement that investors "are cautioned not to give undue weight to such estimates" and the statement that "such information is inherently imprecise." It is not appropriate to directly or indirectly disclaim liability for information in the registration statement.

In response to the Staff's comment, the Company has deleted the statements referenced above.

Use of Proceeds, page 52

13. We note that you intend to use proceeds of this offering to fund the planned development of XEN701. Please expand your disclosure to state the stage of development of XEN701 you expect to reach using the allocated proceeds.

In response to the Staff's comment, the Company has revised the disclosure on page 54 of Amendment No. 1.

Dilution, page 56

14. Please tell us why you are not subtracting your redeemable convertible preferred shares in your calculation of your historical net tangible book value of as of June 30, 2013.

In response to the Staff's comment, the Company advises the Staff that it did not subtract the redeemable convertible preferred shares in its calculation of historical net tangible book value as of June 30, 2013 because such amounts are not considered liabilities for purposes of such calculation.

Management Discussion and Analysis of Financial Condition and Results of Operations, page 60

15. *We note on page 61 and in a risk factor on page 12 that you state that you have not generated substantial royalties on product sales. Please revise your disclosure throughout your prospectus to clarify that you have not generated any revenue from product royalties. Alternatively, please clarify and describe the royalties you have received.*

In response to the Staff's comment, the Company has revised the disclosure on pages 6, 13, 14 and 63 of Amendment No. 1.

Accrued Expenses, page 67

16. *Please disclose whether there have been any material adjustments to your estimates of accrued expenses for the periods presented.*

In response to the Staff's comment, the Company has revised the disclosure on page 70 of Amendment No. 1.

Share-Based Compensation

Valuation of Common Shares, page 69

17. *We have reviewed your share-based compensation disclosures and have the following comments:*

- *Please revise your disclosure to state the events that resulted in an increase in the fair value of the common stock from \$0.55 at December 21, 2012 to \$1.07 on January 1, 2013.*
- *With respect to the January 1, 2013 valuation report, please clarify whether the blend in the income and market approaches resulted in an equal weighting of both methods.*
- *Please update the stock option table on page 70 through the date of effectiveness of your registration statement. Also, please disclose in the filing any new equity issuances such as preferred stock, warrants, etc. through the date of effectiveness.*
- *Please note we may have additional comments on your accounting for stock compensation and related disclosure once you have disclosed an estimated offering price. Please provide quantitative and qualitative disclosures explaining the difference between the estimated offering price and the fair value of the most recent issuance.*

The Company supplementally advises the Staff that no material events effecting the Company's valuation occurred between December 21, 2012 and January 1, 2013. As disclosed on page 73 of Amendment No. 1, the Company elected to perform a retrospective valuation as of January 1, 2013, as that date represented the beginning of a new accounting period and allowed for the full impact of the Company's collaboration with Teva to be considered and included in the valuation.

In response to the second bullet point of the Staff's comment, the Company has revised the disclosure on page 73 of Amendment No. 1.

In response to the first sentence of the third bullet point of the Staff's comment, the Company has revised the stock option table on page 72 of Amendment No. 1. The Company acknowledges the second sentence of the third bullet point of the Staff's comment and will disclose any new equity issuances through the date of effectiveness.

The Company acknowledges the fourth bullet point of the Staff's comment and will provide quantitative and qualitative disclosures explaining the difference between the estimated offering price and the fair value of the most recent issuance once an estimated offering price is determined.

Research and Development Expenses, page 73

18. *For your key research and development projects please disclose the costs incurred during each period presented and to date.*

In response to the Staff's comment, the Company has revised the disclosure on pages 75 and 77 of Amendment No. 1.

Business, page 81

19. *Please amend your disclosure to describe the INDs submitted for XEN402 by indication and disclose when these INDs were filed and by whom. Additionally, please clarify whether you or anyone else has filed INDs for XEN701 or the Selective Inhibitor of Nav1.7 for the Treatment of Pain. If so, provide the same information as requested for the INDs for XEN402.*

In response to the Staff's comment, the Company has revised the disclosure on pages 83, 85 and 86 of Amendment No. 1.

Glybera, page 82

20. *Please disclose how you anticipate physicians will prescribe Glybera for patients suffering from LPLD. In particular, please clarify whether you believe doctors will prescribe Glybera for permanent, indefinite, intermittent or short-term use.*

In response to the Staff's comment, the Company has revised the disclosure on page 85 of Amendment No. 1. The Company supplementally advises the Staff that it is unable to predict how physicians might prescribe Glybera with any degree of certainty at this time. However, as stated in the revised disclosure, the goal of Glybera therapy is to chronically treat LPLD, and this may be achievable through intermittent use.

Programs, page 85

21. *We note that you have a collaboration agreement with Teva to develop XEN402 as an inhibitor of Nav1.7. We also note that you have entered into a collaboration agreement with Genentech to develop inhibitors for Nav1.7. Please expand your disclosure to discuss the differences between these two drugs that both inhibit Nav1.7, and the anticipated patient population for each.*

In response to the Staff's comment, the Company has revised the disclosure on pages 90 and 100 of Amendment No. 1 to discuss the differences between these two drugs. The Company respectfully advises the Staff that the anticipated patient population for XEN402 in the U.S. is disclosed on page 90. The Company

acknowledges the Staff's comment regarding the anticipated patient population for the oral selective Nav1.7 inhibitor developed in collaboration with Genentech, and respectfully advises that this population cannot currently be determined, as the target indication for this product candidate has not yet been selected.

Glybera (alipogene tiparvovec): A Gene Therapy for the Orphan Disease LPLD, page 85

22. *We note on page 85 that you state that you are eligible to receive a double-digit percentage of all compensation received by uniQure. Please revise this disclosure to provide narrower information about the percentage. For example, you may either provide a range of percentages within ten percent or a statement that the percentage is in the teens, twenties, etc. Additionally, we note that you state that you are eligible to receive mid-single digit royalties from uniQure on page 97. Please include this disclosure on page 85.*

In response to the Staff's comment, the Company has revised the disclosure on pages 85 and 101 of Amendment No. 1.

23. *Please quantify the size of the patient population that you and your collaborators are targeting for sales of Glybera.*

The Company acknowledges the Staff's comment and respectfully submits that there is no consensus in the scientific community as to the number of LPLD patients; however, the Company has disclosed on page 89 of Amendment No. 1 the population frequency of LPLD in the U.S. as reported by the National Library of Medicine. The Company understands that uniQure is currently developing an estimate of market size and will supplement this disclosure in a subsequent filing if the information becomes available.

24. *Please clarify whether Glybera has orphan designation in the EU.*

In response to the Staff's comment, the Company has revised the disclosure on page 89 of Amendment No. 1.

25. *We note that you state the results of your Topical XEN402 Phase 2 Trial in EM on page 89. Please indicate the statistical significance of your results by providing a p-value.*

In response to the Staff's comment, the Company has revised the chart on page 93 of Amendment No. 1 to include the requested p-values.

XEN701: An Antisense Oligonucleotide for the Treatment of Anemia of Chronic Kidney Disease, page 94

26. *Please quantify the size of the patient population that you plan to target for sales of XEN701.*

In response to the Staff's comment, the Company has revised the disclosure on page 98 of Amendment No. 1.

Programs in Discovery, page 96

27. ***Please quantify the size of the patient population suffering from DS that you plan to target for sales of your small-molecule sodium channel modulators.***

In response to the Staff's comment, the Company has revised the disclosure on page 101 of Amendment No. 1.

Strategic Alliances, page 97

28. ***We note that you have a license agreement with Memorial University of Newfoundland on page 76. Please disclose the material terms of this agreement under a separate caption, including the patents licensed under this agreement and how they apply to your products, the duration, material termination provisions, and payment terms and prior payments. Additionally, please file this agreement as an exhibit pursuant to Item 601(b)(10) of Regulation S-K. Alternatively, please provide us with an analysis supporting your determination that this agreement is not material to the company.***

The Company acknowledges the Staff's comment regarding the license agreement with Memorial University of Newfoundland ("MUN"); however, the Company respectfully submits that the MUN agreement is not material to the Company, the existing disclosure regarding the agreement is sufficient for an agreement of this nature and that disclosure of the additional details requested would neither be helpful to an investor nor would disclosure of such details alter the total mix of information available regarding the Company.

The Company's agreement with MUN sets forth the terms pursuant to which MUN had collaborated with the Company. Specifically, MUN collected certain DNA samples and provided the Company with a non-exclusive license to use such samples and associated anonymized clinical information. No patents owned by MUN were licensed to the Company pursuant to this agreement. Potential milestone payments owed to MUN pursuant to the terms of the agreement are immaterial to the Company's business and contingent upon filing New Drug Applications related to the Company's pain program. Any potential royalties owed to MUN are contingent upon sales of products resulting from the Company's pain program. Furthermore, on page 80 of Amendment No. 1, the Company includes disclosure regarding the potential royalties owing to MUN.

For the foregoing reasons, the Company respectfully submits that the MUN agreement is not material to the Company and that the existing disclosure is sufficient.

29. ***Please disclose under a separate caption the payment terms, duration, and material termination provisions of your agreement with the University of British Columbia for your license related to Glybera.***

In response to the Staff's comment, the Company has revised the disclosure on page 102 of Amendment No. 1.

Agreement with uniQure for Glybera, page 97

- 30. For the uniQure agreement, please disclose the duration of the agreement, the material termination provisions, and when the licensed patents expire.**

In response to the Staff's comment regarding the duration of the agreement and the material termination provisions, the Company has revised the disclosure on page 102 of Amendment No. 1. The Company acknowledges the Staff's comment regarding disclosure of expiration dates of the licensed patents; however, the Company respectfully submits that the requested information is inherently uncertain and thus would not materially enhance an investor's understanding of the Company's agreement with uniQure. Specifically, the Company supplementally advises the Staff that there is a pending U.S. application in one of the patent families that may receive a patent term adjustment if and when such application is prosecuted to grant. Similarly, one of the relevant European patents is the subject of an application for a supplementary protection certificate in Europe, which, if granted, could provide an additional five years of exclusive rights upon grant. Given these uncertainties, the Company is not able to accurately identify when the licensed patents will expire and therefore submits that any such disclosure would not materially enhance an investor's understanding of the Company's agreement with uniQure. Furthermore, additional information regarding the Glybera patents is included on page 105 of Amendment No. 1.

- 31. We note that you state you will receive a double-digit percentage of all non-royalty compensation that uniQure receives from sublicenses. Please revise your disclosure throughout the registration statement to provide narrower information about the percentage. For example, you may either provide a range of percentages within ten percent or a statement that the percentage is in the teens, twenties, etc.**

In response to the Staff's comment, the Company has revised the disclosure on page 101 of Amendment No. 1.

Agreement with Teva for XEN402, page 98

- 32. For the Teva agreement, please disclose the amount of the opt-in fee required for you to have a minority co-promotion interest, the resulting share of the operating profits that you are entitled, and the duration of the agreement. Additionally, please revise your disclosure throughout the registration statement to provide narrower information about the royalty provisions. For example, you may either provide a range of royalties within ten percent or a statement that the percentage is in the teens, twenties, etc.**

In response to the Staff's comment, the Company has revised the disclosure on page 102 and 103 of Amendment No. 1.

Agreement with Genentech for Selective Inhibitors of Nav1.7, page 99

- 33. Please state the duration of your agreement with Genentech.**

In response to the Staff's comment, the Company has revised the disclosure on page 104 of Amendment No. 1.

- 34. For the Genentech Agreement, we note that you are eligible to receive royalties in the low double-digit range. Please revise your disclosure throughout the registration statement to provide narrower information about the royalty provisions. For example, you may either provide a range of royalties within ten percent or a statement that the percentage is in the teens, twenties, etc.**

In response to the Staff's comment, the Company has revised the disclosure on page 104 of Amendment No. 1.

Agreement with Merck for Cardiovascular Disease, page 99

- 35. For the Merck Agreement, we note that you are eligible to receive royalties in the high single digit to low double-digit range. Please revise your disclosure regarding the low-double digit range throughout the registration statement to provide narrower information about the royalty provisions. For example, you may refer to a range of royalties within ten percent or state that the percentage is in the teens, twenties, etc.**

In response to the Staff's comment, the Company has revised the disclosure on page 104 of Amendment No. 1.

- 36. Please state the duration of the agreement with Merck.**

In response to the Staff's comment, the Company has revised the disclosure on page 105 of Amendment No. 1.

Research and Development, page 101

- 37. Please estimate the amount spent on research and development for the past 3 years ending in December 31, 2012 as required by Regulation S-K Item 101(c)(1)(xi).**

In response to the Staff's comment, the Company has revised the disclosure on page 106 of Amendment No. 1.

Manufacturing, page 102

- 38. We note that there are a limited number of suppliers of XEN701, and the inability to find a suitable replacement could materially impact your business. Please expand your disclosure to state your current relationship and the material termination provision of your contractual agreement with your suppliers for XEN701. Additionally, file these agreements as exhibits pursuant to Item 601(b)(10) of Regulation S-K.**

In response to the Staff's comment, the Company respectfully submits that it does not believe that the identification of any third party which supplies the Company with antisense oligonucleotides, like XEN701, is material to investors or that its current supply agreement with respect to XEN701 is required to be filed as an exhibit under Item 601(b)(10) of Regulation S-K. As disclosed on pages 106 and 107 of Amendment No. 1, there are fewer manufacturers of oligonucleotides than manufacturers of small-molecules. While it is appropriate to disclose this fact about the Company's supply options to prospective

investors, the smaller number of alternative oligonucleotide suppliers is not akin to a sole-source supply arrangement that would make the success of the Company's XEN701 development program contingent upon an uninterrupted supply of oligonucleotides from a single manufacturer. As discussed in greater detail below, there are additional manufacturers of oligonucleotides that could be engaged by the Company if the need arises. While the need to engage new suppliers can be a lengthy process, the risk is not unique to the XEN701 program and the Company's disclosure adequately apprises prospective investors of the risks faced if new suppliers become necessary. Furthermore, the Company advises the Staff that it has on hand supplies of XEN701 sufficient to advance the clinical development of XEN701 through Phase 1 and into a Phase 2a clinical trial.

With respect to the Staff's request that the Company file its agreement with its oligonucleotide supplier, the Company respectfully advises the Staff that:

- such agreement was entered into in the ordinary course of the Company's business and is typical for the kind of business conducted by the Company;
- such agreement relates only to limited quantities required for the Company's clinical development of XEN701, and the Company anticipates entering into other manufacturing agreements for production of XEN701 as the clinical development program advances to a later stage;
- because there are at least six other suppliers capable of manufacturing antisense oligonucleotide drug substances, like XEN701, under current good manufacturing practices in quantities suitable for clinical development, the Company believes that in the event its supplier were to cease providing raw materials to the Company, it would be able to find a suitable replacement;
- the agreement contains no minimum purchase requirements; and
- the agreement is terminable by the Company on short notice without penalty.

Accordingly, because (i) the agreement is entered into the ordinary course of the Company's business and (ii) the Company's business is not substantially dependent on any particular supplier, the Company believes that the identity of any third-party supplier is not material to investors and that any related arrangement need not be filed as an exhibit pursuant to Item 601(b)(10) of Regulation S-K.

Subsequent to the completion of the initial public offering, if the Company enters into an agreement with a third-party manufacturer for commercial-scale production of its clinical drug candidates, the Company will analyze such agreement as to materiality and determine whether disclosure is required and if the agreement is required to be filed as an exhibit to the Company's 1934 Act reports pursuant to Item 601(b)(10) of Regulation S-K.

Orphan Drug Designation, page 107

39. *Please clarify if the FDA has granted orphan designation to any of your products.*

In response to the Staff's comment, the Company has revised the disclosure on page 111 of Amendment No. 1.

Government Regulation Outside of the U.S., page 109

40. *Please clarify if any of your products have received orphan designation in the EU.*

In response to the Staff's comment, the Company has revised the disclosure on page 115 of Amendment No. 1.

Management

Executive Officers, page 115

41. *Please expand your disclosure to include Gary Bridger's business experience between December 2007 and June 2010.*

In response to the Staff's comment, the Company has revised the disclosure on page 120 of Amendment No. 1.

Indemnification Agreements and Directors' and Officers' Liability Insurance, page 123

42. *We note that you will enter into indemnification agreements. Please file the form of these agreements as an exhibit pursuant to Item 601(b)(10) of Regulation S-K.*

The Company acknowledges the Staff's comment and will submit the form of indemnification agreement as soon as practicable.

43. *Please expand your disclosure to explain the limits of indemnification permitted under Canadian law.*

In response to the Staff's comment, the Company has revised the disclosure on page 129 of Amendment No. 1.

Executive Compensation

Executive Employment Arrangements, page 125

44. *Please update your disclosure to include the material terms of the executive employees' amended employment agreements when available.*

The Company acknowledges the Staff's comment and will update the executive compensation disclosure as soon as practicable following finalization of the executive employee's amended employment agreements.

45. *Please file the amended employment agreements between the company and each of Dr. Pimstone and Dr. Goldberg as exhibits pursuant to Item 601(b)(10) of Regulation S-K.*

The Company acknowledges the Staff's comment and will submit the amended employment agreements as soon as practicable.

Certain Relationships and Related Party Transactions
Consulting Services Provided by Genworks, Inc., page 132

46. *If you have a written consulting agreement with Genworks, Inc., please file the agreement as an exhibit pursuant to Item 601(b)(10) of Regulation S-K.*

The Company acknowledges the Staff's comment and has submitted a copy of the consulting agreement with Genworks, Inc. as an exhibit to Amendment No. 1.

Shares Eligible for Future Sale, page 149

47. *Please state the number of shares of common stock that will be restricted securities under Rule 144 upon completion of this offering.*

The Company acknowledges the Staff's comment and will include the requested information in a future submission.

48. *Once available please file copies of each of the lock-up agreements.*

The Company will file the form of lock-up agreement, which will be an exhibit to the underwriting agreement, as soon as practicable.

Notes to Financial Statements

9. Redeemable Convertible Preferred Shares: Conversion, page F-16

49. *With respect to the certain adjustments, please revise your disclosure to specifically state the additional events that cause the conversion rate to change, as your reference to "the like" is ambiguous. In addition, please provide us an analysis of whether the conversion option for all preferred stock issued should be a derivative liability.*

In response to the first sentence of the Staff's comment, the Company has revised the disclosure on page F-16 of Amendment No. 1.

In response to the second sentence of the Staff's comment, the Company advises the Staff that in considering whether the conversion options under the Company's various series of preferred shares are required to be separated as embedded derivatives, the Company has performed a two step analysis:

(1) determining the nature of the host contract and (2) determining whether the conversion option represents an embedded derivative in relation to the host contract.

The first step the Company considered was to determine whether the host contract (i.e., the preferred shares) has characteristics that are more akin to debt or to equity. In making this determination, the Company considered the applicable FASB guidance and SEC Staff speeches. As part of this analysis, the Company noted the following factors that support the treatment of the preferred shares as an equity host:

- the preferred shares have the right to vote,
- there is no collateral attached to the preferred shares,
- the preferred shares have no mandatory redemption feature at a specified future date, and
- the preferred share dividend is non-cumulative.

On the basis of these factors, the Company concluded that the preferred shares represent an equity host.

Having concluded that the host instrument is equity, the Company subsequently considered whether there is a requirement to separate the conversion option or whether such an option is considered to be clearly and closely related to the host instrument. ASC 815-15-25-16 states, "If the host contract encompasses a residual interest in an entity, then its economic characteristics and risks shall be considered that of an equity instrument and an embedded derivative would need to possess principally equity characteristics (related to the same entity) to be considered clearly and closely related to the host contract." As the conversion option allows the holder to exchange the preferred shares for a known number of common shares, changes in the value of the common shares (i.e., equity) would be the main driver of any change in the value of the conversion option. Due to this relationship, the embedded derivative possesses principally equity characteristics. As both the host and the embedded derivative are considered to have equity characteristics, the embedded derivative is considered to be clearly and closely related to the host and should not be separated.

11. Stock Option Plan, page F-17

50. ***We note that the expected volatility remained at 70% for each of the periods presented. Please tell us why the amount did not change for any period and provide us with your calculation. In addition, clarify how you determined that each public companies used in your determination of expected volatility company was similar. Please also tell us whether the volatility was consistently calculated for each period (i.e. daily, monthly, weekly, etc.).***

The Company advises the Staff that as a private company, it must determine an expected volatility by comparison to the actual volatility of a comparable group of public companies. For this determination, the Company used the following group of public companies:

- Jazz Pharmaceuticals Public Limited Company
- Recordati SpA
- Almirall, S.A.
- Optimer Pharmaceuticals
- NewLink Genetics Corporation
- Sangamo Biosciences Inc.
- Endocyte, Inc.
- Trius Therapeutics, Inc.
- Synta Pharmaceuticals Corp.
- DepoMed Inc.
- Anacor Pharmaceuticals Inc.
- Zogenix, Inc.
- BioDelivery Sciences International, Inc.

This group of comparable companies was selected due to their similarity to the Company in terms of stage of development, therapeutic focus area, products offered for sale or financial condition. In addition, several of these companies had recently completed initial public offerings, which contributed to the Company's decision to include them in the comparable group.

Volatility was consistently computed on a weekly basis over each period of time and annualized to arrive at a mean volatility factor of the comparable companies for the respective prior five year period of trading for each measurement date. A period of time less than five years was used for individual comparable companies that had not been publicly traded for at least five years.

Based on the mean volatility calculation, a rounded volatility amount of 70% was used as the expected volatility factor to compute stock-based compensation for stock options granted during each period. The mean volatility calculations for the prior five year historical period for the comparable group at each of the four periods presented are set forth below:

- Year ended December 31, 2012 – 72.0%
- Year ended December 31, 2011 – 66.8%
- Six months ended June 30, 2013 – 69.9%
- Six months ended June 30, 2012 – 71.9%

While the individual mean volatility calculations set forth above do vary, the Company respectfully submits that the differences between the actual volatility calculations and the rounded volatility factor of 70% are immaterial.

13. Collaboration Agreements, page F-20

51. ***For your Genome BC arrangement, please revise your disclosure to comply with ASC 605-25-50-2. It is currently unclear what you are collaborating on and what your deliverables are. In addition, please tell us what the counterparty is receiving for funding your research and development beyond the subscription rights. If the consideration is limited to the subscription rights, please explain the economics of the arrangement to us.***

In response to the Staff's comment, the Company has revised the disclosure on page F-21 of Amendment No. 1. In addition to the subscription rights issued to Genome BC and as currently disclosed in Note 13(a), Genome BC, a not-for-profit organization that provides grants and other funding to various organizations in British Columbia for genomics-based research, is entitled to receive a payment equal to 50% of the total research funding provided by Genome BC to the Company under the funding agreement, in the event that the Company files for marketing approval in any jurisdiction for a hepcidin or hemojuvelin antisense product that arose from the funding agreement.

52. ***For your Genentech and Teva arrangements please disclose why the licenses did not qualify as separate units of accounting pursuant to ASC 605-25-50-2f. In addition, tell us how your statement that you are unable to estimate a fair value for the undelivered items complies with ASC 605-25-30-2 and how this statement impacts your accounting.***

In response to the first sentence of the Staff's comment, the Company has revised the disclosure on pages F-23 and F-24 of Amendment No. 1. In response to the second sentence of the Staff's comment, the Company has deleted the statement that it is unable to estimate a fair value for the undelivered items as it is unnecessary under ASC 605-25-30-2 and does not impact the Company's accounting.

53. ***You disclose several agreements which you are eligible to receive milestone payments. Please revise your disclosure to describe each substantive milestone and the related contingent consideration for each agreement separately. Refer to ASC 605-28-50-2b. In addition, clarify for us why you believe all potential milestone payments under the Merck and Teva agreement are substantive per ASC 605-28-25-2 when you do not appear to be performing any additional work in the Merck agreement and it is unclear why sales milestones are substantive in the Teva agreement.***

In response to the Staff's comment, the Company has revised the disclosure on pages F-21 through F-26 of Amendment No. 1 to describe the different milestone payments related to development, regulatory and sales-based achievements and the aggregate milestone payments for each such group of milestones for each collaboration consistent with ASC 605-28-50-2b. In response to the Staff's request to describe each substantive milestone and the related contingent consideration for each agreement, the Company refers the Staff to the Company's Request for Confidential Treatment dated September 13, 2013 (the "CTR"), which requested confidential treatment of the items addressed in the Staff's comment for the reasons described therein. The Company respectfully submits that disclosure of the substantive milestones and the related contingent consideration would not be useful to investors and would cause competitive harm to the Company. The Company supplementally advises the Staff that, consistent with ASC 605-28-25-2, the Company has revised its disclosure related to the future potential milestone payments under the Merck, Teva and Genentech collaboration agreements.

* * * * *

Please direct your questions or comments regarding the Company's responses or Amendment No. 1 to Troy Foster at (650) 565-3600. Thank you for your assistance.

Sincerely,

WILSON SONSINI GOODRICH & ROSATI
Professional Corporation

/s/ Troy Foster

Troy Foster

Enclosures

cc (w/encl.): Simon Pimstone
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