

Xenon Pharmaceuticals Inc.
Form 10-K
March 07, 2018

or

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2017

or

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF
1934

For the transition period from _____ to _____

Commission file number: 001-36687

XENON PHARMACEUTICALS INC.

(Exact Name of Registrant as Specified in its Charter)

Canada 98-0661854
(State or other jurisdiction (I.R.S. Employer

of incorporation or organization) Identification Number)

200 – 3650 Gilmore Way

Burnaby, British Columbia V5G 4W8

Canada

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(Address of Principal Executive Offices, including zip code)

(Registrant's Telephone Number, Including Area Code): (604) 484-3300

Securities registered pursuant to Section 12(b) of the Act:

| Title of Each Class | Name of Exchange on Which Registered |
|---------------------------------------|---|
| Common Shares, no par value per share | The NASDAQ Stock Market LLC (The NASDAQ Global Market) |

Securities registered pursuant to Section 12(g) of the Act: None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes No

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. Yes No

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes No

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§229.405) is not contained herein, and will not be contained, to the best of the registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an emerging growth company. See definitions of "large accelerated filer", "accelerated filer," "smaller reporting company," and "emerging growth 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
Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

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Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Securities Exchange Act of 1934). Yes No

The aggregate market value of the voting and non-voting common shares held by non-affiliates of the registrant, based on the closing sale price of the registrant's common shares on the last business day of its most recently completed second fiscal quarter, as reported on The NASDAQ Global Market, was approximately \$43.4 million. Common shares held by each executive officer and director and by each other person who may be deemed to be an affiliate of the registrant, have been excluded from this computation. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

The number of outstanding common shares of the registrant, no par value per share, as of March 2, 2018 was 18,002,499.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive Proxy Statement to be filed with the Securities and Exchange Commission in connection with the registrant's 2018 Annual Meeting of Shareholders, which will be filed subsequent to the date hereof, are incorporated by reference into Part III of this Form 10-K. Such Proxy Statement will be filed with the Securities and Exchange Commission not later than 120 days following the end of the registrant's fiscal year ended December 31, 2017.

XENON PHARMACEUTICALS INC.

FORM 10-K

For the Fiscal Year Ended December 31, 2017

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PART I

Forward-Looking Statements

Certain statements contained in this Annual Report on Form 10-K may constitute forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended and Canadian securities laws. The words or phrases “would be,” “will allow,” “intends to,” “may,” “believe,” “plan,” “will likely result,” “are expected to,” “will continue,” “is anticipated,” “estimate,” “project,” or similar expressions or the negative of such words or phrases, are intended to identify “forward-looking statements.” You should read these statements carefully because they discuss future expectations, contain projections of future results of operations or financial condition, or state other “forward-looking” information. These statements relate to our future plans, objectives, expectations, intentions and financial performance and the assumptions that underlie these statements. These forward-looking statements include, but are not limited to:

- our ability to identify additional products or product candidates either from our internal research efforts or through acquiring or in-licensing other product candidates or technologies;
- the initiation, timing, cost, progress and success of our research and development programs, pre-clinical studies, and clinical trials;
- our ability to advance product candidates into, and successfully complete, clinical trials;
- our ability to recruit sufficient numbers of patients for our current and future clinical trials for orphan or more common indications;
- 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 timing and magnitude of potential milestone payments under our product acquisition and in-licensing agreements;
- the implementation of our business model and strategic plans;
- our ability to develop and commercialize product candidates for orphan and niche indications independently;
- our commercialization, marketing and manufacturing capabilities and strategy;
- 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 any future products;
- the timing of, and our and our collaborators’ ability to obtain and maintain, regulatory approvals for our product candidates;
- our ability to maintain and establish collaborations;
- our expectations regarding market risk, including interest rate changes and foreign currency fluctuations;
- our belief in the sufficiency of our cash, cash equivalents and marketable securities to meet our needs for at least the next 12 months;
- our 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.

These forward-looking statements are subject to certain risks and uncertainties that could cause actual results to differ materially from those anticipated in the forward-looking statements. Factors that might cause such a difference include, but are not limited to, those discussed in this report in Part I, Item 1A — “Risk Factors,” and elsewhere in this report. Forward-looking statements are based on our management’s beliefs and assumptions and on information currently available to our management. These statements, like all statements in this report, speak only as of their date, and we undertake no obligation to update or revise these statements in light of future developments. In this report, “we,” “our,” “us,” “Xenon,” and “the Company” refer to Xenon Pharmaceuticals Inc. and its subsidiary. Unless otherwise noted, all dollar amounts in this report are expressed in United States dollars.

This Annual Report on Form 10-K includes our trademarks and registered trademarks, including the Xenon logo and other trademarks or service marks of Xenon. Each other trademark, trade name or service mark appearing in this Annual Report on Form 10-K belongs to its holder.

Item 1. Business Overview

We are a clinical stage biopharmaceutical company focused on developing innovative therapeutics to improve the lives of patients with neurological disorders. Building upon our extensive knowledge of human genetics and diseases caused by mutations in ion channels, known as channelopathies, we are advancing a novel product pipeline of central nervous system, or CNS, therapies to address areas of high unmet medical need, such as epilepsy and pain.

To date, our pharmaceutical collaborations have generated in aggregate over \$160.0 million in non-equity funding with the potential to provide us with future milestone payments, as well as royalties on product sales. Our current pharmaceutical partners include Genentech, a member of the Roche Group, and Merck & Co., Inc., or Merck (through its affiliate, Essex Chemie AG).

Our clinical development pipeline includes:

✕ XEN1101 is a Kv7 potassium channel opener being developed for the treatment of epilepsy including: treatment-resistant adult and pediatric focal seizures; rare, pediatric forms of epilepsy, such as EIEE7, an early infantile epileptic encephalopathy associated with mutations in the KCNQ2 gene that cause loss-of-function in the Kv7.2 potassium channel; and potentially other neurological disorders. In October 2017, we initiated a randomized, double-blind, placebo-controlled Phase 1 clinical trial to evaluate the safety, tolerability and pharmacokinetics of both single ascending doses, or SAD, and multiple ascending doses, or MAD, of XEN1101 in healthy subjects. The XEN1101 Phase 1 clinical trial includes a pharmacodynamic biomarker read-out from a transcranial magnetic stimulation, or TMS, study, designed to assess XEN1101’s ability and potency to modulate cortical excitability, thereby demonstrating activity in the target CNS tissue. We expect to present interim Phase 1 results in May 2018. The release of the complete Phase 1 results, including the Phase 1b TMS data, is anticipated in the second half of 2018. We anticipate initiating a Phase 2 proof-of-concept trial evaluating XEN1101’s efficacy as a treatment for adult focal seizures by year end. We also intend to explore a parallel plan to advance XEN1101 into rare, pediatric forms of epilepsy as soon as feasible thereafter;

✕ XEN901 is a potent, highly selective Nav1.6 sodium channel inhibitor being developed for the treatment of epilepsy including treatment resistant adult and pediatric focal seizures, as well as rare, pediatric forms of epilepsy, such as EIEE13, an early infantile epileptic encephalopathy due to gain-of-function mutations in the SCN8A gene that encodes the Nav1.6 sodium channel. In February 2018, we initiated a randomized, double-blind, placebo-controlled Phase 1 clinical trial to evaluate XEN901’s safety, tolerability and pharmacokinetics in both SAD and MAD cohorts of approximately 64 healthy subjects in total. Upon completion of the Phase 1 clinical trial, a read-out of results is anticipated in the second half of 2018, followed by a Phase 2 proof-of-concept trial evaluating XEN901’s efficacy as a treatment for adult focal seizures. We also intend to pursue a parallel plan to advance XEN901 into rare, pediatric

forms of epilepsy as soon as feasible thereafter;

• We have identified an additional clinical stage, ion channel program, XEN007 (active ingredient flunarizine), to expand our existing neurology-focused product pipeline. XEN007 is a CNS-acting calcium channel blocker that directly modulates Cav2.1, which is a critical calcium channel implicated in the pathophysiology of hemiplegic migraine, or HM, a rare and debilitating neurological disorder afflicting approximately 60,000 people in the U.S. Flunarizine has been used outside of the U.S. in the prevention of chronic migraine and has been reported to have clinical benefit in HM case studies. Xenon's clinical development plans include a proposed strategy to develop XEN007 as the first treatment specifically approved for HM anywhere in the world. We have received Orphan Drug Designation from the U.S. Food and Drug Administration, or FDA, for XEN007 for the treatment of HM. In addition, we have entered into key agreements in order to access regulatory files and manufacturing support to potentially enable the accelerated clinical development of XEN007 directly into a Phase 2 clinical trial. We are currently examining various development strategies for XEN007 with key opinion leaders and leading clinicians, as well as exploring options for potential partnerships for this program; and

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•We have an ongoing collaboration with Genentech focused on developing novel inhibitors of Nav1.7 for the treatment of pain. Genentech has completed a Phase 1 clinical trial for GDC-0310, which is an oral, selective Nav1.7 small-molecule inhibitor developed for the potential treatment of pain. Guidance around the future clinical development of GDC-0310 will be updated once ongoing pre-clinical studies are completed and the final results are analyzed by Genentech.

Our Strategy

Our goal is to build a self-sustaining, fully-integrated, and profitable company that discovers, develops and commercializes innovative CNS therapeutics, including novel, selective ion channel modulators. We intend to expand our pipeline with therapeutic candidates from our internal research efforts, such as XEN901, and through the acquisition or in-licensing of other technologies or product candidates, such as XEN1101.

Our strategy includes:

•Focusing on orphan and niche disease market opportunities that we can independently develop and commercialize ourselves.

•Selectively establishing additional partnerships enabling us to access large commercial indications while leveraging the benefits of those collaborations to expand our internal capabilities.

•Further leveraging our discovery platform and insights into disease biology to identify novel targets and additional product candidates.

A significant focus of our discovery efforts has been on human channelopathies, enabling us to develop strong capabilities in small molecule ion channel drug discovery. Our ion channel discovery capability is founded upon our understanding of the genetics of channelopathies combined with our proprietary biology and medicinal chemistry assets and know-how. We, along with our collaborators at Genentech, identified new binding sites on ion channels which, in turn, led to the discovery of highly-selective voltage-gated sodium channel inhibitors, which may have safety and efficacy advantages over non-selective sodium channel inhibitors.

While the pharmaceutical industry has shown significant interest in channelopathies, a general inability to target ion channels selectively with a pharmaceutical agent has been a limitation to the development of effective therapeutics. We believe we have developed a core competence in developing highly-selective small-molecule ion channel inhibitors, and we believe we can use this know-how to develop a pipeline of novel ion channel inhibitors for diseases in areas of high unmet medical need.

Our Pipeline

Our pipeline is summarized in the following figure, which shows our own proprietary product candidates and our partnered pain program:

Our Product Candidates

XEN1101, A Selective Kv7 Potassium Channel Modulator for the Treatment of Epilepsy

We are developing XEN1101, a Kv7 potassium channel opener, for the treatment of epilepsy including: treatment-resistant adult and pediatric focal seizures; rare pediatric forms of epilepsy, such as EIEE7, an early infantile epileptic encephalopathy associated with mutations in the KCNQ2 gene that cause loss-of-function in the Kv7.2 potassium channel; as well as potentially other neurological disorders. We acquired XEN1101 from 1st Order Pharmaceuticals pursuant to an asset purchase agreement in April 2017. For a more detailed description of the terms of this agreement with 1st Order, see “—Collaborations, Commercial and License Agreements” below.

The Kv7 potassium channel opener mechanism has been clinically validated as an effective adjunctive treatment for treatment-resistant focal seizures as demonstrated with ezogabine, an earlier generation Kv7 opener. XEN1101’s unique composition is chemically designed to improve upon potency, selectivity and PK of ezogabine, and is not expected to have ezogabine’s composition-specific skin and eye pigmentary issues.

In addition to XEN1101’s strong pre-clinical data, and the clinical validation from the use of ezogabine, there is strong human genetic validation to support the use of XEN1101 as a potential treatment for epilepsy. The KCNQ2 gene encodes for the Kv7.2 voltage-gated potassium channel. Loss-of-function missense mutations in KCNQ2 can cause an extremely severe epilepsy disorder characterized by multiple, daily, treatment-resistant seizures often presenting within the first week of life. This human genetic validation further underpins the important role KCNQ2 plays in limiting the hyper-excitatory state of the brain and as a target for the prevention of seizures in humans.

Clinical Development

In October 2017, we initiated a randomized, double-blind, placebo-controlled Phase 1 clinical trial to evaluate XEN1101's safety, tolerability and pharmacokinetics in both SAD and MAD cohorts of healthy subjects. The XEN1101 Phase 1 clinical trial includes a pharmacodynamic biomarker read-out from a TMS study, designed to assess XEN1101's ability and potency to modulate cortical excitability, thereby demonstrating activity in the target CNS tissue. Xenon has completed a Phase 1a pilot TMS study in 8 healthy subjects and has now begun a double-blind, placebo-controlled, randomized cross-over Phase 1b TMS study in 15 healthy subjects.

Xenon expects to present interim Phase 1 results – including preliminary pharmacokinetic, tolerability and safety data from 42 subjects, along with a read-out from the Phase 1a pilot TMS study – at the 14th EILAT Conference on New Antiepileptic Drugs and Devices to be held in Madrid, Spain in May 2018. The release of the complete Phase 1 results, including the Phase 1b TMS data, is anticipated in the second half of 2018. Xenon anticipates initiating a Phase 2 proof-of-concept trial evaluating XEN1101's efficacy as a treatment for adult focal seizures by year end. Xenon also intends to explore a parallel plan to advance XEN1101 into rare, pediatric forms of epilepsy as soon as feasible thereafter.

About Focal Seizures

A focal seizure is localized within the brain and can either stay localized or spread to the entire brain, which is typically categorized as a secondary generalized seizure. Focal seizures are the most common type of seizure experienced by people with epilepsy. The treatment of an individual patient with focal seizures is currently focused on reduction of seizure frequency, with seizure freedom as the ultimate goal. Focal seizures (simple, complex and secondarily generalized tonic-clonic) account for approximately 60% of seizures (GlobalData Report 2017) of which approximately 33% are considered resistant to current treatments (Epilepsy Foundation). It is estimated that the addressable population in the United States could include approximately 460,000 adults and 70,000 pediatric epilepsy patients with refractory seizures.

About Early Infantile Epileptic Encephalopathy (EIEE7)

Mutations in the KCNQ2 gene result in loss-of-function in the Kv7.2 potassium channel that can cause a rare, extremely severe, single-gene epilepsy disorder known as EIEE7 that typically presents with seizures within the first week of life. These seizures can occur multiple times a day and are often difficult to treat. Typically, the seizures are associated with abnormal brain wave patterns on EEG. While the seizures in EIEE7 often resolve within months to years, many children sustain some degree of permanent developmental impairment involving one or more domains (motor, social, language, cognition). This can range from mild to severe depending on a number of different factors. Some children may also have autistic features.

XEN901, A Selective Nav1.6 Sodium Channel Inhibitor for the Treatment of Epilepsy

We are developing XEN901, a potent, highly selective Nav1.6 sodium channel inhibitor, for the treatment of epilepsy, including treatment resistant adult and pediatric focal seizures, as well as rare, pediatric forms of epilepsy, such as EIEE13, an early infantile epileptic encephalopathy associated with gain-of-function mutations in the SCN8A gene, which encodes the Nav1.6 sodium channel. By selectively targeting Nav1.6, it is anticipated that XEN901 may achieve efficacy conferred by this well-validated epilepsy target, but with a potentially improved therapeutic index compared with currently available non-selective sodium channel inhibitors.

There is strong human genetic validation supporting the rationale for treating epilepsy by blocking the Nav1.6 sodium channel. Nav1.6 is the most highly expressed sodium channel in the excitatory pathways in the CNS. When mutations

in the SCN8A gene result in a gain of function in the Nav1.6 sodium channel, children can present with a very severe form of epilepsy. This early infantile epileptic encephalopathy is known as EIEE13. We have examined XEN901 in a pre-clinical model of genetically defined epilepsy as well as models representative of focal seizures. These studies showed that XEN901 is efficacious against seizures in both an SCN8A (Nav1.6) gain-of-function model, which is designed to be predictive of the pediatric genetic epilepsy EIEE13, and in the maximal electroshock seizure, or MES, model, which is designed to be predictive of adult focal seizures. When compared to phenytoin in both the SCN8A and MES models, XEN901 achieved the same degree of efficacy as phenytoin at one thousand fold lower brain exposures. XEN901 also was observed to have an improved therapeutic index relative to phenytoin as assessed by tests of rodent behavior and motor impairment.

Clinical Development

In February 2018, we initiated a randomized, double-blind, placebo-controlled Phase 1 clinical trial to evaluate XEN901's safety, tolerability and pharmacokinetics in both SAD and MAD cohorts of approximately 64 healthy subjects in total. Upon completion of the Phase 1 clinical trial, a read-out of results is anticipated in the second half of 2018, followed by a Phase 2 proof-of-concept trial evaluating XEN901's efficacy as a treatment for adult focal seizures. We also intend to pursue a parallel plan to advance XEN901 into rare, pediatric forms of epilepsy as soon as feasible thereafter. For a description of focal seizures, which is a potential indication for a Phase 2 XEN901 clinical trial, see “—XEN1101, A Selective Kv7 Potassium Channel Modulator for the Treatment of Epilepsy—About Focal Seizures” above.

About Early Infantile Epileptic Encephalopathy (EIEE13)

Mutations in the SCN8A gene result in a gain-of-function in the Nav1.6 sodium channel that can cause a rare, extremely severe, single-gene epilepsy disorder known as EIEE13, which typically presents with seizure onset between birth and 18 months of age. Most children diagnosed with EIEE13 have seizures that can occur multiple times a day and are often difficult to treat. Other symptoms include learning difficulties, muscle spasms, low or high muscle tone, poor coordination, developmental delay, and features similar to autism. The extent of physical disability leaves some children able to make little or no voluntary movement. Most children will have trouble learning to speak, and some will need assistance from feeding tubes to get the nourishment they need to grow.

XEN007, A Cav2.1 Calcium Channel Inhibitor for the Treatment of Hemiplegic Migraine

We have identified an additional clinical stage, ion channel program, XEN007 (active ingredient flunarizine), to complement our neurology-focused product pipeline. XEN007 is a CNS-acting calcium channel inhibitor that directly modulates Cav2.1, which is a critical calcium channel implicated in the pathophysiology of HM, a rare and debilitating neurological disorder afflicting approximately 60,000 people in the U.S. Flunarizine has been used outside of the U.S. in the prevention of chronic migraine and has been reported to have clinical benefit in HM case studies. Our clinical development plans include a proposed strategy to develop XEN007 as the first treatment specifically approved for HM anywhere in the world. We have received Orphan Drug Designation from the FDA for XEN007 for the treatment of HM. In addition, we have entered into key agreements in order to access regulatory files and manufacturing support to potentially enable the accelerated clinical development of XEN007 directly into a Phase 2 clinical trial. We are currently examining various development strategies for XEN007 with key opinion leaders and leading clinicians, as well as exploring options for potential partnerships for this program.

We believe that there is strong human genetic validation supporting the use of XEN007 for the treatment of HM. At least three different genes have been implicated in HM, all of which can promote excessive glutamatergic (excitatory) neurotransmission leading to cortical spreading depression which mediates the progressive symptoms characteristic of HM. HM patients may have mutations in one of these three causal ion channel genes. In particular, gain-of-function mutations in CACNA1A, the gene that encodes for Cav2.1, have been shown to increase the activity of Cav2.1 and thereby enhance excitatory neurotransmission. This increase in Cav2.1 activity is therefore thought to play an important causal role in HM. In contrast, the suppression of the channel activity by XEN007, both in HM patients with or without mutant Cav2.1, has the potential to dampen the excessive excitatory neurotransmission, thereby mediating a beneficial effect in HM. These genetic causes of HM suggest that XEN007 may be well suited for the treatment of HM, which has been supported by case study reports. Other neurologic disorders are also being considered for future development of XEN007 in both adult and pediatric populations.

New Pipeline Opportunities

Given our expertise in ion channel drug discovery, our efforts are concentrated on the identification of ion channel targets where we believe novel selective modulators might represent significant therapeutic advances, with a particular focus on CNS-related orphan indications. We intend to expand our pipeline from our internal research efforts and through the acquisition or in-licensing of other product candidates or technologies.

Our Partnered Programs

Selective Inhibitors of Nav1.7 for the Treatment of Pain

In December 2011, we entered into a collaborative research and license agreement with Genentech and its affiliate, F. Hoffman-La Roche Ltd, or Roche, to discover and develop selective oral inhibitors of Nav1.7 for the treatment of pain. For a more detailed description of the terms of this agreement with Genentech, see “—Collaborations, Commercial and License Agreements” below. Based on our discovery of Nav1.7 deficiency underlying the rare human disease called congenital indifference to pain, or CIP, where individuals with CIP are unable to feel pain, we believe that Nav1.7 is a highly-validated target for the treatment of pain. Our Genentech collaboration is focused on discovering and developing oral drugs that selectively target Nav1.7.

Clinical Development

We have an ongoing collaboration with Genentech focused on developing novel inhibitors of Nav1.7 for the treatment of pain. Genentech has completed a Phase 1 clinical trial for GDC-0310, which is an oral, selective Nav1.7 small-molecule inhibitor developed for the potential treatment of pain. Guidance around the future clinical development of GDC-0310 will be updated once ongoing pre-clinical studies are completed and the final results are analyzed by Genentech.

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 as a single agent or in combination with existing analgesics that work through different mechanisms. 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.

Additional Collaborative Work with Genentech

We formed a second collaboration with Genentech in March 2014 for pain genetics, with a focus on rare phenotypes where individuals have an inability to perceive pain or where individuals have non-precipitated spontaneous severe pain. We believe these phenotypes may unlock new key molecular regulators of pain signaling in humans, which we will seek to validate as targets for new pain drugs. In March 2017, the research term for this second collaboration agreement was extended until March 2018. To date, Genentech has paid us a \$1.5 million upfront payment and two \$0.25 million milestone payments related to the identification of novel pain targets in September 2015 and July 2017. For a more detailed description of the terms of our collaborations with Genentech, see “—Collaborations, Commercial and License Agreements” below.

Selective Small-Molecule Inhibitors of Targets for the Treatment of 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. For a more detailed description of the terms of our agreement with Merck, see “—Collaborations, Commercial and License Agreements” below. In 2012, Merck exercised its option to obtain an exclusive license to a target for cardiovascular disease and compound 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.

Collaborations, Commercial and License Agreements

Asset Purchase Agreement with 1st Order Pharmaceuticals, Inc.

In April 2017, we entered into an asset purchase agreement with 1st Order Pharmaceuticals, Inc., or 1st Order, pursuant to which we acquired all rights with respect to XEN1101 (previously known as 1OP2198). XEN1101 was previously acquired by 1st Order from an affiliate of Valeant Pharmaceuticals International, Inc., or Valeant. Pursuant to the terms of the agreement, we also assumed certain obligations due to Valeant from 1st Order pursuant to the terms of their agreement, including potential milestone and royalty payments.

Under the terms of the agreement, we paid 1st Order an upfront fee of approximately \$0.4 million and a \$0.7 million milestone in 2017 upon achieving a clinical development milestone. Future potential payments to both 1st Order and Valeant include \$1.0 million in clinical development milestones, up to \$13.0 million in regulatory milestones, and up to approximately \$33.6 million in sales-based and other milestones, which includes a \$1.5 million milestone that may be payable pre-commercially, plus a mid-to-high single digit percentage royalty on commercial sales.

The agreement contains customary representations, warranties and covenants by us and 1st Order. Each party has agreed, subject to certain conditions and limitations, to indemnify the other party for breaches of representations, warranties and covenants and for losses arising from certain assumed/excluded liabilities, as applicable.

Agreements with Genentech for Selective Inhibitors of Nav1.7 and Pain Genetics

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, a \$5.0 million milestone payment for the selection of a compound for development and an \$8.0 million milestone payment upon the approval by Health Canada of the clinical trial application, or CTA. Genentech provided funding to us for certain of our full-time equivalents, or FTEs, performing the research collaboration plan, which concluded in December 2016. We are eligible to receive pre-commercial and commercial milestone payments with respect to the licensed products totaling up to an additional \$613.0 million, comprised of up to \$45.5 million in pre-clinical 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 until the date that is ten years after first commercial sale on a country-by-country basis, plus a low single-digit percentage for large molecule inhibitors of Nav1.7 for a period of ten years from first commercial sale on a country-by-country basis.

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 us, 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 us to enable us to develop and commercialize certain terminated products outside of the collaboration.

In May 2015, we amended the collaborative research and license agreement to leverage the work performed in our ongoing Nav1.7 pain collaboration with Genentech for use in our research and development program directed towards modulators of Nav1.6 for use in the field of treating epilepsy. Pursuant to the amendment, we obtained a worldwide, non-exclusive, revocable license under intellectual property exclusively licensed by us to Genentech and Genentech intellectual property developed under the Nav1.7 collaboration that is necessary or useful to make and use certain Nav1.6 modulators for use in the field, excluding commercialization. We obtained a right of first negotiation for a

certain period of time to obtain a worldwide, exclusive license under the intellectual property previously licensed by us to commercialize certain Nav1.6 modulators to treat any disease in the field. We also granted Genentech a right of first negotiation to enter into a drug research and development collaboration with us for our Nav1.6 program. Genentech can terminate the license upon 90 days' notice after the third anniversary of the amendment or at any time upon our uncured material breach.

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Pursuant to the amendment, we granted Genentech a worldwide exclusive license under intellectual property developed under our Nav1.6 program. The license permits Genentech to develop and commercialize compounds identified or first made in our Nav1.6 program for all uses outside the field of epilepsy and to develop and commercialize compounds (other than certain compounds identified or first made in our Nav1.6 program) for all uses. If Genentech reaches certain development milestones for and/or sells certain compounds identified or first made in our Nav1.6 program that are covered by a patent licensed to Genentech under the amendment, products containing such compound would be included in the products subject to the royalty and milestone obligations payable to us under the original agreement. The collaborative research and license agreement was amended in December 2015 to extend the term of the research program and, in March 2016, the agreement was amended again, pursuant to which we obtained a non-sublicensable, non-transferable, royalty free, non-exclusive license to make, use and test certain collaboration compounds developed under the Nav1.7 collaboration for internal research purposes during the term of the agreement.

In March 2014, we entered into an additional agreement with Genentech for pain genetics, which is focused on identifying genetic targets associated with rare phenotypes where individuals have an inability to perceive pain or where individuals have non-precipitated spontaneous severe pain. Pursuant to the terms of this agreement, any intellectual property arising out of the collaboration will be jointly owned by us and Genentech. We have also granted Genentech a time-limited, exclusive right of first negotiation on a target-by-target basis to form joint drug discovery collaborations. Under the terms of this agreement, Genentech paid us an upfront payment of \$1.5 million, two \$0.25 million milestone payments related to the identification of novel pain targets in September 2015 and July 2017, and we are eligible for an additional \$1.5 million in milestone payments. The agreement terminates upon the expiration of Genentech's time-limited, exclusive right of first negotiation which shall be exercisable throughout the research term. Genentech may terminate the agreement with three months advance notice anytime on or after the 12 month 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 for 90 days. In March 2017, the research term for this agreement was extended until March 2018.

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 and paid us \$2.0 million 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 December 31, 2017, 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 pre-clinical 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 in countries where such products are covered by a valid composition or method of use claim of a Xenon or Merck patent or, if not covered by such claims, royalties in the mid single-digit range for ten years after first commercial sale of such products.

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.

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.

Termination Agreement with Teva

On March 7, 2018, we and Teva Pharmaceuticals International GmbH and Teva Canada Limited, or together Teva, entered into a termination agreement terminating by mutual agreement the collaborative development and license agreement dated December 7, 2012, as amended. We and Teva agreed to terminate the collaborative development and license agreement after Teva informed us that it no longer intends to further develop TV-45070. For additional information regarding the terms of the collaborative development and license agreement, see the section captioned “Business—Strategic Alliances—Agreement with Teva for TV-45070” in our Annual Report on Form 10-K filed with the Securities and Exchange Commission on March 8, 2017.

Pursuant to the termination agreement and subject to receipt by us of an order from the Ontario Securities Commission, or OSC, Teva has agreed to transfer and assign 1,000,000 of our common shares held by Teva Canada Limited to us for cancellation. Teva will also return, license or assign to us certain intellectual property including certain patent rights. The termination agreement requires us to pay a low single-digit percentage royalty to Teva based on net sales of approved products, if any, resulting from any continued development and commercialization of TV-45070 by us during the period that assigned or licensed patents cover such products. Teva will also transfer regulatory filings related to TV-45070 to us.

The termination agreement will become effective on the date specified by us in a written notice to Teva. The effective date will be after the date that we receive the OSC order granting us exemptive relief from the requirements related to issuer bids under applicable Canadian securities laws in connection with the transfer and assignment to us by Teva Canada Limited of the 1,000,000 common shares and not earlier than 10 business days from the date that we issue a press release announcing the termination agreement. We have made an application to the OSC for the OSC order and expect the effective date to be on or about March 22, 2018.

The termination agreement includes customary representations, warranties, indemnities, releases and covenants of us and Teva.

Intellectual Property

As part of our business strategy, we generally file patent applications disclosing and claiming drug targets and their novel uses, 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, the EU, 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 December 31, 2017, we owned, co-owned or licensed 61 issued U.S. patents and approximately 12 pending U.S. patent applications, including provisional and non-provisional filings. We also owned, co-owned or licensed an additional 780 pending and granted counterpart applications worldwide, including 227 country-specific validations of 15 European patents.

As of December 31, 2017, we owned two issued U.S. patents related to XEN1101, and methods of making and using XEN1101 and certain related compounds. The issued patents are expected to expire between 2028 and 2029 (absent any extensions of term). In addition, we have 10 foreign issued patents (exclusive of European patent national validations) and have filed nine pending corresponding applications in various foreign jurisdictions relating to XEN1101 and certain related compounds.

As of December 31, 2017, we have filed a PCT international patent application as well as a U.S. non-provisional patent application directed to XEN901 and methods of making and using XEN901 and certain related compounds. Any patents issuing from these applications are expected to expire in 2037 (absent any extensions of term).

As of December 31, 2017, we have filed a PCT international patent application as well as a U.S. non-provisional patent application directed to certain of our selective inhibitors of Nav1.6 (exclusive of XEN901), as well as methods of making and using the same. Any patents issuing from these applications are expected to expire in 2037 (absent any extensions of term).

As of December 31, 2017, we, together with Genentech, co-owned two issued U.S. patents, one pending U.S. patent application and 28 pending counterpart patent applications worldwide relating to GDC-0310 and methods of making and using GDC-0310 and certain related compounds. The issued patents, as well as any patents issuing from these applications are expected to expire in 2034 (absent any extensions of term).

As provided for in the termination agreement entered on March 7, 2018, Teva will assign to us one issued U.S. patent, two pending U.S. patent applications and a further two pending PCT international patent applications relating to TV-45070. The issued U.S. patent is expected to expire in 2036 (absent any extensions of term) and any patents issuing from these applications are expected to expire in 2037 (absent any extensions of term). For a more detailed description of the terms of our termination agreement with Teva, see “—Collaborations, Commercial and License Agreements” above. Excluding the patents included in the terms of the termination agreement, as of December 31, 2017, we owned 17 issued U.S. patents and three pending U.S. patent applications related to TV-45070, and methods of making and using TV-45070 and certain related compounds. The issued patents are expected to expire between 2026 and 2034 (absent any extensions of term). In addition, we have 80 foreign issued patents (exclusive of European patent national validations) and have filed 73 pending corresponding applications in various foreign jurisdictions relating to TV-45070 and certain related compounds.

Competition

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

Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, pre-clinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we, or our collaborators, do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early stage companies may also prove to be significant competitors, particularly through collaboration arrangements with large and established companies.

Our commercial opportunities could be reduced or eliminated if our competitors develop and commercialize products or therapies that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA, European Medicines Agency, or EMA, or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third party payers.

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

The key competitive factors affecting the success of all of our product candidates, if approved, are likely to be their efficacy, safety, convenience, price, the effectiveness of alternative products, the level of competition and the availability of coverage, and adequate reimbursement from government and other third party payers. Our product candidates that are in clinical development may compete with various therapies and drugs, both in the marketplace and currently under development.

Selective Inhibitors of Nav1.7 for the Treatment of Pain

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, gabapentin, and pregabalin. We are also aware of development programs at several pharmaceutical and biotechnology companies that are developing Nav1.7 inhibitors or other sodium channel inhibitors for the treatment of pain, including Amgen Inc., AstraZeneca PLC, Biogen Inc., Dainippon Sumitomo Co., Ltd., Eli Lilly and Company, Merck, NeuroQuest Inc., Vertex Pharmaceuticals Inc., Voyager Therapeutics, Inc. and Chromocell Corporation in collaboration with its partner Astellas Pharma 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 Nav1.8 inhibitors.

XEN901 and XEN1101 for the Treatment of Epilepsy

If XEN901 or XEN1101 were approved for the treatment of epilepsy, we anticipate that they could potentially compete with each other and other anti-epileptic drugs, or AEDs, which typically can be categorized into four classes by AED mechanism: modulation of voltage-gated ion channels, enhancement of GABA-mediated inhibitory neurotransmission, reduction of glutamate-mediated excitatory neurotransmission, and SV2A modulation. Commonly used AEDs include phenytoin, levetiracetam, carbamazepine, clobazam, lamotrigine, valproate, oxcarbazepine, topiramate, lacosamide and perampanel. There are currently no FDA-approved treatments indicated for the early infantile epileptic encephalopathies EIEE7 or EIEE13. We are not aware of other companies that are developing selective Nav1.6 inhibitors for the treatment of epilepsy. There are other AEDs in development that could potentially compete with XEN1101 or XEN901, including products in development from UCB, Inc., Zogenix, Inc., GW Pharmaceuticals, Sage Therapeutics, Marinus Pharmaceuticals, Inc., SciFluor Lifesciences, Inc., Knopp Biosciences LLC, and Upsher-Smith Laboratories, Inc.

Government Regulation

We are developing small-molecule product candidates, which are regulated as drugs by the FDA. Within the FDA, the Center for Drug Evaluation and Research, or CDER, regulates drugs. Drugs are subject to regulation under the Federal Food, Drug, and Cosmetic Act, or FD&C Act, and other federal, provincial, state, local and foreign statutes and regulations. The FD&C Act and corresponding regulations govern, among other things, the testing, manufacturing, safety, efficacy, labeling, packaging, storage, record keeping, distribution, import, export, reporting, advertising and other promotional practices involving drugs. FDA approval must be obtained before clinical testing of drugs 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 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 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 product may be marketed in the U.S. generally involves the following:

- completion of nonclinical laboratory tests and animal studies according to good laboratory practices, or GLPs, and applicable requirements for the humane use of laboratory animals or other applicable regulations;
- submission to the FDA of an application for an IND, which must become effective before human clinical studies may begin;
- performance of adequate and well-controlled human clinical studies according to the FDA's regulations commonly referred to as good clinical practices, or GCPs, and any additional requirements for the protection of human research subjects and their health information, to establish the safety and efficacy of the proposed product for its intended use;

submission to the FDA of an NDA for drug products for marketing approval that includes substantial evidence of safety, efficacy, 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; and
FDA review and approval of the NDA.

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

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

Phase 2. The drug is evaluated in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine 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. During all phases of clinical development, regulatory agencies require extensive monitoring and auditing of all clinical activities, clinical data, and clinical study investigators.

Concurrent with clinical studies, companies usually complete additional animal studies and must also develop additional information about the physical characteristics of the drug as well as finalize a process for manufacturing the product in commercial quantities in accordance with GMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other requirements, the sponsor must develop methods for testing the identity, strength, quality, potency and purity of the final drug. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

U.S. Review and Approval Processes

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

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

Within 60 days following submission of the application, the FDA reviews an NDA 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 information. In this event, the NDA must be resubmitted with the additional information. The resubmitted application also is

subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review of the NDA. The FDA reviews the application to determine, among other things, whether the proposed product is safe and 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 must submit a proposed REMS; the FDA will not approve the application without a REMS, if required.

Notwithstanding the submission of relevant data and information, the FDA may ultimately decide that the NDA does not satisfy its regulatory criteria for approval and deny approval. Data obtained from clinical studies are not always conclusive and the FDA may interpret data differently than we interpret the same data. If the agency decides not to approve the marketing application, the FDA will issue a complete response letter 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, 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 pursuant to a REMS request, or otherwise limit the scope of any approval.

One of the performance goals agreed to by the FDA under the PDUFA is to complete its review of 90% of standard NDAs within ten months from filing and 90% of priority NDAs 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.

Fast Track Designation

The FDA has various programs, including Fast Track, which are intended to expedite the process for the development and review of drugs. Even if a drug qualifies for one or more of these programs, the FDA may later decide that the drug no longer meets the conditions for qualification. Generally, drugs that are eligible for these programs are those for serious or life-threatening conditions, those with the potential to address unmet medical needs, and those that offer meaningful benefits over existing treatments. For example, Fast Track is a process designed to expedite the FDA's review of drugs that treat serious or life-threatening diseases or conditions and fill unmet medical needs. Under the Fast Track process, drugs that offer major advances in treatment or provide a treatment where no adequate therapy exists, may also receive priority review by the FDA, or review within six months of the filing of an NDA compared to a traditional review time of ten months. Although Fast Track and priority review do not affect the standards for approval of a drug, for Fast Track designated drugs, the FDA will also attempt to facilitate early and frequent meetings with a sponsor of a Fast Track designated drug, to expedite such drug's review and development.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the U.S., or more than 200,000 individuals in the U.S. and for which there is no reasonable expectation that the cost of developing and making a drug available in the U.S. for this type of disease or condition will be recovered from sales of the product. We have received orphan drug designation from the FDA for XEN007 (active ingredient flunarizine), a drug we are evaluating internally for the potential treatment of hemiplegic migraine. Orphan product designation must be requested before submitting an NDA. After the FDA grants 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 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 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 ten years of exclusivity.

Post-Approval Requirements

Maintaining 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 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, 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 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 drugs .

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 manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with GMPs and other laws. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain GMP compliance. Discovery of problems with a product after approval may result in restrictions on a product, manufacturer, or holder of an approved NDA, including withdrawal of the product from the market. In addition, changes to the manufacturing process or facility generally require prior FDA approval before being implemented and other types of changes to the approved product, such as adding new indications and additional labeling claims, are also subject to further FDA review and approval.

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 plus the time between the submission date of an NDA 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 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.

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 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.

Global Anti-Corruption Laws

The U.S. Foreign Corrupt Practices Act and the Canadian Corruption of Foreign Public Officials Act, the U.S. Travel Act, the OECD Anti-Bribery Convention, Title 18 United States Code section 201, and any other applicable domestic or foreign anti-corruption or anti-bribery laws to which we are subject prohibit corporations and individuals from engaging in certain activities to obtain or retain business or to influence a person working in an official capacity. It is illegal to pay, offer to pay or authorize the payment of anything of value to any foreign government official, government staff member, political party or political candidate in an attempt to obtain or retain business or to otherwise influence a person working in an official capacity. We may also be held liable for the acts of our third party agents under the U.S. Foreign Corrupt Practices Act, Canadian Corruption of Foreign Public Officials Act, and other applicable anti-corruption and anti-bribery laws. Noncompliance with these laws could subject us to investigations, sanctions, settlements, prosecution, other enforcement actions, disgorgement of profits, significant fines, damages, other civil and criminal penalties or injunctions, suspension or debarment from contracting with certain persons, the loss of export privileges, whistleblower complaints, reputational harm, adverse media coverage, and other collateral consequences. Any investigations, actions or sanctions or other previously mentioned harm could have a material negative effect on our business, operating results and financial condition.

Government Regulation Outside of the U.S.

In addition to regulations in the U.S., we will be subject to a variety of regulations in other jurisdictions governing, among other things research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing and export and import of drugs. Generally, before a new drug can be marketed, considerable data demonstrating its quality, safety and efficacy must be obtained, organized into a format specific for each regulatory authority, submitted for review and approved by the regulatory authority. Whether or not we obtain FDA approval for a product, 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 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. The EU clinical trials legislation currently is undergoing a transition process mainly aimed at harmonizing and streamlining clinical-trial authorization, simplifying adverse-event reporting procedures, improving the supervision of clinical trials and increasing their transparency. Recently enacted Clinical Trials Regulation EU No 536/2014 is intended to ensure that the rules for conducting clinical trials in the EU are identical; however, it has not

yet been fully implemented.

To obtain regulatory approval of an investigational drug under EU regulatory systems, we must submit a marketing authorization application, or MAA. The application used to file the NDA in the U.S. is similar to that required in the EU, with the exception of, among other things, country-specific document requirements. 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 ten 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 ten years of market exclusivity for the approved therapeutic indication. The application for orphan drug designation must be submitted before the application for marketing authorization. The applicant will receive a fee reduction for the marketing authorization application if the orphan drug designation has been granted, but not if the designation is still pending at the time the marketing authorization is submitted. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

The 10-year market exclusivity may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan designation, for example, if the product is sufficiently profitable not to justify maintenance of market exclusivity. Additionally, marketing authorization may be granted to a similar 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 payers. Third-party payers include government programs such as Medicare or Medicaid, managed care plans, private health insurers, and other organizations. These third-party payers 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 payers 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 payer interest. We expect that the pharmaceutical industry will experience pricing pressures due to the trend toward managed

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

Some third-party payers also require pre-approval 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 payers, that coverage or an adequate level of reimbursement will be available or that the third-party payers' reimbursement policies will not adversely affect our ability to sell our products profitably.

In addition, in most foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing and reimbursement vary widely from country to country. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, products launched in the European Union do not follow price structures of the United States and generally prices tend to be significantly lower.

Healthcare Reform

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

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 payers often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the Medicare Modernization Act may result in a similar reduction in payments from private payers.

Enacted in March 2010, the Patient Protection and Affordable Care Act, as amended, or PPACA, is a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against healthcare fraud and abuse, add new transparency requirements for healthcare and health insurance industries, impose new taxes and fees on pharmaceutical and medical device manufacturers and impose additional health policy reforms. Among other things, PPACA revises the definition of "average 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. PPACA may continue to place 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 PPACA was enacted. These new laws may result in 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 PPACA, 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 payers. 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.

The Trump administration and Congress have made changes to current health care laws and may continue to attempt broad sweeping changes to existing health care laws. We face uncertainties that might result from modification or repeal of any of the provisions of the PPACA, including as a result of current and future executive orders and legislative actions. The impact of those changes on us and the pharmaceutical industry as a whole is currently unknown. Any changes to the PPACA are likely to have an impact on our results of operations, and may have a material adverse effect on our result of operations. We cannot predict what other healthcare programs and regulations will ultimately be implemented at the federal or state level or the effect of any future legislation or regulation in the United States may have on our business.

In addition, different pricing and reimbursement schemes exist in other countries. In the European Community, governments influence the price of pharmaceutical products through their pricing and reimbursement rules and control of national healthcare systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may be marketed only once a reimbursement price has been agreed upon. Some of these countries may require, as 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, 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 PPACA, 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 PPACA provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act (discussed below) or the civil monetary penalties statute, which imposes fines against any person who is determined to have presented or caused to be presented claims to a federal healthcare program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent. Additionally, many states have adopted laws similar to the federal Anti-Kickback Statute, and some of these state prohibitions apply to referral of patients for healthcare items or services reimbursed by any third-party payer, not only the Medicare and

Medicaid programs in at least some cases, and do not contain safe harbors.

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

In addition, we may be subject to, or our marketing activities may be limited by, data privacy and security regulation 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 included expansion of HIPAA's privacy and security standards called the Health Information Technology for Economic and Clinical Health Act, or HITECH. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable to "business associates"—independent contractors or agents of covered entities that create, receive, maintain, or transmit protected health information in connection with providing a service for or on behalf of a covered entity. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney's fees and costs associated with pursuing federal civil actions.

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, pursuant to a similar federal requirement, manufacturers must 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 discloses the reported information on a publicly available website. 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, 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.

Environmental Matters

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

Employees

As of December 31, 2017, we had 81 employees, including 77 full-time employees. Of our employees, 52 were primarily engaged in research and development, 25 of whom hold a Ph.D. or M.D. (or equivalent) degree. None of our employees are represented by a labor union. We have not experienced any work stoppages, and we consider our relations with our employees to be good.

Research and Development

We have committed, and expect to continue to commit, significant resources to developing new product candidates. We have assembled an experienced research and development team with scientific and clinical development personnel. Our research and development expenses for the years ended December 31, 2017, 2016, and 2015 were \$25.6 million, \$19.8 million, and \$15.2 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 pre-clinical 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 source. However, the manufacturing processes for each of our product candidates vary and sourcing adequate supplies may be made more difficult depending on the type of product candidate involved. Our product candidates generally can be manufactured in reliable and reproducible synthetic processes from readily available starting materials. This chemistry generally is amenable to scale-up and does not require unusual equipment in the manufacturing process.

Corporate Information

We were incorporated in the Province of British Columbia on November 5, 1996 under the predecessor to the Business Corporations Act (British Columbia) under the name "Xenon Bioresearch Inc." We continued from British Columbia to the federal jurisdiction pursuant to Section 187 of the Canada Business Corporations Act, or the CBCA, on May 17, 2000 and concurrently changed our name to "Xenon Genetics Inc." We registered as an extra-provincial company in British Columbia on July 10, 2000 and changed our name to "Xenon Pharmaceuticals Inc." on August 24, 2004. We have one wholly-owned subsidiary as at December 31, 2017, Xenon Pharmaceuticals USA Inc., which was incorporated in Delaware on December 2, 2016. Our principal executive offices are located at 200 – 3650 Gilmore Way, Burnaby, British Columbia, Canada V5G 4W8, and our telephone number is (604) 484-3300. We are a reporting issuer in British Columbia, Alberta and Ontario, but our shares are not listed on any recognized Canadian stock exchange. Our common shares trade on The NASDAQ Global Market under the symbol "XENE."

Where You Can Find Additional Information

We make available free of charge through our investor relations website, <http://www.xenon-pharma.com>, our annual reports, quarterly reports, current reports, proxy statements and all amendments to those reports as soon as reasonably practicable after such material is electronically filed or furnished with the U.S. Securities and Exchange Commission, or SEC. These reports may also be obtained without charge by contacting Investor Relations, Xenon Pharmaceuticals Inc., 200 – 3650 Gilmore Way, Burnaby, British Columbia, Canada V5G 4W8, e-mail: investors@xenon-pharma.com. Our Internet website and the information contained therein or incorporated therein are not intended to be incorporated into this Annual Report on Form 10-K. In addition, the public may read and copy any materials we file or furnish with the SEC at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549 or may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. Moreover, the SEC maintains an Internet site that contains reports, proxy and information statements, and other information regarding reports that we file or furnish electronically with them at www.sec.gov. Additional information related to Xenon is also available on SEDAR at www.sedar.com.

Item 1A. Risk Factors

You should carefully consider the following risk factors, in addition to the other information contained in this report, including the section of this report captioned "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our financial statements and related notes. If any of the events described in the following risk factors and the risks described elsewhere in this report occurs, our business, operating results and financial condition could be seriously harmed. This report on Form 10-K also contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those anticipated in the forward-looking statements as a result of factors that are described below and elsewhere in this report.

Risks Related to Our Financial Condition and Capital Requirements

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

We are a clinical stage biotechnology company and, other than the years ended December 31, 2014 and 2013, we have recorded net losses in each annual reporting period since inception in 1996, and we do not expect to have sustained profitability for the foreseeable future. We had net losses of \$30.7 million for the year ended December 31, 2017 and an accumulated deficit of \$173.4 million as of December 31, 2017, which were driven by expenses incurred in connection with our research and development programs and from general and administrative costs associated with our operations.

We have devoted most of our financial resources to research and development, including our clinical and pre-clinical development activities. To date, we have financed our operations through the sale of equity securities, funding received from our licensees and collaborators, debt financing and, to a lesser extent, government funding. We have not generated any significant revenue from product sales and our product candidates will require substantial additional investment before they will provide us with any revenue.

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

- continue our research and pre-clinical and clinical development of our product candidates;

- expand the scope of our clinical studies for our current and prospective product candidates;
- initiate additional pre-clinical, clinical or other studies for our product candidates;
 - change or add additional manufacturers or suppliers;
- seek regulatory and marketing approvals for any of our product candidates that successfully complete clinical studies;
- seek to identify and validate additional product candidates;
- acquire or in-license other product candidates and technologies;
- make milestone or other payments under our in-license or other agreements, including, without limitation, payments to Memorial University of Newfoundland, 1st Order Pharmaceuticals, Inc., an affiliate of Valeant Pharmaceuticals International, Inc. and other third parties;
- maintain, protect and expand our intellectual property portfolio;

- establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval;
- create additional infrastructure to support our operations and our product development and planned future commercialization efforts; and
- experience any delays or encounter issues with any of the above.

Our expenses could increase beyond expectations for a variety of reasons, including if we are required by the 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 significant royalty revenue from product sales and may never become profitable on a U.S. GAAP basis.

Our ability to generate meaningful revenue and achieve profitability on a U.S. GAAP basis depends on our ability, alone or with strategic collaborators, to successfully complete the development of, and obtain the regulatory approvals necessary to commercialize, our product candidates. Substantially all of our revenue since inception has consisted of upfront and milestone payments associated with our collaboration and license agreements. Revenue from these agreements is dependent on successful development of our product candidates by us or our collaborators. We have not generated any significant royalty revenue from product sales, and do not otherwise anticipate generating revenue from product sales for the foreseeable future, if ever. If any of our product candidates fail in clinical trials or do not gain regulatory approval, or if any of our future products, if any, once approved, fail to achieve market acceptance or adequate market share, we may never become profitable. Although we were profitable for the years ended December 31, 2014 and 2013, we may not be able to sustain profitability in subsequent periods. Our ability to generate future revenue from product sales depends heavily on our success, and the success of our collaborators, in:

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

The scope of our future revenue will also depend upon the size of any markets in which our product candidates receive approval and the availability of insurance coverage and the availability and amount of reimbursement from third-party payers for future products, if any. If we are unable to achieve sufficient revenue to become profitable and remain so, our financial condition and operating results will be negatively impacted, and the market price of our common shares might be adversely impacted.

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

Since our inception, we have dedicated most of our resources to the discovery and development of our proprietary pre-clinical and clinical product candidates, and we expect to continue to expend substantial resources doing so for the foreseeable future. These expenditures will include costs associated with research and development, potential milestone payments to third parties, manufacturing of product candidates and products approved for sale, conducting pre-clinical experiments and clinical trials and obtaining and maintaining regulatory approvals, as well as commercializing any products later approved for sale. During the year ended December 31, 2017, we incurred approximately \$25.6 million of costs associated with research and development, exclusive of costs incurred by our collaborators in developing our product candidates.

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

- the number and characteristics of the future product candidates we pursue either from our internal research efforts or through acquiring or in-licensing other product candidates or technologies;
 - the scope, progress, results and costs of independently researching and developing any of our future product candidates, including conducting pre-clinical research and clinical trials;
 - whether our existing collaborations continue to generate substantial milestone payments and, ultimately, royalties on future approved products for us;
- the timing of, and the costs involved in, obtaining regulatory approvals for any future product candidates we develop independently;
- the timing and magnitude of potential milestone payments under our product acquisition and in-license agreements;
- the cost of commercializing any future products we develop independently that are approved for sale;
- the cost of manufacturing our future product candidates and products, if any;
- our ability to maintain existing collaborations and to establish new collaborations, licensing or other arrangements and the financial terms of such agreements;
- the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing patents, including litigation costs and the outcome of such litigation; and
- the timing, receipt and amount of sales of, or royalties on, our future products, if any.

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

Based on our research and development plans and our timing expectations related to the progress of our programs, we expect that our existing cash and cash equivalents and marketable securities as of the date of this report will enable us to fund our operating expenses and capital expenditure requirements for at least the next 12 months.

Our operating plan may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings, government or other third-party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements or a combination of these approaches. Raising funds in the future may present additional challenges and future financing may not be available in sufficient amounts or on terms acceptable to us, if at all.

We are party to a loan and security agreement that contains operating and financial covenants that may restrict our business and financing activities and we may be required to repay the outstanding indebtedness in an event of default, which could have a materially adverse effect on our business.

In December 2017, we entered into a loan and security agreement with Silicon Valley Bank providing for term loans to us with an aggregate principal amount of up to \$15.0 million, in three tranches of \$7.0 million, \$5.0 million, and \$3.0 million, respectively. The initial tranche of \$7.0 million was funded in December 2017.

Borrowings under this loan and security agreement are secured by substantially all of our assets except intellectual property and subject to certain other exceptions. The loan and security agreement restricts our ability, among other things, to:

- sell, transfer or otherwise dispose of any of our business assets or property, subject to limited exceptions;
- make material changes to our business or management;
- enter into transactions resulting in significant changes to the voting control of our stock;
- make certain changes to our organizational structure;
- consolidate or merge with other entities or acquire other entities;
- incur additional indebtedness or create encumbrances on our assets;
- pay dividends, other than dividends paid solely in our common shares, or make distributions on and, in certain cases, repurchase our capital stock;
- enter into certain transactions with our affiliates;
- repay subordinated indebtedness; or
- make certain investments.

In addition, we are required under our loan agreement and security agreement to comply with various affirmative covenants. The covenants and restrictions and obligations in our loan and security agreement, as well as any future financing agreements that we may enter into, may restrict our ability to finance our operations, engage in business activities or expand or fully pursue our business strategies. Our ability to comply with these covenants may be affected by events beyond our control, and we may not be able to meet those covenants. A breach of any of these covenants could result in a default under the loan and security agreement, which could cause all of the outstanding indebtedness under the facility to become immediately due and payable and eliminate our eligibility to receive additional loans under the agreement.

If we are unable to generate sufficient cash available to repay our debt obligations when they become due and payable, either when they mature, or in the event of a default, we may not be able to obtain additional debt or equity financing on favorable terms, if at all, which may negatively impact our business operations and financial condition.

Raising additional capital may cause dilution to our existing shareholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.

The terms of any financing arrangements we enter into may adversely affect the holdings or the rights of our shareholders and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our common shares to decline. The sale of additional equity or convertible securities also would dilute all of our shareholders. In December 2017, we entered into a loan and security agreement with Silicon Valley Bank, which is secured by substantially all of our assets except intellectual property, and requires us to comply with various affirmative and negative covenants. The incurrence of additional indebtedness would result in increased fixed payment obligations and, potentially, the imposition of additional restrictive covenants. Such additional covenants could include limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. We could also be required to seek funds through arrangements with collaborators or otherwise at an earlier stage than otherwise would be desirable resulting in the loss of rights to some of our product candidates or other unfavorable terms, any of which may have a material adverse effect on our business, operating results and prospects. In addition, any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates.

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 the market price of our common shares could require us to delay or abandon development or commercialization plans. In addition, there is a risk that one or more of our current collaborators, service providers, manufacturers and other partners would not survive or be able to meet their commitments to us under such circumstances, which could directly affect our ability to attain our operating goals on schedule and on budget.

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

As of December 31, 2017, approximately 36% of our cash and cash equivalents and marketable securities was denominated in Canadian dollars. Historically, a significant portion of our operating expenses have been in Canadian dollars and the majority of our revenue has been in U.S. dollars.

Prior to December 31, 2014, our functional currency was the Canadian dollar. On January 1, 2015, our functional currency changed from the Canadian dollar to the U.S. dollar based on our analysis of the changes in the primary economic environment in which we operate. As a result, changes in the exchange rate between the Canadian dollar and the U.S. dollar could materially impact our reported results of operations and distort period to period comparisons. In particular, to the extent that foreign currency-denominated (i.e., non-U.S. dollar) monetary assets do not equal the amount of our foreign currency denominated monetary liabilities, foreign currency gains or losses could arise and materially impact our financial statements. As a result of such foreign currency fluctuations, it could be more difficult to detect underlying trends in our business and results of operations. In addition, to the extent that fluctuations in currency exchange rates cause our results of operations to differ from our expectations or the expectations of our investors, the market 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 aim to maintain a natural currency hedge against fluctuations in the U.S./Canadian foreign exchange rate by matching the amount of U.S. dollar and Canadian dollar investments to the expected amount of future U.S. dollar and Canadian dollar obligations, respectively. Any hedging technique we implement may fail to be effective. If our hedging activities are not effective, changes in currency exchange rates may have a more significant impact on the market price of our common shares.

Risks Related to Our Business

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

Our clinical product candidates, which include XEN1101, XEN901 and GDC-0310, along with our pre-clinical compounds, are in varying stages of development and will require substantial clinical development, testing and regulatory approval prior to commercialization. It may be several more years before these product candidates or any of our other product candidates receive marketing approval, if ever. If any of our product candidates fail to become approved products, our business, growth prospects, operating results and financial condition may be adversely

affected and a decline in the market price of our common shares could result.

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, governmental agencies, as well as public and private research institutions. Any product candidates that we or our collaborators successfully develop and commercialize will compete with existing products and any new products that may become available in the future.

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

Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, pre-clinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we, or our collaborators, do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early stage companies may also prove to be significant competitors, particularly through collaboration arrangements with large and established companies.

Our commercial opportunities could be reduced or eliminated if our competitors develop and commercialize products or therapies that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA, EMA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected by decisions made by insurers or other third-party payers.

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

If XEN901 or XEN1101 were approved for the treatment of epilepsy, we anticipate that they could potentially compete with each other and other anti-epileptic drugs, or AEDs, which typically can be categorized into four classes by AED mechanism: modulation of voltage-gated ion channels, enhancement of GABA-mediated inhibitory neurotransmission, reduction of glutamate-mediated excitatory neurotransmission, and SV2A modulation. Commonly used AEDs include phenytoin, levetiracetam, carbamazepine, clobazam, lamotrigine, valproate, oxcarbazepine, topiramate, lacosamide and perampanel. There are currently no FDA-approved treatments indicated for the early infantile epileptic encephalopathies EIEE7 or EIEE13. We are not aware of other companies that are developing selective Nav1.6 inhibitors for the treatment of epilepsy. There are other AEDs in development that could potentially compete with XEN1101 or XEN901, including products in development from UCB, Inc., Zogenix, Inc., GW Pharmaceuticals, Sage Therapeutics, Marinus Pharmaceuticals, Inc., SciFluor Lifesciences, Inc., Knopp Biosciences LLC, and Upsher-Smith Laboratories, Inc.

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, gabapentin, and pregabalin. We are also aware of development programs at several pharmaceutical and biotechnology companies that are developing Nav1.7 inhibitors or other sodium channel inhibitors for the treatment of pain, including Amgen Inc., AstraZeneca PLC, Biogen Inc., Dainippon Sumitomo Co., Ltd., Eli Lilly and Company, Merck, NeuroQuest Inc., Vertex Pharmaceuticals Inc., Voyager Therapeutics, Inc. and Chromocell Corporation in collaboration with its partner Astellas Pharma 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 Nav1.8 inhibitors.

We have no marketed proprietary 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. 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 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 discovering, acquiring or in-licensing product candidates in addition to XEN1101, XEN901, XEN007 and GDC-0310, our ability to expand our business and achieve our strategic objectives may be impaired.

We have built a product development pipeline by identifying product candidates either from our internal research efforts or through acquiring or in-licensing other product candidates. To date, our internal discovery efforts have yielded multiple development candidates, including GDC-0310 and XEN901. Both our internal discovery efforts and our assessment of potential acquisition or in-licensing opportunities require substantial technical, financial and human resources, regardless of whether we identify any viable product candidates.

If we are unable to identify additional product candidates suitable for clinical development and commercialization either from our internal research efforts or through acquiring or in-licensing other product candidates or technologies, we may not be able to obtain product revenue in future periods, which likely would result in significant harm to our financial position and adversely impact the market price of our common shares.

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

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

Our drug discovery efforts may initially show promise in identifying additional potential product candidates, yet fail to yield viable product candidates for clinical development or commercialization. Such failure may occur for many reasons, including the following: any product candidate may, on further study, be shown to have serious or unexpected side effects or other characteristics that indicate it is unlikely to be safe or otherwise does not meet applicable regulatory criteria; and any product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all.

If our discovery activities fail to identify novel targets for drug discovery, or such targets prove to be unsuitable for treating human disease, or 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.

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. Simon Pimstone, our Chief Executive Officer and President, and Mr. Ian Mortimer, our Chief Financial Officer and Chief Operating Officer, as well as other employees. 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 regulators, provide accurate information to the FDA, EMA and other regulators, comply with data privacy and security and healthcare fraud and abuse laws and regulations in the U.S. and abroad, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. Additionally, laws regarding data privacy and security, including the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, as well as comparable laws in non-U.S. jurisdictions, may impose obligations with respect to safeguarding the privacy, use, security and transmission of individually identifiable health information such as genetic material or information we obtain through our direct-to-patient web-based recruitment approach for identifying patients with rare or extreme phenotypes or patients identified for clinical trials.

Various laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Any misconduct could also involve the improper use of information obtained in the course of clinical studies, which could result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of conduct applicable to all of our employees, officers, directors, agents and representatives, including consultants, but it is not always possible to identify and deter misconduct, and the precautions we take to detect and prevent misconduct may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws and regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

We may encounter difficulties in managing our growth, including headcount, and expanding our operations successfully.

Our business strategy involves continued development and, where development is successful, commercialization of select product candidates for orphan and niche indications. In order to execute on this strategy, we will need to build out a regulatory, sales, manufacturing, distribution and marketing infrastructure and expand our development capabilities or contract with third parties to provide these capabilities and infrastructure for us. To achieve this, we will need to identify, hire and integrate personnel who have not worked together as a group previously.

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

Drs. Simon Pimstone and Y. Paul Goldberg each devote a small amount of their time to clinical work outside of their duties at our company, conducting, generally, two to three outpatient clinics per month on average. Future growth will impose significant added responsibilities on members of management, and our management may need to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities.

If we are unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate and grow revenue could be reduced, and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize product candidates and compete effectively will depend, in

part, on our ability to effectively manage any future growth.

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

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

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

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

- different regulatory requirements for initiating clinical trials and maintaining approval of drugs in foreign countries;
- reduced protection for intellectual property rights in certain countries;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, political instability or open conflict in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations of doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in North America;
- likelihood of potential or actual violations of domestic and international anti-corruption laws, such as the U.S. Foreign Corrupt Practices Act and the U.K. Bribery Act, or of U.S. and international export control and sanctions regulations, which likelihood may increase with an increase of operations in foreign jurisdictions;
- 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.

We believe that we may be deemed a passive foreign investment company for the taxable year ended December 31, 2017, which could result in adverse tax consequences for U.S. holders of our common shares.

Generally, for any taxable year in which 75% or more of our gross income is passive income, or at least 50% of the average quarterly value of our assets (which may be determined in part by the market value of our common shares, which is subject to change) are held for the production of, or produce, passive income, we would be characterized as a passive foreign investment company, or PFIC, for U.S. federal income tax purposes. Based on the price of our common shares and the composition of our gross assets, we believe that we may be deemed a PFIC for the taxable year ended December 31, 2017, and we could be a PFIC in subsequent years. Based on the composition of our gross income and gross assets, we do not believe that we were a PFIC for the taxable years ended December 31, 2016 and 2015. 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 future taxable years.

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

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

net capital gains for each year for which we may be a PFIC. U.S. holders should consult their own tax advisors with respect to making this election and the related reporting requirements.

A U.S. holder may also mitigate the adverse tax consequences by timely making a mark-to-market election. Generally, for each year that we meet the PFIC gross income or asset test, an electing U.S. holder would include in gross income the increase in the value of its common shares during each of its taxable years and deduct from gross income the decrease in the value of such shares during each of its taxable years. A mark-to-market election may be made and maintained only if our common shares are regularly traded on a qualified exchange, including The NASDAQ Global Market, or NASDAQ. Whether our common shares are regularly traded on a qualified exchange is an annual determination based on facts that, in part, are beyond our control. Accordingly, a U.S. holder might not be eligible to make a mark-to-market election to mitigate the adverse tax consequences if we are characterized as a PFIC. U.S. holders should consult their own tax advisors with respect to the possibility of making this election. In addition, our PFIC status may deter certain U.S. investors from purchasing our common shares, which could have an adverse impact on the market price of our common shares.

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

There is a risk that we may become subject to income tax in jurisdictions outside of Canada and the United States, if under the laws of any such jurisdiction, we are considered to be carrying on a trade or business there or earn income that is considered to be sourced there and we do not qualify for an exemption. In jurisdictions where we do not believe we are subject to tax, we can provide no certainty that tax authorities in those jurisdictions will not subject one or more tax years to examination. Tax examinations are often complex as tax authorities may disagree with the treatment of items reported by us, the result of which could have a material adverse effect on our operating results and financial condition.

Acquisitions 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 pre-clinical and clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. 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 pre-clinical studies or clinical trials;
 - the data collected from clinical trials of our product candidates may not be sufficient to support the submission of a New Drug Application, or NDA, or other submission or to obtain regulatory approval in the U.S. or elsewhere;
 - the FDA, EMA 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;

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

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

We could also encounter delays if a clinical trial is suspended or terminated by us, by our collaborators, by the IRBs of the institutions in which such trial is being conducted, by any Data Safety Monitoring Board for such trial, or by the FDA, EMA or other regulatory authorities. Such authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA, EMA or other regulatory authorities resulting in the imposition of a clinical hold, product candidate manufacturing problems, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. In addition, delays can occur due to safety concerns arising from trials or other clinical data regarding another company's product candidate in the same compound class as one of ours.

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 period during which we may have the exclusive right to commercialize our products under patent protection 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 product candidates – including XEN1101 and XEN901 for the treatment of epilepsy and GDC-0310 for the treatment of pain – 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 pre-clinical 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 some of our product candidates, we are seeking to develop treatments for diseases for which there is relatively limited clinical experience, and our clinical trials may use novel end points and measurement methodologies or subjective patient feedback, which adds a layer of complexity to our clinical trials and may delay regulatory approval. In addition, our focus on orphan and niche markets may cause us to select target indications that are in more challenging therapeutic areas. Clinical trials for pain, the indication for which GDC-0310 is being developed, are inherently difficult to conduct. The primary measure of pain is based on 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, from patient to patient, and from site to site within a clinical study. The placebo effect also tends to have a more significant impact in pain trials.

If our product candidates are not shown to be both safe and effective in clinical trials, we will not be able to obtain regulatory approval or commercialize these product candidates and products. In such case, we would need to develop other compounds and conduct associated pre-clinical testing and clinical trials, as well as potentially seek additional financing, all of which would have a material adverse effect on our business, growth prospects, operating results, financial condition and results of operations.

We 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, such as early infantile epileptic encephalopathies, or EIEEs, present significant recruitment challenges for clinical trials and a full understanding of the size of these populations is still relatively unknown. Many of these patients may not be suitable or available 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 product candidates 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. XEN007, a drug we are evaluating internally for the potential treatment of hemiplegic migraine, has received orphan drug designation from the FDA. If we seek orphan drug designations for other indications or in other jurisdictions, we may fail to receive such orphan drug designations and, even if we succeed, such orphan drug designations may fail to result in or maintain orphan drug exclusivity upon approval, which would harm our competitive position.

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

The results of pre-clinical studies and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. Interpretation of results from early, usually smaller, studies that suggest a clinically meaningful response in some patients, requires caution. Results from later stages of clinical trials enrolling more patients may fail to show the desired safety and efficacy results or otherwise fail to be consistent with the results of earlier trials of the same product candidate. Later clinical trial results may not replicate earlier clinical trials for a variety of reasons, including differences in trial design, different trial endpoints (or lack of trial endpoints in exploratory studies), patient population, number of patients, patient selection criteria, trial duration, drug dosage and formulation and lack of statistical power in the earlier studies. These uncertainties are enhanced where the diseases 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.

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

As product candidates are developed through pre-clinical to late stage clinical trials towards approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods and formulation, are altered along the way in an effort to optimize processes and results. Such changes carry the risk that they will not achieve these intended objectives. Any of these changes could cause our product candidates to perform differently and affect the results of planned clinical trials or other future clinical trials conducted with the altered materials. This could delay completion of clinical trials, require the conduct of bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidates and/or jeopardize our or our collaborators’ ability to commence product sales and generate revenue.

Even if we obtain and maintain approval for our product candidates from one jurisdiction, we may never obtain approval for our product candidates in other jurisdictions, which would limit our market opportunities and adversely affect our business.

Sales of our approved products, if any, will be subject to the regulatory requirements governing marketing approval in the countries in which we obtain regulatory approval, and we plan to seek regulatory approval to commercialize our product candidates in North America, the EU and in additional foreign countries. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries and regulatory approval in one country does not ensure approval in any other country, while a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory approval process in others. For example, approval in the U.S. by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one foreign regulatory authority does not ensure approval by the FDA or regulatory authorities in other countries. Approval procedures vary among jurisdictions and can be lengthy and expensive, and involve requirements and administrative review periods different from, and greater than, those in the U.S., including additional pre-clinical studies or clinical trials. Even if our product candidates are approved, regulatory approval for any product may be withdrawn by the regulatory authorities in a particular jurisdiction.

Even if a product is approved, the FDA, the EMA or another applicable regulatory authority, as the case may be, may limit the indications for which the product may be marketed, require extensive warnings on the product labeling or require expensive and time-consuming 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 EU also have their own requirements for approval of product candidates with which we must comply prior to marketing in those countries. Obtaining foreign regulatory approvals and compliance with such foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our current and any future products, in certain countries.

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

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

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

Risks Related to 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.

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 qualified sales and marketing personnel or develop alternative sales channels;
- the inability of sales personnel to obtain access to physicians or an inadequate 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 successful in entering into arrangements with third parties to sell, market, and distribute our product candidates or may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties, and any of these third parties may fail to devote the necessary resources and attention to sell, market, and distribute our current or any future products effectively.

Even if we receive regulatory approval to commercialize any of the product candidates that we develop independently, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense.

Any regulatory approvals that we receive for our product candidates we commercialize will be subject to limitations on the approved indicated uses for which the product may be marketed or subject to certain conditions of approval, and may contain requirements for potentially costly post-approval trials, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the marketed product.

For any approved product, we will need to ensure continued compliance with extensive regulations and requirements regarding the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for the product. These requirements include submissions of safety and other post-approval information and reports, as well as continued compliance with current good manufacturing practices, or cGMP, and current good clinical practices, or cGCP, for any clinical trials that we or our collaborators conduct post-approval. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- 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;
- and
- injunctions or the imposition of civil or criminal penalties.

Occurrence of any of the foregoing could have a material and adverse effect on our business and results of operations.

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. 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 payers have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payers are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that coverage and reimbursement will be available for any product that we or any collaborator commercialize and, if reimbursement is available, the level of reimbursement. In addition, coverage and reimbursement may impact the demand for, or the price of, any product candidate for which we or a collaborator obtains marketing approval. If coverage and reimbursement are not available or reimbursement is available only to limited levels, we or our collaborators may not be able to successfully commercialize any product candidate for which marketing approval is obtained.

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

Our target patient populations in orphan and niche indications, such as EIEE7 and EIEE13 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.

For example, in 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, collectively, the PPACA, was enacted and includes measures that have significantly changed, or will significantly change, the way healthcare is financed by both governmental and private insurers.

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. Our future products, if any, might not be considered medically reasonable and necessary for a specific indication or cost-effective by third-party payers. An adequate level of reimbursement might not be available for such products and third-party payers' reimbursement policies might adversely affect our or our collaborators' ability to sell any future products profitably.

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

The Trump administration and Congress may also attempt broad sweeping changes to the current health care laws, including PPACA. The impact of any such changes on us and the pharmaceutical industry as a whole is currently unknown. Any changes to the PPACA are likely to have an impact on our results of operations, and may have a material adverse effect on our result of operations. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the U.S. or abroad. If we or our collaborators are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or our collaborators are not able to maintain regulatory compliance, our product candidates may lose any marketing approval that may have been obtained and we may not achieve or sustain profitability, which would adversely affect our business.

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

In most foreign countries, particularly those in the EU, prescription drug pricing and/or reimbursement is subject to governmental control. In those countries that impose price controls, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we or our collaborators may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies.

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

Risks Related to Our Dependence on Third Parties

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

We have no control over the resources, time and effort that our collaborators may devote to our programs and limited access to information regarding or resulting from such programs. We are dependent on our collaborators, including 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, commercialization of a product or payment of royalties or milestone payments, any of which could result in a delay in milestones, royalty payments or termination of a program and possibly resulting in costly litigation or arbitration which may divert management attention and resources;
- a collaborator may not adequately protect the intellectual property rights associated with a product or product candidate; 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 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 significant 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 pre-clinical 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, EMA and other regulatory agencies. They are also subject to periodic unannounced inspections by the FDA, EMA and other regulatory agencies. Any subsequent discovery of problems with a product, or a manufacturing or laboratory facility used by us or our collaborators, may

result in restrictions on the product or on the manufacturing or laboratory facility, including product recall, suspension of manufacturing, product seizure or a voluntary withdrawal of the drug from the market. Any failure by our third-party manufacturers to comply with cGMP or any failure to deliver sufficient quantities of product candidates in a timely manner, could lead to a delay in, or failure to obtain, regulatory approval of any of our product candidates.

We rely on third parties to monitor, support, conduct, and/or oversee clinical trials of the product candidates that we are developing independently and, in some cases, to maintain regulatory files for those product candidates. We may not be able to obtain regulatory approval for our product candidates or commercialize any products that may result from our development efforts, if we are not able to maintain or secure agreements with such third parties on acceptable terms, if these third parties do not perform their services as required, or if these third parties fail to timely transfer any regulatory information held by them to us.

We rely on entities outside of our control, which may include academic institutions, CROs, hospitals, clinics and other third-party collaborators, to monitor, support, conduct and/or oversee pre-clinical and clinical studies of our current and future product candidates. As a result, we have less control over the timing and cost of these studies and the ability to recruit trial subjects than if we conducted these trials with our own personnel.

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

Ultimately, we are responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards, and our reliance on third parties does not relieve us of our regulatory responsibilities.

We and our CROs are required to comply with cGCP regulations and guidelines enforced by the FDA, the competent authorities of the member states of the European Economic Area and comparable foreign regulatory authorities for products in clinical development. Regulatory authorities enforce these cGCP regulations through periodic inspections of clinical trial sponsors, principal investigators and clinical trial sites. If we or any of our CROs fail to comply with applicable cGCP regulations, the clinical data generated in our clinical trials may be deemed unreliable and our submission of marketing applications may be delayed or the FDA, EMA or another regulatory authority may require us to perform additional clinical trials before approving our marketing applications. Upon inspection, the FDA, EMA or another regulatory authority could determine that any of our clinical trials fail or have failed to comply with applicable cGCP regulations. In addition, our clinical trials must be conducted with product produced under the cGMP regulations enforced by the FDA, EMA and other regulatory authorities, 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 or unenforceable, be interpreted in a manner that does not adequately protect our current product or any future products, or fail to otherwise provide us with any competitive advantage. The patent position of biotechnology and pharmaceutical companies is generally uncertain because it involves complex legal and factual considerations. The standards applied by the U.S. Patent and Trademark Office, or USPTO, and foreign patent offices in granting patents are not always applied uniformly or predictably. For example, there is no uniform worldwide policy regarding patentable subject matter or the scope of claims allowable in biotechnology and pharmaceutical patents. Consequently, patents may not issue from our pending patent applications. As such, we do not know the degree of future protection that we will have on our proprietary products and technology, if any, and a failure to obtain adequate intellectual property protection with respect to our product candidates and proprietary technology could have a material adverse impact on our business.

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

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

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

The following examples are illustrative:

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

- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may fail to develop additional proprietary technologies that are patentable;
- the laws of certain foreign countries may not protect our intellectual property rights to the same extent as the laws of the U.S., or we may fail to apply for or obtain adequate intellectual property protection in all the jurisdictions in which we operate; and
- the patents of others may have an adverse effect on our business, for example by preventing us from marketing one or more of our product candidates for one or more indications.

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

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

Filing, prosecuting 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. For example, currently, some of these rights relating to the patent portfolios for GDC-0310 are held by Genentech.

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

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

Competitors may infringe our patents or the patents of our licensors. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that a patent of ours or one of our licensors is not valid or is unenforceable, or may refuse to stop the other party in such infringement proceeding from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated, held unenforceable or interpreted narrowly, and could put any of our patent applications at risk of not yielding an issued patent.

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

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

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

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

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

Defending against claims of patent infringement, misappropriation of trade secrets or other violations of intellectual property rights could be costly and time consuming, regardless of the outcome. Thus, even if we were to ultimately prevail, or to settle at an early stage, such litigation could burden us with substantial unanticipated costs. In addition, litigation or threatened litigation could result in significant demands on the time and attention of our management team, distracting them from the pursuit of other company business. Claims that our product candidates or the sale or use of our future products infringe, misappropriate or otherwise violate third-party intellectual property rights could therefore have a material adverse impact on our business.

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

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

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

If third parties successfully assert their intellectual property rights against us, we might be barred from using certain aspects of our technology, or barred from developing and commercializing certain products. Prohibitions against using certain technologies, or prohibitions against commercializing certain products, could be imposed by a court or by a settlement agreement between us and a plaintiff. In addition, if we are unsuccessful in defending against allegations that we have infringed, misappropriated or otherwise violated patent or other intellectual property rights of others, we may be forced to pay substantial damage awards to the plaintiff. There is inevitable uncertainty in intellectual property litigation and we could lose, even if the case against us is weak or flawed. If litigation leads to an outcome unfavorable to us, we may be required to obtain a license from the intellectual property owner in order to continue our research and development programs or to market any resulting product. It is possible that the necessary license will not be available to us on commercially acceptable terms, or at all. Alternatively, we may be required to modify or redesign our current or future products, if any, in order to avoid infringing or otherwise violating third-party intellectual property rights. This may not be technically or commercially feasible, may render those products less competitive, or may delay or prevent the entry of those products to the market. Any of the foregoing could limit our research and development activities, our ability to commercialize one or more product candidates, or both.

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

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

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

Under our existing license and other agreements, including those associated with our XEN1101 program, 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 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 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 June 13, 2013, the U.S. Supreme Court decision in *Association for Molecular Pathology v. Myriad Genetics, Inc.*, held that isolated DNA sequences are not patentable. In December 2014, the USPTO issued its Interim Guidance on Patent Subject Matter Eligibility, in which it extended Myriad's "marked difference" standard for patent subject matter eligibility to all potential natural products. This standard applies to patent claims that recite not only nucleic acids (such as DNA in Myriad), but also other subject matter that could be considered a natural product, such as peptides, proteins, extracts, organisms, antibodies, chemicals, and minerals. As a consequence of the Myriad decision and the USPTO's Interim Guidance, if any of our future product candidates utilize isolated DNA, peptides, proteins or the like, we will not be able to obtain patents in the U.S. claiming such novel gene targets that we discover, which could limit our ability to prevent third parties from developing drugs directed against such targets.

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

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

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

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

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

Intellectual property litigation may lead to unfavorable publicity that harms our reputation and causes the market price of our common shares to decline.

During the course of any intellectual property litigation, there could be public announcements of the initiation of the litigation as well as results of hearings, rulings on motions, and other interim proceedings in the litigation. If securities analysts or investors regard these announcements as negative, the perceived value of our existing products, programs or intellectual property could be diminished. Accordingly, the market price of our common shares may decline. Such announcements could also harm our reputation or the market for our future products, which could have a material adverse effect on our business.

Risks Related to Our Industry

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our current and any future products.

We face an inherent risk of product liability as a result of the clinical testing of our product candidates, and we will face an even greater risk if we commercialize any product candidates. For example, we may be sued if any of our product candidates, including any that are developed in combination with other therapies, allegedly causes injury or is found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability and a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Even successful defense would require significant financial and management resources. There is also risk that third parties we have agreed to indemnify could incur liability. Regardless of the merits or eventual outcome, liability claims may result in:

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

• a decline in the market price of our common shares.

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We currently carry product liability insurance of \$10,000,000 CAD per occurrence and \$10,000,000 CAD aggregate limit. We believe our product liability insurance coverage is appropriate relative to our current clinical programs; however, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. If and when we obtain marketing approval for product candidates, we intend to expand our insurance coverage to include the sale of commercial products; however, we may then be unable to obtain product liability insurance on commercially reasonable terms or in adequate amounts. On occasion, large judgments have been awarded in class action lawsuits based on drugs or medical treatments that had unanticipated adverse effects. A successful product liability claim or series of claims brought against us could cause the market price of our common shares to decline and, if judgments exceed our insurance coverage, could adversely affect our future results of operations and business.

Patients with certain of the diseases 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 future relationships with customers and third-party payers, if any, in the U.S. and elsewhere will be subject, directly or indirectly, to applicable federal and state anti-kickback, fraud and abuse, false claims, transparency, health information privacy and security, and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, administrative burdens, and diminished profits and future earnings.

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

- 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 their behalf, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

the federal Open Payments program; and

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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.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

Our research and development activities involve the controlled use of potentially harmful biological materials as well as hazardous materials, chemicals, and various radioactive compounds typically employed in molecular and cellular biology. For example, we routinely use cells in culture and we employ small amounts of radioisotopes. We cannot completely eliminate the risk of accidental contamination or injury from the use, storage, handling, or disposal of these materials through our maintenance of up-to-date licensing and training programs. In the event of contamination or injury, we could be held liable for damages that result, and any liability could exceed our resources. We currently carry insurance covering certain claims arising from our use of these materials. However, if we are unable to maintain our insurance coverage at a reasonable cost and with adequate coverage, our insurance may not cover any liability that may arise. We are subject to U.S. and Canadian federal, provincial, and local laws and regulations governing the use, storage, handling, and disposal of these materials and specified waste products. Complying with regulations regarding the use of these materials could be costly, and if we fail to comply with these regulations, it could have a material adverse effect on our operations and profitability.

We or the third parties upon whom we depend may be adversely affected by earthquakes or other natural disasters and our business continuity and disaster recovery plans may not adequately protect us from serious disaster.

Our headquarters are located in Burnaby, British Columbia, Canada. We are vulnerable to natural disasters such as earthquakes that could disrupt our operations. If a natural disaster, power outage, fire or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as the manufacturing facilities of our third-party contract manufacturers, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. Although we carry insurance for earthquakes and other natural disasters, we may not carry sufficient business interruption insurance to compensate us for all losses that may occur. The disaster recovery and business continuity plans we have in place may not be adequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result

of a natural disaster or earthquake, which could have a material adverse effect on our business. In addition, we may lose samples or other valuable data. The occurrence of any of the forgoing could have a material adverse effect on our business.

Risks Related to Our Common Shares

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

The market price of our common shares has fluctuated in the past and is likely to be volatile in the future. As a result of this volatility, investors may experience losses on their investment in our common shares. The market price for our common shares may be influenced by many factors, including the following:

- announcements by us or our competitors of new products, product candidates or new uses for existing products, significant contracts, commercial relationships or capital commitments and the timing of these introductions or announcements;

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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;

- unanticipated serious safety concerns related to the use of any of our products and product candidates;
- results from or delays of clinical trials of our product candidates;
- failure to obtain or delays in obtaining or maintaining product approvals or clearances from regulatory authorities;
- adverse regulatory or reimbursement announcements;
- announcements by us or our competitors of significant acquisitions, strategic collaborations, joint ventures or capital commitments;
- the results of our efforts to discover or develop additional product candidates;
- 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;
- sales of common shares by us or our shareholders in the future, as well as the overall trading volume of our common shares;
- failure to comply with covenants or make required payments under loan agreements;
- changes in the structure of healthcare payment systems;
- commencement of, or our involvement in, litigation;
- general economic, industry and market conditions in the pharmaceutical and biotechnology sectors and other factors that may be unrelated to our operating performance or the operating performance of our competitors, including changes in market valuations of similar companies; and
- the other factors described in this “Risk Factors” section.

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

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

The market price of our common shares could decline as a result of sales of a large number of our common shares or the perception that these sales could occur. These sales, or the possibility that these sales may occur, also might make it more difficult for us to sell equity securities in the future at a time and at a price that we deem appropriate.

In addition, in the future, we may issue additional common shares 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 the market price of our common shares to decline.

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

Provisions in our articles and our by-laws, as well as certain provisions under the Canada Business Corporations Act, or CBCA, and applicable Canadian securities laws, may discourage, delay or prevent a merger, acquisition or other change in control of us that shareholders may consider favorable, including transactions in which they might otherwise receive a premium for their common shares. These provisions could also limit the price that investors might be willing to pay in the future for our common shares, thereby depressing the market price of our common shares. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our shareholders to replace or remove our current management by making it more difficult for shareholders to replace members of our board of directors. Among other things, these provisions include the following:

- shareholders cannot amend our articles unless such amendment is approved by shareholders holding at least two-thirds of the shares entitled to vote on such approval;
- 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 CBCA or under any applicable Canadian securities law that has the effect of delaying or deterring a change in control could limit the opportunity for our shareholders to receive a premium for their common shares, and could also affect the price that some investors are willing to pay for our common shares.

U.S. civil liabilities may not be enforceable against us, our directors, or our officers.

We are governed by the CBCA and our principal place of business is in Canada. Many of our directors and officers reside outside of the U.S., and all or a substantial portion of their assets as well as all or a substantial portion of our assets are located outside the U.S. As a result, it may be difficult for investors to effect service of process within the U.S. upon us and certain of our directors and officers or to enforce judgments obtained against us or such persons, in U.S. courts, in any action, including actions predicated upon the civil liability provisions of U.S. federal securities laws or any other laws of the U.S. Additionally, rights predicated solely upon civil liability provisions of U.S. federal securities laws or any other laws of the U.S. may not be enforceable in original actions, or actions to enforce judgments obtained in U.S. courts, brought in Canadian courts, including courts in the Province of British Columbia.

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

We are governed by the CBCA and other relevant laws, which may affect the rights of shareholders differently than those of a company governed by the laws of a U.S. jurisdiction, and may, together with our charter documents, have the effect of delaying, deferring or discouraging another party from acquiring control of our company by means of a tender offer, a proxy contest or otherwise, or may affect the price an acquiring party would be willing to offer in such an instance. The material differences between the CBCA and Delaware General Corporation Law, or DGCL, that may have the greatest such effect include, but are not limited to, the following: (i) for material corporate transactions (such as mergers and amalgamations, other extraordinary corporate transactions or amendments to our articles) the CBCA generally requires a two-thirds majority vote by shareholders, whereas DGCL generally only requires a majority vote; and (ii) under the CBCA a holder of 5% or more of our common shares can requisition a special meeting of shareholders, whereas such right does not exist under the DGCL.

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

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

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

We are an “emerging growth company,” as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. For as long as we continue to be an “emerging growth company,” we may choose to take advantage of exemptions from various reporting requirements applicable to other public companies that are not “emerging growth companies,” including, but not limited to, not being required to have our independent registered public accounting firm audit our internal control over financial reporting under Section 404, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved. We could be an “emerging growth company” for up to five years following the completion of our initial public offering, although, if we have more than \$1.07 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 the market price of our common shares may be more volatile.

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

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

As a public company, and particularly after we cease to be an “emerging growth company,” we will incur significant legal, accounting and other expenses. In addition, the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, and the related rules and regulations subsequently implemented by the Securities and Exchange Commission, or SEC, the applicable Canadian securities regulators and NASDAQ impose numerous requirements on public companies, including requiring changes in corporate governance practices. Also, the Securities Exchange Act of 1934, as amended, or the Exchange Act, requires, among other things, that we file annual, quarterly and current reports with respect to our business and operating results. Our management and other personnel have and will continue to devote a substantial amount of time to compliance with these laws and regulations. These requirements have increased and will continue to increase our legal, accounting, and financial compliance costs and have made and will continue to make some activities more time-consuming and costly. For example, these rules and regulations make it difficult and expensive for us to maintain director and officer liability insurance and we may be required to accept reduced policy limits and coverage or to incur substantial costs to maintain the same or similar coverage. These rules and regulations could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors or our board committees or as executive officers.

The Sarbanes-Oxley Act requires, among other things, that we assess the effectiveness of our internal control over financial reporting annually and the effectiveness of our disclosure controls and procedures quarterly. In particular,

Section 404 of the Sarbanes-Oxley Act, or Section 404, requires us to perform system and process evaluation and testing of our internal control over financial reporting to allow management to report on, and our independent registered public accounting firm potentially to attest to, the effectiveness of our internal control over financial reporting. As an “emerging growth company” we expect to avail ourselves of the exemption from the requirement that our independent registered public accounting firm attest to the effectiveness of our internal control over financial reporting under Section 404. However, we may no longer avail ourselves of this exemption when we cease to be an “emerging growth company.” When our independent registered public accounting firm is required to undertake an assessment of our internal control over financial reporting, the cost of our compliance with Section 404 will correspondingly increase. Our compliance with applicable provisions of Section 404 will require that we incur substantial accounting expense and expend significant management time on compliance-related issues as we implement additional corporate governance practices and comply with reporting requirements. Moreover, if we are not able to comply with the requirements of Section 404 applicable to us in a timely manner, or if we or our independent registered public accounting firm identifies deficiencies in our internal control over financial reporting that are deemed to be material weaknesses, the market price of our common shares could decline and we could be subject to sanctions or investigations by the SEC or other regulatory authorities, which would require additional financial and management resources.

Furthermore, investor perceptions of our company may suffer if deficiencies are found, and this could cause a decline in the market price of our common shares. Irrespective of compliance with Section 404, any failure of our internal control over financial reporting could have a material adverse effect on our stated operating results and harm our reputation. If we are unable to implement these requirements effectively or efficiently, it could harm our operations, financial reporting, or financial results and could result in an adverse opinion on our internal controls from our independent registered public accounting firm.

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

Effective internal controls over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with Section 404 or any subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the market price of our common shares.

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

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

As of December 31, 2017, options to purchase 2,339,905 of our common shares with a weighted-average exercise price of \$7.41 per common share were outstanding. The exercise of any of these options would result in dilution to current shareholders. Further, because we will need to raise additional capital to fund our clinical development programs, we may in the future sell substantial amounts of common shares or securities convertible into or exchangeable for common shares. Pursuant to our equity incentive plans, our compensation committee (or a subset or delegate thereof) is authorized to grant equity-based incentive awards to our employees, directors and consultants. Future option grants and issuances of common shares under our share-based compensation plans may have an adverse effect on the market price of our common shares.

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

We are at risk of securities class action litigation.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology companies have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

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

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

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

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

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

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

We have broad discretion in the application of the net proceeds to us from our December 2017 debt financing and September 2016 public equity offering of our common shares. You may not agree with our decisions, and our use of the proceeds and our existing cash and cash equivalents and marketable securities may not improve our results of operation or enhance the value of our common shares. The results and effectiveness of the use of proceeds are uncertain, and we could spend the proceeds in ways that you do not agree with or that do not improve our results of operations or enhance the value of our common shares. Our failure to apply these funds effectively could have a material adverse effect on our business, delay the development of our product candidates and cause the market price of our common shares to decline. In addition, until the net proceeds are used, they may be placed in investments that do not produce significant income or that may lose value.

We do not anticipate paying any cash dividends on our common shares in the foreseeable future.

We do not currently intend to pay any cash dividends on our common shares in the foreseeable future. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common shares may be investors' sole source of gain for the foreseeable future.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

Our headquarters are located in Burnaby, British Columbia, where we occupy approximately 41,332 square feet of office and laboratory space. The term of the lease expires in March 2022. We currently pay an aggregate of approximately \$107,474 per month in base rent, property tax, common area maintenance fees and management fees, and the landlord holds a security deposit equal to approximately \$72,394.

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Our U.S. office is located in Boston, Massachusetts, where we occupy on a month-to-month basis approximately 215 square feet.

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.

Item 3. 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.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Shareholder Matters and Issuer Purchases of Equity Securities

Market Information

Our common shares have been traded on The NASDAQ Global Market since November 5, 2014 under the symbol "XENE." Prior to such time, there was no public market for our common shares. The following table sets forth the high and low sales prices per common share as reported on The NASDAQ Global Market for the periods indicated.

| | High | Low |
|---------------------------------------|--------|--------|
| Year Ended December 31, 2018 | | |
| First Quarter (through March 2, 2018) | \$4.45 | \$2.70 |
| Year Ended December 31, 2017 | | |
| Fourth Quarter | \$3.50 | \$2.10 |
| Third Quarter | \$3.50 | \$2.25 |
| Second Quarter | \$4.45 | \$2.85 |
| First Quarter | \$9.95 | \$3.95 |
| Year Ended December 31, 2016 | | |
| Fourth Quarter | \$8.75 | \$7.35 |
| Third Quarter | \$8.56 | \$5.88 |
| Second Quarter | \$7.72 | \$5.65 |
| First Quarter | \$8.42 | \$6.31 |

On March 2, 2018, the last reported sale price of our common shares was \$4.40 per share.

Holders

As of March 2, 2018, there were approximately 166 holders of record of our common shares. The actual number of shareholders is greater than this number of record holders and includes shareholders who are beneficial owners but whose common shares are held in street name by brokers and other nominees.

Dividends

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.

Canadian withholding tax at a rate of 25% (subject to reduction under the provisions of any applicable income tax treaty or convention to which Canada is a signatory) will be payable on the gross amount of a dividend on our common shares paid or credited, or deemed to be paid or credited, to a holder of our common shares who, for purposes of the Income Tax Act (Canada), is not (and is not deemed to be) resident in Canada, or a Non-Resident of Canada Holder. The Canadian withholding tax 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 our common shares to a Non-Resident of Canada Holder who is a resident of the U.S.

for purposes of the Canada U.S. Tax Convention (1980), or the Convention, is the beneficial owner of 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 company that owns (or, for purposes of the Convention, is considered to own) at least 10% of our voting shares, to 5%. Not all persons who are residents of the U.S. for purposes of the Convention will qualify for the benefits of the Convention. A Non-Resident of Canada Holder who is a resident of the U.S. is advised to consult his or her tax advisor in this regard. The rate of withholding tax on dividends is also reduced under other bilateral income tax treaties to which Canada is a signatory.

Securities Authorized for Issuance under Equity Compensation Plans

The information concerning our equity compensation plans is incorporated by reference herein to our Proxy Statement for the 2018 Annual Meeting of Shareholders to be filed with the SEC within 120 days after the end of our fiscal year ended December 31, 2017.

Performance Graph

This performance graph shall not be deemed “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or the Exchange Act, or incorporated by reference into any of our filings under the Securities Act of 1933, as amended, or the Exchange Act, except as shall be expressly set forth by specific reference in such filing.

The following stock performance graph illustrates a comparison of the total cumulative shareholder return on our common shares from November 5, 2014, which is the date our common shares commenced trading on The NASDAQ Global Market, through December 31, 2017, to two indices: the NASDAQ Composite Index and the NASDAQ Biotechnology Index. The graph assumes an initial investment of \$100 on November 5, 2014, and that any dividends were reinvested. The comparisons in the graph are required by the Securities and Exchange Commission and are not intended to forecast or be indicative of possible future performance of our common shares.

Recent Sales of Unregistered Securities

On December 18, 2017, we issued Silicon Valley Bank a warrant to purchase 50,411 of our common shares at a price per share of \$2.43. If Silicon Valley Bank advances a second tranche of funding pursuant to the loan and security agreement, the number of common shares exercisable pursuant to the warrant will increase by 36,008. If Silicon Valley Bank advances a third tranche of funding pursuant to the loan and security agreement, the number of common shares exercisable pursuant to the warrant will increase by 21,604. In no event will the number of common shares issuable pursuant to the exercise of the warrant exceed 108,023 in the aggregate. The issuance of the warrant was exempt from registration under the Securities Act of 1933, as amended, pursuant to Section 4(a)(2) thereof as a transaction by an issuer not involving a public offering and exempt from the prospectus requirements under applicable Canadian securities laws as Silicon Valley Bank is an “accredited investor”, as such term is defined in section 1.1 of National Instrument 45-106 - Prospectus Exemptions.

Issuer Repurchases of Equity Securities

None.

Item 6. Selected Financial Data

The following selected financial data is derived from our audited consolidated financial statements and should be read in conjunction with, and is qualified in its entirety by, Item 7, “Management’s Discussion and Analysis of Financial Condition and Results of Operations,” and Item 8, “Financial Statements and Supplementary Data” contained elsewhere in this Annual Report on Form 10-K. The selected Statements of Operations Data for the years ended December 31, 2017, 2016 and 2015 and Balance Sheet Data as of December 31, 2017 and 2016 have been derived from our audited consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K. The selected Statements of Operations Data for the years ended December 31, 2014 and 2013 and Balance Sheet Data as of December 31, 2015, 2014 and 2013 have been derived from our audited financial statements that are not included in this Annual Report on Form 10-K. Historical results are not necessarily indicative of future results. Our audited annual consolidated financial statements have been prepared in U.S. dollars and in accordance with U.S. Generally Accepted Accounting Principles.

| | Year Ended December 31, | | | | |
|---|---|------------|------------|----------|----------|
| | 2017 | 2016 | 2015 | 2014 | 2013 |
| | (in thousands except per share amounts) | | | | |
| Statement of Operations Data: | | | | | |
| Revenue: | | | | | |
| Collaboration revenue | \$309 | \$1,767 | \$15,573 | \$28,366 | \$27,352 |
| Royalties | 2 | 36 | 4 | 4 | 4 |
| | 311 | 1,803 | 15,577 | 28,370 | 27,356 |
| Operating expenses: | | | | | |
| Research and development | 25,573 | 19,828 | 15,152 | 11,768 | 12,303 |
| General and administrative | 7,313 | 6,792 | 9,786 | 5,496 | 5,341 |
| Total operating expenses | 32,886 | 26,620 | 24,938 | 17,264 | 17,644 |
| Income (loss) from operations | (32,575) | (24,817) | (9,361) | 11,106 | 9,712 |
| Other income (expense): | | | | | |
| Interest income | 477 | 504 | 542 | 568 | 338 |
| Interest expense | — | — | — | — | (64) |
| Foreign exchange gain (loss) | 1,394 | 1,316 | (6,933) | 1,344 | 2,035 |
| Gain on write-off and disposal of assets | — | — | — | — | 11 |
| Net income (loss) | (30,704) | (22,997) | (15,752) | 13,018 | 12,032 |
| Net income attributable to participating securities | — | — | — | — | 8,199 |
| Net income (loss) attributable to common shareholders | \$(30,704) | \$(22,997) | \$(15,752) | \$13,018 | \$3,833 |
| Net income (loss) per share—basic ⁽¹⁾ | \$(1.71) | \$(1.48) | \$(1.10) | \$4.11 | \$2.87 |
| Net income (loss) per share—diluted ⁽¹⁾ | \$(1.72) | \$(1.48) | \$(1.10) | \$3.28 | \$1.91 |
| Weighted-average common shares outstanding used | | | | | |
| in computing basic net income (loss) per share ⁽¹⁾ | 17,985 | 15,493 | 14,282 | 3,166 | 1,338 |
| Weighted-average common shares outstanding used | | | | | |
| in computing diluted net income (loss) per share ⁽¹⁾ | 18,002 | 15,493 | 14,282 | 3,964 | 2,009 |

As of December 31,
2017 2016 2015 2014 2013
(in thousands)

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| Balance Sheet Data: | | | | | |
|--|----------|----------|----------|----------|----------|
| Cash, cash equivalents and marketable securities | \$43,667 | \$64,146 | \$58,651 | \$84,041 | \$49,276 |
| Working capital ⁽²⁾ | 40,738 | 62,089 | 57,951 | 70,460 | 31,384 |
| Total assets | 46,121 | 67,487 | 63,949 | 87,418 | 54,487 |
| Loan payable | 6,804 | — | — | — | — |
| Redeemable convertible preferred shares | — | — | — | — | 102,488 |
| Total shareholders' equity (deficit) | 35,934 | 63,901 | 61,034 | 72,779 | (78,372) |

- (1) See Note 5 to our consolidated financial statements appearing elsewhere in this report 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) Certain comparative figures, which comprise working capital, have been reclassified to conform to the consolidated financial statement presentation adopted for the current year.

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

You should read the following discussion and analysis together with Part II, Item 6 — “Selected Financial Data” and our consolidated financial statements and notes included elsewhere in this Annual Report. The following discussion contains forward-looking statements that involve risks and uncertainties. Our actual results could differ from those expressed or implied in any forward-looking statements as a result of various factors, including those set forth under the caption Part I, Item 1A — “Risk Factors.” Throughout this discussion, unless the context specifies or implies otherwise, the terms “Xenon,” “we,” “us,” and “our” refer to Xenon Pharmaceuticals Inc. and its subsidiary.

Overview

We are a clinical stage biopharmaceutical company focused on developing innovative therapeutics to improve the lives of patients with neurological disorders. Building upon our extensive knowledge of human genetics and diseases caused by mutations in ion channels, known as channelopathies, we are advancing – both independently and with our collaborators – a novel product pipeline of central nervous system, or CNS, therapies to address areas of high unmet medical need, such as epilepsy and pain.

To date, our pharmaceutical collaborations have generated in aggregate over \$160.0 million in non-equity funding with the potential to provide us with future milestone payments, as well as royalties on product sales. Our current pharmaceutical partners include Genentech, a member of the Roche Group, and Merck & Co., Inc., or Merck (through its affiliate, Essex Chemie AG).

Our clinical development pipeline includes:

• XEN1101 is a Kv7 potassium channel opener being developed for the treatment of epilepsy including: treatment-resistant adult and pediatric focal seizures; rare, pediatric forms of epilepsy, such as EIEE7, an early infantile epileptic encephalopathy associated with mutations in the KCNQ2 gene that cause loss-of-function in the Kv7.2 potassium channel; and potentially other neurological disorders. In October 2017, we initiated a randomized, double-blind, placebo-controlled Phase 1 clinical trial to evaluate the safety, tolerability and pharmacokinetics of both single ascending doses, or SAD, and multiple ascending doses, or MAD, of XEN1101 in healthy subjects. The XEN1101 Phase 1 clinical trial includes a pharmacodynamic biomarker read-out from a transcranial magnetic stimulation, or TMS, study, designed to assess XEN1101's ability and potency to modulate cortical excitability, thereby demonstrating activity in the target CNS tissue. We expect to present interim Phase 1 results in May 2018. The release of the complete Phase 1 results, including the Phase 1b TMS data, is anticipated in the second half of 2018. We anticipate initiating a Phase 2 proof-of-concept trial evaluating XEN1101's efficacy as a treatment for adult focal seizures by year end. We also intend to explore a parallel plan to advance XEN1101 into rare, pediatric forms of epilepsy as soon as feasible thereafter;

• XEN901 is a potent, highly selective Nav1.6 sodium channel inhibitor being developed for the treatment of epilepsy including treatment resistant adult and pediatric focal seizures, as well as rare, pediatric forms of epilepsy, such as EIEE13, an early infantile epileptic encephalopathy due to gain-of-function mutations in the SCN8A gene that encodes the Nav1.6 sodium channel. In February 2018, we initiated a randomized, double-blind, placebo-controlled Phase 1 clinical trial to evaluate XEN901's safety, tolerability and pharmacokinetics in both SAD and MAD cohorts of approximately 64 healthy subjects in total. Upon completion of the Phase 1 clinical trial, a read-out of results is anticipated in the second half of 2018, followed by a Phase 2 proof-of-concept trial evaluating XEN901's efficacy as a treatment for adult focal seizures. We also intend to pursue a parallel plan to advance XEN901 into rare, pediatric forms of epilepsy as soon as feasible thereafter;

• We have identified an additional clinical stage, ion channel program, XEN007 (active ingredient flunarizine), to expand our existing neurology-focused product pipeline. XEN007 is a CNS-acting calcium channel blocker that directly modulates Cav2.1, which is a critical calcium channel implicated in the pathophysiology of hemiplegic migraine, or HM, a rare and debilitating neurological disorder afflicting approximately 60,000 people in the U.S.

Flunarizine has been used outside of the U.S. in the prevention of chronic migraine and has been reported to have clinical benefit in HM case studies. Xenon's clinical development plans include a proposed strategy to develop XEN007 as the first treatment specifically approved for HM anywhere in the world. We have received Orphan Drug Designation from the U.S. Food and Drug Administration, or FDA, for XEN007 for the treatment of HM. In addition, we have entered into key agreements in order to access regulatory files and manufacturing support to potentially enable the accelerated clinical development of XEN007 directly into a Phase 2 clinical trial. We are currently examining various development strategies for XEN007 with key opinion leaders and leading clinicians, as well as exploring options for potential partnerships for this program; and

• We have an ongoing collaboration with Genentech focused on developing novel inhibitors of Nav1.7 for the treatment of pain. Genentech has completed a Phase 1 clinical trial for GDC-0310, which is an oral, selective Nav1.7 small-molecule inhibitor developed for the potential treatment of pain. Guidance around the future clinical development of GDC-0310 will be updated once ongoing pre-clinical studies are completed and the final results are analyzed by Genentech.

We have funded our operations through the sale of equity securities, funding received from our licensees and collaborators, debt financing and, to a lesser extent, government funding. For 2017, 2016, and 2015, we recognized revenues of approximately \$0.3 million, \$1.8 million, and \$15.6 million, respectively, consisting primarily of funding and payments from our collaborators. Though our revenue from our collaboration and license agreements resulted in net income of \$13.0 million for the year ended December 31, 2014 and \$12.0 million for the year ended December 31, 2013, we do not expect to have sustained profitability for the foreseeable future. We had net losses of \$30.7 million for the year ended December 31, 2017 and an accumulated deficit of \$173.4 million as of December 31, 2017, from expenses incurred in connection with our research programs and from general and administrative costs associated with our operations.

We have not generated any significant royalty revenue from product sales, and do not otherwise anticipate generating revenue from product sales for the foreseeable future, if ever. 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 at least the next 12 to 24 months. We anticipate that our expenses will increase as we:

- continue our research and pre-clinical and clinical development of our product candidates either from our internal research efforts or through acquiring or in-licensing other product candidates or technologies;
- 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 or other agreements;
- maintain, protect and expand our intellectual property portfolio;
- attract, hire and retain skilled personnel; and
- create additional infrastructure to support our operations 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. We have not generated any significant royalty revenue from product sales, and do not otherwise anticipate generating revenue from product sales for the foreseeable future, if ever. Over our history, we have entered into several collaboration agreements, the most significant of which, with respect to revenue, are described at “Business – Strategic Alliances” and “Note 11” of the consolidated financial statements included elsewhere in this Annual Report on Form 10-K.

The following table is a summary of revenue recognized from our current and former collaboration and licensing agreements for each of the years ended December 31, 2017, 2016 and 2015 (in thousands):

Year Ended December
31,

| | 2017 | 2016 | 2015 |
|--------------------------------|-------|---------|----------|
| Teva: | | | |
| Recognition of upfront payment | \$— | \$— | \$10,897 |
| Research funding | 59 | 116 | 112 |
| Genentech: | | | |
| Recognition of upfront payment | — | 157 | 725 |
| Research funding | — | 1,494 | 3,589 |
| Milestone payments | 250 | — | 250 |
| Total collaboration revenue | \$309 | \$1,767 | \$15,573 |

Pursuant to the terms of our former collaborative development and license 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 a single unit of accounting. As such, the \$41.0 million upfront payment was recognized as revenue ratably over the expected period of research performance of pre-commercial activities, which was the three-year period from December 2012 through December 2015.

Pursuant to the terms of our March 2014 genetics collaborative agreement with Genentech, we received an upfront payment of \$1.5 million. We determined that the various deliverables under this agreement should be considered as a single unit of accounting. As such, the \$1.5 million upfront payment was recognized as revenue ratably over the expected period of research performance, which was the two-year period from March 2014 to March 2016. In September 2015, we received a \$0.25 million milestone payment for the identification of a novel pain target under this agreement which was recognized upon achievement in September 2015. In July 2017, we received a \$0.25 million milestone payment for the identification of a second novel pain target under this agreement which was recognized upon achievement in July 2017.

As our other internal and partnered products are in various stages of clinical and pre-clinical development, we do not expect to generate any revenue from product sales for at least the next several years. We expect that revenue for the next several years may be derived from 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.

As of December 31, 2017, we have recognized all deferred revenue from upfront payments received under our existing collaboration and licensing agreements.

Operating Expenses

The following table summarizes our operating expenses for the years ended December 31, 2017, 2016 and 2015 (in thousands):

| | Year Ended December 31, | | |
|----------------------------|-------------------------|----------|----------|
| | 2017 | 2016 | 2015 |
| Research and development | \$25,573 | \$19,828 | \$15,152 |
| General and administrative | 7,313 | 6,792 | 9,786 |
| Total operating expenses | \$32,886 | \$26,620 | \$24,938 |

Research and Development Expenses

Research and development expenses represent costs incurred to conduct research and development of our other proprietary product candidates, including any acquired or in-licensed product candidates or technology, as well as to support research and development on our product candidates under current and former collaboration agreements.

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

Project-specific expenses reflect costs directly attributable to our clinical development candidates and our pre-clinical candidates once nominated and selected for further development, including pre-clinical and discovery costs supporting a development candidate. All remaining research and development expenses are reflected in pre-clinical, discovery and other program expenses. 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 proprietary product candidates through clinical development, advance our internal drug discovery programs into pre-clinical 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, pre-clinical studies and clinical trial activities as well as third-party acquisition, 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 pre-clinical 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 at least the next 12 to 24 months.

General and Administrative Expenses

General and administrative expenses consist primarily of salary, related benefits and stock-based compensation of our executive, finance, legal, business development and administrative functions, travel expenses, allocated facility-related and information technology costs not otherwise included in research and development expenses, director compensation, director's and officer's insurance premiums, investor relations costs and professional fees for auditing, tax and legal services, including legal expenses for intellectual property protection. General and administrative expenses also include fair value adjustments of certain liability classified stock option awards.

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.

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 levels of cash and investment balances and low interest earned on such balances. We anticipate that our interest income will continue to fluctuate depending on timing of payments from collaborative partners, our cash and investment balances, and interest rates.

Foreign Exchange Gain (Loss). Net foreign exchange gains and losses consisted of gains and losses from the impact of foreign exchange fluctuations on our monetary assets and liabilities that are denominated in currencies other than the U.S. dollar (principally the Canadian dollar). We will continue to incur substantial expenses in Canadian dollars and will remain subject to risks associated with foreign currency fluctuations. See "Quantitative and Qualitative Disclosures About Market Risk – Foreign Currency Exchange Risk" below for additional information.

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 consolidated 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 consolidated 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.

The significant accounting policies that we believe to be most critical in fully understanding and evaluating our financial results are revenue recognition, research and development costs and stock-based compensation. See "Note 3" of the consolidated financial statements for additional information.

Revenue recognition:

Revenue recognition is a critical accounting estimate due to the magnitude and nature of the revenues we receive.

Our primary sources of revenue have been derived from non-refundable upfront payments, funding for research and development services, and milestone payments under various collaboration agreements. 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. Revenues associated with multiple element arrangements are attributed to the various elements based on their relative fair values or are recognized as a single unit of accounting when relative fair values are not determinable.

Non-refundable upfront payments are recorded as deferred revenue on 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 need to make estimates as to what period the services will be delivered as these payments are deferred and amortized into collaboration revenue over the estimated period of our ongoing involvement. The actual period of our ongoing involvement may differ from the estimated period determined at the time the payment is initially received and recorded as deferred revenue. This may result in a different amount of revenue that should have been recorded in the period and a longer or shorter period of revenue amortization. When an estimated period changes, we amortize the remaining deferred revenue over the estimated remaining time to completion.

We recognize funding related to full-time equivalent staffing funded through collaboration agreements as revenue on a gross basis as we perform or deliver such related services in accordance with the agreement terms, provided that we will receive payment for such services upon standard payment terms.

We recognize 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. Payments received upon the occurrence of milestones that are non-substantive are deferred and recognized as revenue over the estimated period of performance applicable to the associated collaborative agreement.

Research and development costs:

Research and development costs is a critical accounting estimate due to the magnitude of and the many assumptions that are required to calculate third-party accrued and prepaid research and development expenses.

We incur development activity costs, such as pre-clinical costs, manufacturing costs and clinical trial costs paid to contract research organizations, investigators and other vendors who conduct certain product development activities on our behalf. The amount of 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. We monitor these factors and adjust our estimates accordingly.

Stock-based compensation:

Stock-based compensation is a critical accounting estimate due to the magnitude of and the many assumptions that are required to calculate stock-based compensation expense.

We grant stock options to employees, directors and officers pursuant to our stock option plan. Compensation expense is recorded using the fair value method. We calculate the fair value of stock options using the Black-Scholes option-pricing model which requires that certain assumptions, including the expected life of the option and expected volatility of the stock, be estimated at the time that the options are granted.

Prior to our initial public offering, or IPO, our shares did not have a readily available market; therefore, we lack company-specific historical and implied volatility information. Consequently, we estimated the expected volatility of our stock options based on a combination of our available historical volatility information and a historical volatility analysis of peers that are similar with respect to industry, stage of development, size, and financial leverage. The expected term of our stock options has been determined utilizing our available historical data and we recognize forfeitures as they occur. We amortize the fair value of stock options using the straight-line method over the vesting period of the options.

Results of Operations

Comparison of Years Ended December 31, 2017 and 2016

The following table summarizes the results of our operations for the years ended December 31, 2017 and 2016 together with changes in those items (in thousands):

| | Year Ended December 31, | | Change |
|-------------------------------------|-------------------------|-------------|--------------------------------------|
| | 2017 | 2016 | 2017 vs. 2016 Increase/(Decrease) |
| Collaboration revenue | \$ 309 | \$ 1,767 | \$ (1,458) |
| Royalties | 2 | 36 | (34) |
| Research and development expenses | 25,573 | 19,828 | 5,745 |
| General and administrative expenses | 7,313 | 6,792 | 521 |
| Other: | | | |
| Interest income | 477 | 504 | (27) |
| Foreign exchange gain | 1,394 | 1,316 | 78 |
| Net loss | \$ (30,704) | \$ (22,997) | \$ (7,707) |

Revenue

We recognized revenue of \$0.3 million for the year ended December 31, 2017, compared to \$1.8 million for the year ended December 31, 2016, a decrease of \$1.5 million. In 2016, we recognized revenue related to the upfront payment from our March 2014 genetics collaborative agreement with Genentech, which was fully recognized by March 2016. The remaining decrease was mainly due to the expiration of our full-time equivalent, or FTE, funding from Genentech in late 2016 as we shifted resources from supporting our collaborations to our proprietary programs, partially offset by a \$0.25 million milestone payment recognized in July 2017 under the March 2014 genetics collaborative agreement with Genentech.

Research and Development Expenses

The following table summarizes research and development expenses for the years ended December 31, 2017 and 2016 together with changes in those items (in thousands):

| | Year Ended December 31, | | Change |
|---|-------------------------|-----------|--------------------------------------|
| | 2017 | 2016 | 2017 vs. 2016 Increase/(Decrease) |
| Collaboration expenses | \$ 120 | \$ 1,114 | \$ (994) |
| XEN801 expenses | 1,353 | 5,877 | (4,524) |
| XEN901 and Nav1.6 pre-clinical and discovery expenses | 10,157 | 9,559 | 598 |
| XEN1101 expenses | 5,885 | — | 5,885 |
| Pre-clinical, discovery and other program expenses | 8,058 | 3,278 | 4,780 |
| Total research and development expenses | \$ 25,573 | \$ 19,828 | \$ 5,745 |

Research and development expenses were \$25.6 million for the year ended December 31, 2017, compared to \$19.8 million for the year ended December 31, 2016. The increase of \$5.7 million was primarily attributable to spending on our XEN1101 product candidate which was acquired in April 2017 and increased spending on our pre-clinical, discovery and other internal programs as well as on our XEN901 product candidate. These increases were partially offset by a decrease in XEN801 expenses, a product candidate which is no longer being developed, and a decrease in collaboration expenses.

General and Administrative Expenses

The following table summarizes general and administrative expenses for the years ended December 31, 2017 and 2016 together with changes in those items (in thousands):

| | Year Ended December 31, | | Change |
|-------------------------------------|-------------------------|----------|--------------------------------------|
| | 2017 | 2016 | 2017 vs. 2016 Increase/(Decrease) |
| General and administrative expenses | \$ 7,313 | \$ 6,792 | \$ 521 |

General and administrative expenses were \$7.3 million for the year ended December 31, 2017, compared to \$6.8 million for the year ended December 31, 2016. The increase of \$0.5 million was primarily attributable to increased costs for business development activities and salaries and benefits.

Other Income

The following table summarizes our other income for the years ended December 31, 2017 and 2016 together with changes in those items (in thousands):

| | Year Ended December 31, | | Change |
|---------------|-------------------------|----------|--------------------------------------|
| | 2017 | 2016 | 2017 vs. 2016 Increase/(Decrease) |
| Other income: | \$ 1,871 | \$ 1,820 | \$ 51 |

Other income did not change significantly for the year ended December 31, 2017, as compared to the year ended December 31, 2016.

Comparison of Years Ended December 31, 2016 and 2015

The following table summarizes the results of our operations for the years ended December 31, 2016 and 2015 together with changes in those items (in thousands):

| | Year Ended December 31, | | Change |
|-------------------------------------|-------------------------|--------------|--------------------------------------|
| | 2016 | 2015 | 2016 vs. 2015 Increase/(Decrease) |
| Collaboration revenue | \$ 1,767 | \$ 15,573 | \$ (13,806) |
| Royalties | 36 | 4 | 32 |
| Research and development expenses | 19,828 | 15,152 | 4,676 |
| General and administrative expenses | 6,792 | 9,786 | (2,994) |
| Other: | | | |
| Interest income | 504 | 542 | (38) |
| Foreign exchange gain (loss) | 1,316 | (6,933) | 8,249 |
| Net income (loss) | \$ (22,997) | \$ (15,752) | \$ (7,245) |

Revenue

We recognized revenue of \$1.8 million for the year ended December 31, 2016, compared to \$15.6 million for the year ended December 31, 2015, a decrease of \$13.8 million. In 2015, we recognized revenues relating to the upfront payment from the former collaborative agreement with Teva which was fully recognized by December 2015 as well as revenue related to the upfront payment from our March 2014 collaborative agreement with Genentech which was fully recognized by March 2016. The remaining decrease was due to less FTE funding from Genentech as we shifted resources from supporting our collaborations to our proprietary programs.

Research and Development Expenses

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The following table summarizes research and development expenses for the years ended December 31, 2016 and 2015 together with changes in those items (in thousands):

| | Year Ended December 31, | | Change |
|---|-------------------------|-----------|--------------------------------------|
| | 2016 | 2015 | 2016 vs. 2015 Increase/(Decrease) |
| Collaboration expense | \$ 1,114 | \$ 2,762 | \$ (1,648) |
| XEN801 expenses | 5,877 | 4,446 | 1,431 |
| Pre-clinical and discovery program expenses | 12,837 | 7,944 | 4,893 |
| Total research and development expenses | \$ 19,828 | \$ 15,152 | \$ 4,676 |

65

Research and development expenses were \$19.8 million for the year ended December 31, 2016, compared to \$15.2 million for the year ended December 31, 2015. The increase of \$4.7 million was primarily attributable to increased spending on our pre-clinical and discovery programs, mostly related to our Nav1.6 sodium channel inhibitor program, as well as additional expenses for our XEN801 program which entered Phase 2 clinical development in February 2016, but which is no longer being developed. These increases were partially offset by a decrease in Genentech collaboration expenses.

General and Administrative Expenses

The following table summarizes general and administrative expenses for the years ended December 31, 2016 and 2015 together with changes in those items (in thousands):

| | Change | | |
|-------------------------------------|-------------------------|----------|---------------------|
| | Year Ended December 31, | | 2016 vs. 2015 |
| | 2016 | 2015 | Increase/(Decrease) |
| General and administrative expenses | \$ 6,792 | \$ 9,786 | \$ (2,994) |

General and administrative expenses were \$6.8 million for the year ended December 31, 2016, compared to \$9.8 million for the year ended December 31, 2015, a decrease of \$3.0 million. During 2015, we recognized a \$1.7 million expense due to a fair value adjustment upon the reclassification of stock option awards granted to directors and certain consultants to liability classification. The remaining change is due to one-time severance costs resulting from an internal reorganization and acceleration of stock-based compensation expense for certain consultants that occurred in 2015.

Other Income (Expense)

The following table summarizes our other income (expense) for the years ended December 31, 2016 and 2015 together with changes in those items (in thousands):

| | Change | | |
|-------------------------|-------------------------|-------------|---------------------|
| | Year Ended December 31, | | 2016 vs. 2015 |
| | 2016 | 2015 | Increase/(Decrease) |
| Other income (expense): | \$ 1,820 | \$ (6,391) | \$ 8,211 |

Other income was \$1.8 million for the year ended December 31, 2016, compared to other expense of \$6.4 million for the year ended December 31, 2015. The change of \$8.2 million was primarily driven by the change in foreign exchange gain (loss) arising largely from the translation of cash and cash equivalents and marketable securities denominated in Canadian dollars to U.S. dollars. We recorded a foreign exchange gain of \$1.3 million in 2016, compared to a \$6.9 million foreign exchange loss in 2015, largely due to a 3% increase as compared to a 16% decrease in the value of the Canadian dollar for the years ended December 31, 2016 and 2015, respectively.

Liquidity and Capital Resources

To date, we have financed our operations primarily through funding received from collaboration and license agreements, private placements of our common and preferred shares, public offerings of our common shares, debt

financing and government funding. As of December 31, 2017, we had cash and cash equivalents and marketable securities of \$43.7 million. In September 2016, we completed an underwritten public offering of 3,450,000 of our common shares at a public offering price of \$7.50 per common share. We received approximately \$24.3 million of proceeds, net of underwriting discounts and commissions but before offering expenses. In December 2017, we entered into a loan and security agreement with Silicon Valley Bank, or the Bank, for a term loan of up to \$15.0 million. The initial tranche of \$7.0 million was funded in December 2017. For additional information regarding our loan and security agreement with the Bank, see “—Contractual Obligations and Commitments—Term Loan” below.

We have incurred significant operating losses since inception. We had a \$30.7 million net loss for the year ended December 31, 2017 and an accumulated deficit of \$173.4 million from inception through December 31, 2017. We expect to continue to incur significant expenses in excess of our revenue 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 pre-clinical and clinical development of our product candidates; expand the scope of our current studies for our product candidates; initiate additional pre-clinical, clinical or other studies for our product candidates, including under our collaboration agreements; change or add manufacturers or suppliers; seek regulatory and marketing approvals for any of our product candidates that successfully complete clinical studies; seek to identify, evaluate and validate additional product candidates; acquire or in-license other product candidates and technologies; make milestone or other payments under our product acquisition and in-license agreements, including, without limitation, payments to the Memorial University of Newfoundland, or MUN, 1st Order Pharmaceuticals, Inc., or 1st Order, Valeant Pharmaceuticals International, Inc., or Valeant, and other third parties; 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 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 make milestone payments under our agreements with them and additional borrowings under our loan and security agreement that may become available upon achievement of certain clinical and financial milestones, we do 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:

- the number and characteristics of the future product candidates we pursue either from our internal research efforts or through acquiring or in-licensing other product candidates or technologies;
 - the scope, progress, results and costs of independently researching and developing any of our future product candidates, including conducting pre-clinical research and clinical trials;
 - whether our existing collaborations continue to generate substantial milestone payments and, ultimately, royalties on future approved products for us;
- the timing of, and the costs involved in, obtaining regulatory approvals for any future product candidates we develop independently;
- the timing and magnitude of potential milestone payments under our product acquisition and in-license agreements;
- the cost of commercializing any future products we develop independently that are approved for sale;
- the cost of manufacturing our future product candidates and products, if any;
- our ability to maintain existing collaborations and to establish new collaborations, licensing or other arrangements and the financial terms of such 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 of, or royalties on our collaborators' product candidates, and our future products, if any.

Based on our research and development plans and our timing expectations related to the progress of our programs, we expect that our existing cash and cash equivalents and marketable securities as of the date of this report will enable us to fund our operating expenses and capital expenditure requirements for at least the next 12 months. 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, 2017, 2016 and 2015 (in thousands):

| | Year Ended December 31, | | |
|---|-------------------------|------------|------------|
| | 2017 | 2016 | 2015 |
| Net cash used in operating activities | \$(28,726) | \$(19,567) | \$(18,103) |
| Net cash provided by (used in) investing activities | 24,294 | (47,842) | 10,194 |
| Net cash provided by financing activities | 7,070 | 23,964 | 278 |

Operating Activities

Net cash used in operating activities totaled \$28.7 million in 2017 as compared to \$19.6 million in 2016 and \$18.1 million in 2015. The increase in cash used in operating activities was primarily related to an increase in research and development expenses, a decrease in revenue, and changes in working capital. Cash used in operating activities in 2015 includes a \$3.2 million prepayment to Medpace, Inc., or Medpace, for future clinical development services.

Investing Activities

Net cash provided by investing activities totaled \$24.3 million in 2017 as compared to \$47.8 million used in 2016 and \$10.2 million provided in 2015. The change was driven by the maturity of marketable securities, net of purchases during 2017, as compared to the purchase of marketable securities in 2016 and the maturity of marketable securities during 2015.

Financing Activities

Net cash provided by financing activities totaled \$7.1 million in 2017 as compared to \$24.0 million in 2016 and \$0.3 million in 2015. In December 2017, we received net proceeds of \$6.9 million from the issuance of a term loan and in September 2016, we received net proceeds of \$23.8 million from the issuance of common shares in an underwritten public offering.

Contractual Obligations and Commitments

The following summarizes our significant contractual obligations as of December 31, 2017 (in thousands):

| Contractual Obligations | Total | Less Than | | More Than | |
|--------------------------------------|-----------------|----------------|----------------|----------------|-------------|
| | | 1 Year | 1 To 3 Years | 3 To 5 Years | 5 Years |
| Operating leases ⁽¹⁾ | \$5,122 | \$1,225 | \$2,456 | \$1,441 | \$ — |
| Term loan ⁽²⁾ | 7,000 | 700 | 5,600 | 700 | — |
| Total contractual obligations | \$12,122 | \$1,925 | \$8,056 | \$2,141 | \$ — |

(1) Represents future minimum lease payments under an operating lease in effect as of December 31, 2017 for our current facility in Burnaby, British Columbia, Canada.

(2) Excluding interest payments and final payment fee of 6.5% of the principal amount.

Term Loan

In December 2017, we entered into a Loan and Security Agreement, or Loan Agreement, with the Bank, pursuant to which the Bank agreed to extend term loans to us with an aggregate principal amount of up to \$15.0 million, in three tranches. We borrowed an initial tranche of \$7.0 million.

The second tranche of \$5.0 million, or the Second Tranche Advance, is available at our option at any time from the occurrence of the Tranche 2 Event through March 31, 2019. The third and final tranche of \$3.0 million, or the Third Tranche Advance, is available at our option at any time from the occurrence of the Tranche 3 Event through September 30, 2019. The Tranche 2 Event means delivery by us to the Bank of evidence that we have, on or before March 31, 2019, (i) obtained net new capital of at least \$12.5 million and (ii) at least two programs in clinical development, at least one of which is in Phase 2. The Tranche 3 Event means delivery by us to the Bank of evidence that we have, on or before September 30, 2019, achieved positive Phase 2 data on at least one program.

Borrowings under the Loan Agreement accrues interest at a floating per annum rate of 0.5% above the prime rate, which interest is payable monthly commencing in January 2018. The initial tranche is interest only until September 30, 2018, followed by 30 months of equal principal and interest payments, maturing on March 31, 2021. If the second tranche is advanced, then both the first and second tranches will be interest only until March 31, 2019, followed by 24 months of equal principal and interest payments, maturing on March 31, 2021. The third tranche, if advanced, will be interest only until September 30, 2019, followed by 24 months of equal principal and interest payments, maturing on September 30, 2021. In addition, we are required to pay a final payment fee of 6.5% of the principal amount extended on the date of repayment of the outstanding term loan.

We may prepay all, but not less than all, of the loaned amount subject to a prepayment fee of 3.0% of the outstanding principal if prepaid prior to the first anniversary of the effective date of the Loan Agreement, 2.0% if prepaid on or after the first anniversary, but prior to the second anniversary, or 1.0%, if prepaid on or after the second anniversary but prior to the applicable maturity date. As security for its obligations under the agreement, we granted the Bank a first priority security interest on substantially all of our assets except our intellectual property and subject to certain other exceptions.

The Loan Agreement contains customary representations and warranties, events of default (including an event of default upon the occurrence of a material impairment on the Bank's security interest over the collateral, and a material adverse change in our company) and affirmative and negative covenants, including, among others, covenants that limit or restrict our ability to incur indebtedness, grant liens, merge or consolidate, dispose of assets, make investments, make acquisitions, enter into certain transactions with affiliates, engage in any new line of business, pay dividends or make distributions, or repurchase stock, in each case subject to certain exceptions. Upon the occurrence and during the continuance of an event of default, a default interest rate will apply that is 5.0% above the otherwise applicable interest rate.

In connection with the Loan Agreement, we issued a warrant to the Bank to purchase 50,411 of our common shares at a price per share of \$2.43. The Bank will receive additional common shares exercisable pursuant to the warrant in connection with the second and third tranches, if and when advanced by the Bank. In no event will the number of common shares issuable pursuant to the exercise of the warrant exceed 108,023 in the aggregate. The warrant is immediately exercisable, has a 10-year term, and contains a cashless exercise provision.

The contractual obligations table above excludes the following material contractual commitments:

In August 2015, we entered into a priority access agreement with Medpace for the provision of certain clinical development services. Under the terms of the agreement, we committed to using Medpace non-exclusively for clinical development services over the five year term of the agreement. In consideration for priority access to Medpace resources and preferred service rates, we committed to \$7.0 million of services over the term of the agreement, \$1.7 million of which was prepaid upon signing of the agreement and an additional \$1.3 million was paid in December 2015. Any portion of the \$3.0 million payment made during 2015 that is not used within the first three years of the agreement term will be forfeited to Medpace. If we do not meet the commitment to retain Medpace for \$7.0 million of services during the term of the agreement, we agreed to give Medpace the exclusive right to perform all of our subsequent outsourced clinical development work until such \$7.0 million commitment has been satisfied, subject to the availability of appropriate Medpace resources and reasonable service rates. If we decide not to retain Medpace for the provision of clinical development services, we may satisfy our obligations under the priority access agreement by paying Medpace an amount equal to half of the unsatisfied portion of the \$7.0 million minimum commitment. See "Note 12(b)" and "Note 14" of the consolidated financial statements for additional information.

In March 2017, we entered into a license, manufacture and supply agreement with a pharmaceutical contract manufacturing organization for the access and use of certain regulatory documents as well as for the manufacture and

supply of clinical and commercial drug product to support the development of XEN007. Under the terms of the agreement, we paid an upfront fee of \$0.5 million CAD and will be required to pay a low single-digit percentage royalty on net sales of any products developed and commercialized under the agreement.

In April 2017, we acquired XEN1101 (previously known as 1OP2198) from 1st Order pursuant to an asset purchase agreement. 1st Order previously acquired 1OP2198 from an affiliate of Valeant, and we have assumed certain financial responsibilities under that agreement. Under the terms of the agreement, we paid an upfront fee of approximately \$0.4 million and milestone payments in 2017 totaling \$0.7 million, which we expensed as research and development. Future potential payments to both 1st Order and Valeant include \$1.0 million in clinical development milestones, up to \$13.0 million in regulatory milestones, and up to approximately \$33.6 million in sales-based and other milestones, which includes a \$1.5 million milestone that may be payable pre-commercially, plus a mid-to-high single-digit percentage royalty on commercial sales.

In July 2017, we entered into a license agreement with a pharmaceutical company for the access and use of certain regulatory documents to support the development of XEN007. Under the terms of the agreement, we paid an upfront fee of \$1.0 million, which we expensed as research and development. Future potential payments include \$2.0 million in clinical development milestones, up to \$7.0 million in regulatory milestones, plus a low-to-mid single-digit percentage royalty on net sales of any products developed and commercialized under the agreement.

Inflation

We do not believe that inflation has had a material effect on our business, financial condition or results of operations in the last three fiscal years.

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 Transactions, and Director Independence.”

Outstanding Share Data

As of March 2, 2018, we had 18,002,499 common shares issued and outstanding and outstanding stock options to purchase an additional 2,306,997 common shares.

Recent Accounting Pronouncements

In May 2014, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update, or ASU, 2014-09, Revenue from Contracts with Customers (ASC 606) to clarify the principles of recognizing revenue and to develop a common revenue standard that would remove inconsistencies in revenue requirements, leading to improved comparability of revenue recognition practices across entities and industries. The standard, as subsequently amended, stipulates that an entity should recognize revenue to depict the transfer of promised goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. The new guidance will be effective for public entities for fiscal years and interim periods within those years, beginning after December 15, 2017. We plan to adopt the standard under the modified retrospective approach on January 1, 2018 and have identified one ongoing significant collaboration agreement with respect to revenue, the collaborative research and license agreement with Genentech, described in “Note 14” of our consolidated financial statements. We have evaluated the new guidance and do not expect a material impact on the Company’s financial statements as a result of the application of the guidance on revenue previously recognized under this agreement.

In February 2016, the FASB issued ASU 2016-02, Leases (Topic 842): Recognition and Measurement of Financial Assets and Financial Liabilities. The update requires the recognition of lease assets and lease liabilities by lessees for those leases classified as operating leases under previous U.S. GAAP. The new guidance retains a distinction between finance leases and operating leases, with cash payments from operating leases classified within operating activities in the statement of cash flows. These amendments will be effective for public entities for fiscal years and interim periods within those years, beginning after December 15, 2018. We are currently evaluating the new guidance to determine the impact it will have on our consolidated financial statements.

Item 7A. Quantitative and Qualitative Disclosures 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

On January 1, 2015, our functional currency changed from the Canadian dollar to the U.S. dollar based on our analysis of the changes in the primary economic environment in which we operate.

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 U.S. dollars, particularly those denominated in Canadian dollars. We also hold non-U.S. dollar denominated cash and cash equivalents, marketable securities, accounts receivable and accounts payable, which are denominated in Canadian dollars.

Changes in foreign currency exchange rates can create significant foreign exchange gains or losses to us. Our current foreign currency risk is with the Canadian dollar, as a majority of our non-U.S. dollar denominated expenses are denominated in Canadian dollars and a significant portion of our cash and cash equivalents and marketable securities are held in Canadian dollars. To limit our exposure to volatility in currency markets, we estimate our anticipated expenses that will be denominated in Canadian and U.S. dollars and then purchase a corresponding amount of Canadian or U.S. dollars 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 Canadian dollars held. At December 31, 2017, we held cash and cash equivalents and marketable securities of \$15.6 million denominated in Canadian dollars. A hypothetical 10% increase (decrease) in the value of the Canadian dollar would result in a foreign exchange gain (loss) of \$1.6 million being recorded in the Statement of Operations and Comprehensive Income (Loss) on the translation of these Canadian dollar cash and cash equivalent and marketable securities balances into the U.S. dollar functional currency.

Interest Rate Risk

An additional market risk we face is interest rate risk. We had cash and cash equivalents and marketable securities of \$43.7 million as of December 31, 2017. 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 and marketable securities.

In addition, we had an outstanding balance of \$7.0 million under our Loan Agreement as of December 31, 2017, of which \$0.7 million was due within 12 months. The interest rate on borrowings under the Loan Agreement with the Bank accrues at a floating per annum rate of 0.5% above the prime rate. A 10% change in interest rates during any of the periods presented would not have had a material impact on our consolidated financial statements.

Item 8. Financial Statements and Supplementary Data
XENON PHARMACEUTICALS INC.

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Year ended December 31, 2017

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Report of Independent Registered Public Accounting Firm

To the Stockholders and Board of Directors
Xenon Pharmaceuticals Inc.:

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Xenon Pharmaceuticals Inc. (the Company) as of December 31, 2017 and 2016, the related consolidated statements of operations and comprehensive loss, shareholders' equity, and cash flows for each of the years in the three year period ended December 31, 2017, and the related notes (collectively, the consolidated financial statements). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2017 and 2016, and the results of its operations and its cash flows for each of the years in the three year period ended December 31, 2017, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these consolidated financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB and in accordance with the ethical requirements that are relevant to our audit of the financial statements in Canada.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits, we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ KPMG LLP

Chartered Professional Accountants

We have served as the Company's auditor since 1999

Vancouver, British Columbia
March 7, 2018

XENON PHARMACEUTICALS INC.

Consolidated Balance Sheets

(Expressed in thousands of U.S. dollars except share amounts)

| | December 31, 2017 | December 31, 2016 |
|--|-------------------------|-------------------------|
| Assets | | |
| Current assets: | | |
| Cash and cash equivalents | \$20,486 | \$17,095 |
| Marketable securities | 23,181 | 47,051 |
| Accounts receivable | 438 | 200 |
| Prepaid expenses and other current assets | 716 | 1,329 |
| | 44,821 | 65,675 |
| Prepaid expenses, long-term | 230 | 408 |
| Property, plant and equipment, net (note 6) | 1,070 | 1,404 |
| Total assets | \$46,121 | \$67,487 |
| Liabilities and shareholders' equity | | |
| Current liabilities: | | |
| Accounts payable and accrued expenses (note 7) | 3,383 | 3,586 |
| Loan payable, current portion (note 8) | 700 | — |
| | 4,083 | 3,586 |
| Loan payable, long-term (note 8) | 6,104 | — |
| | \$10,187 | \$3,586 |
| Shareholders' equity: | | |
| Common shares, without par value; unlimited shares authorized; issued and | | |
| outstanding: 17,998,420 (December 31, 2016 - 17,930,590) (note 9b) | 173,841 | 173,246 |
| Additional paid-in capital | 36,471 | 34,326 |
| Accumulated deficit | (173,388) | (142,681) |
| Accumulated other comprehensive loss | (990) | (990) |
| | \$35,934 | \$63,901 |
| Total liabilities and shareholders' equity | \$46,121 | \$67,487 |
| Collaboration agreements (note 11) | | |
| Commitments and contingencies (note 12) | | |
| Subsequent event (note 16) | | |

The accompanying notes are an integral part of these consolidated financial statements.

XENON PHARMACEUTICALS INC.

Consolidated Statements of Operations and Comprehensive Loss

(Expressed in thousands of U.S. dollars except share and per share amounts)

| | Year Ended December 31, | | |
|---|-------------------------|------------|------------|
| | 2017 | 2016 | 2015 |
| Revenue: | | | |
| Collaboration revenue (note 11) | \$ 309 | \$ 1,767 | \$ 15,573 |
| Royalties | 2 | 36 | 4 |
| | 311 | 1,803 | 15,577 |
| Operating expenses: | | | |
| Research and development | 25,573 | 19,828 | 15,152 |
| General and administrative | 7,313 | 6,792 | 9,786 |
| | 32,886 | 26,620 | 24,938 |
| Loss from operations | (32,575) | (24,817) | (9,361) |
| Other income (expense): | | | |
| Interest income | 477 | 504 | 542 |
| Foreign exchange gain (loss) | 1,394 | 1,316 | (6,933) |
| Net loss and comprehensive loss | (30,704) | (22,997) | (15,752) |
| Net loss per common share (note 5): | | | |
| Basic | \$(1.71) | \$(1.48) | \$(1.10) |
| Diluted | \$(1.72) | \$(1.48) | \$(1.10) |
| Weighted-average common shares outstanding (note 5): | | | |
| Basic | 17,985,061 | 15,493,474 | 14,281,837 |
| Diluted | 18,001,759 | 15,493,474 | 14,281,837 |

The accompanying notes are an integral part of these consolidated financial statements.

XENON pharmaceuticals INC.

Consolidated Statement of Shareholders' Equity

(Expressed in thousands of U.S. dollars except share amounts)

| | Common shares Shares | Amount | Additional paid-in capital | Accumulated deficit | Accumulated other comprehensive income (loss) ⁽¹⁾ | Total shareholders' equity |
|--|-------------------------|-----------|-------------------------------|---------------------|--|-------------------------------|
| Balance as of December 31, | | | | | | |
| 2014 | 14,181,333 | \$147,157 | \$ 30,346 | \$ (103,734) | \$ (990) | \$ 72,779 |
| Net loss for the year | | | | (15,752) | | (15,752) |
| Stock-based compensation expense | | | 2,077 | | | 2,077 |
| Issued pursuant to exercise of stock options | 204,003 | 1,477 | (992) | (207) | | 278 |
| Fair value adjustment upon reclassification of stock options (note 31) | | | 1,652 | | | 1,652 |
| Balance as of December 31, | | | | | | |
| 2015 | 14,385,336 | \$148,634 | \$ 33,083 | \$ (119,693) | \$ (990) | \$ 61,034 |
| Net loss for the year | | | | (22,997) | | (22,997) |
| Issuance of common shares, net of issuance costs | 3,450,000 | 23,832 | | | | 23,832 |
| Stock-based compensation | | | 2,186 | | | 2,186 |

| | | | | | | |
|--------------------------------|------------|------------|-----------|-------------|----|---------|
| expense | | | | | | |
| Issued pursuant to exercise of | | | | | | |
| stock options | 95,254 | 780 | (657 |) | 9 | 132 |
| Fair value adjustment upon | | | | | | |
| reclassification of stock | | | | | | |
| options (note 31) | | | (286 |) | | (286 |
| Balance as of December 31, | | | | | | |
| 2016 | 17,930,590 | \$ 173,246 | \$ 34,326 | \$ (142,681 |) | \$ (990 |
| Net loss for the year | | | | (30,704 |) | (30,704 |
| Stock-based compensation | | | | | | |
| expense | | | 2,460 | | | 2,460 |
| Issued pursuant to exercise of | | | | | | |
| stock options | 67,830 | 595 | (415 |) | (3 |) |
| Issuance of warrants | | | 100 | | | 100 |
| Balance as of December 31, | | | | | | |
| 2017 | 17,998,420 | \$ 173,841 | \$ 36,471 | \$ (173,388 |) | \$ (990 |

(1)December 31, 2017, our accumulated other comprehensive loss is entirely related to historical cumulative translation adjustments from the application of U.S. dollar reporting when the functional currency of the Company was the Canadian dollar as described in note 3m.

The accompanying notes are an integral part of these consolidated financial statements.

XENON PHARMACEUTICALS INC.

Consolidated Statements of Cash Flows

(Expressed in thousands of U.S. dollars)

| | Year Ended December 31, | | |
|---|-------------------------|------------|------------|
| | 2017 | 2016 | 2015 |
| Operating activities: | | | |
| Net loss | \$(30,704) | \$(22,997) | \$(15,752) |
| Items not involving cash: | | | |
| Depreciation | 649 | 864 | 1,038 |
| Amortization of discount on term loan | 11 | — | — |
| Stock-based compensation | 2,236 | 2,161 | 3,729 |
| Unrealized foreign exchange (gain) loss | (1,474) | (1,300) | 6,902 |
| Changes in operating assets and liabilities: | | | |
| Accounts receivable | (232) | 121 | (107) |
| Prepaid expenses, and other current assets | 613 | 571 | (1,214) |
| Prepaid expenses, long term | 178 | 686 | (1,094) |
| Accounts payable and accrued expenses | (3) | 484 | 17 |
| Deferred revenue | — | (157) | (11,622) |
| Net cash used in operating activities | (28,726) | (19,567) | (18,103) |
| Investing activities: | | | |
| Purchases of property, plant and equipment | (315) | (279) | (551) |
| Purchase of marketable securities | (28,007) | (47,563) | — |
| Proceeds from marketable securities | 52,616 | — | 10,745 |
| Net cash provided by (used in) investing activities | 24,294 | (47,842) | 10,194 |
| Financing activities: | | | |
| Proceeds from issuance of term loan, net of issuance costs (note 8) | 6,893 | — | — |
| Issuance of common shares pursuant to exercise of stock options | 177 | 132 | 278 |
| Issuance of common shares, net of issuance costs (note 9a) | — | 23,832 | — |
| Net cash provided by financing activities | 7,070 | 23,964 | 278 |
| Effect of exchange rate changes on cash and cash equivalents | 753 | 1,889 | (5,744) |
| Increase (decrease) in cash and cash equivalents | 3,391 | (41,556) | (13,375) |
| Cash and cash equivalents, beginning of year | 17,095 | 58,651 | 72,026 |
| Cash and cash equivalents, end of year | \$20,486 | \$17,095 | \$58,651 |
| Supplemental disclosures: | | | |
| Interest received | \$740 | \$341 | \$659 |
| Supplemental disclosures of non-cash transactions: | | | |
| Fair value of options exercised on a cashless basis | 25 | 404 | 744 |

The accompanying notes are an integral part of these consolidated financial statements.

XENON PHARMACEUTICALS INC.

Notes to Consolidated Financial Statements

(Expressed in thousands of U.S. dollars except share and per share amounts)

1. Nature of the business:

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 clinical stage biopharmaceutical company focused on developing innovative therapeutics to improve the lives of patients with neurological disorders. Building upon its extensive knowledge of human genetics and diseases caused by mutations in ion channels, known as channelopathies, the Company is advancing a novel product pipeline of central nervous system therapies to address areas of high unmet medical need, such as epilepsy and pain.

The Company has incurred significant operating losses since inception. As of December 31, 2017, the Company had an accumulated deficit of \$173,388 and a \$30,704 net loss for the year ended December 31, 2017. Management expects to continue to incur significant expenses in excess of revenue and to incur operating losses for the foreseeable future. To date, the Company has financed its operations primarily through funding received from collaboration and license agreements, private placements of common and preferred shares, public offerings of common shares, debt financing, and government funding.

Until such time as the Company can generate substantial product revenue, if ever, management expects to finance the Company’s cash needs through a combination of collaboration agreements and equity or debt financings. The continuation of the research and development activities and the future commercialization of its products are dependent on the Company’s ability to successfully raise additional funds when needed. It is not possible to predict either the outcome of future research and development programs or the Company’s ability to continue to fund these programs in the future.

2. Basis of presentation:

These consolidated financial statements are presented in U.S. dollars.

The accompanying audited consolidated financial statements of the Company have been prepared in accordance with United States generally accepted accounting principles (“U.S. GAAP”).

The Company has one wholly-owned subsidiary as at December 31, 2017, Xenon Pharmaceuticals USA Inc., which was incorporated in Delaware on December 2, 2016.

These consolidated financial statements include the accounts of the Company and its wholly-owned subsidiary. All intercompany transactions and balances have been eliminated on consolidation.

3. Significant accounting policies:

(a) Use of estimates:

The preparation of the consolidated financial statements in conformity with U.S. GAAP requires management 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 timing of revenue recognition, the determination of stock-based compensation and the amounts recorded as accrued 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. Cash equivalents are recorded at cost plus accrued interest. The carrying value of these cash equivalents approximates their fair value.

(c) Marketable securities:

Marketable securities are investments with original maturities exceeding three months, and have remaining maturities of less than one year. Marketable securities accrue interest based on a fixed interest rate for the term. The carrying value of marketable securities is recorded at cost plus accrued interest, which approximates their fair value.

(d) Intellectual Property

The costs incurred in establishing and maintaining patents for intellectual property developed internally are expensed in the period incurred.

(e) Property, plant and equipment:

Property, plant and equipment are stated at cost less accumulated depreciation and/or accumulated impairment losses, if any. Repairs and maintenance costs are expensed in the period incurred.

Property, plant and equipment are amortized over their estimated useful lives using the straight-line method based on the following rates:

| Asset | Rate |
|--------------------------------|--|
| 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 |

(f) 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. No impairment of long-lived assets was noted during the years ended December 31, 2017 and 2016.

(g) Concentration of credit risk and of significant customers:

Financial instruments that potentially subject the Company to significant concentrations of credit risk consist primarily of cash and cash equivalents. Cash and cash equivalents were held at major financial institutions in Canada and the United States. Such deposits may be in excess of insured limits in the event of non-performance by the institutions; however, the Company does not anticipate non-performance.

Collaborators whose collaboration research and development revenue accounted for 10% or more of total revenues were as follows:

| | Year ended December 31, | | |
|-----------|-------------------------|---------|---------|
| | 2017 | 2016 | 2015 |
| Genentech | \$250 | \$1,651 | \$4,563 |
| Teva | 59 | 116 | 11,010 |

(h) Financial instruments and fair value:

We measure certain financial instruments and other items at fair value.

To determine the fair value, we use the fair value hierarchy for inputs 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).

Level 1 - Unadjusted quoted prices in active markets for identical instruments.

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 or 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).

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.

Assets and liabilities are classified based on the lowest level of input that is significant to the fair value measurements. Changes in the observability of valuation inputs may result in a reclassification of levels for certain securities within the fair value hierarchy.

The Company's Level 1 assets include cash and cash equivalents and marketable securities with quoted prices in active markets. The carrying amount of accounts receivables, accounts payable and accrued expenses approximates fair value due to the nature and short-term of those instruments. As quoted prices for the liability classified stock options, included in the consolidated balance sheet as accounts payable and accrued expenses, are not readily available, the Company has used a Black-Scholes pricing model to estimate fair value using Level 3 inputs as defined above. The Company's term loan, which was finalized in December 2017, bears interest at a rate that approximates prevailing market rates for instruments with similar characteristics and, accordingly, the carrying value of the loan approximates fair value.

(i) 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. Revenues associated with multiple element arrangements are attributed to the various elements based on their relative fair values or are recognized as a single unit of accounting when relative fair values are not determinable.

Non-refundable upfront payments are recorded as deferred revenue on 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.

The Company recognizes 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. Payments received upon the occurrence of milestones that are non-substantive are deferred and recognized as revenue over the estimated period of performance applicable to the associated collaborative agreement.

(j) Research and development costs:

Research and development costs are expensed in the period incurred.

Certain development activity costs, such as pre-clinical costs, manufacturing costs and clinical trial costs, 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 expenses recognized in a period related to service agreements is based on estimates of the work performed using the 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. Payments made to third parties under these arrangements in advance of the receipt of the related services are recorded as prepaid expenses until the services are rendered.

(k) Stock-based compensation:

The Company grants stock options to employees, directors and officers pursuant to a stock option plan described in note 9c.

Employee stock-based compensation expense is measured at the grant date, based on the estimated fair value of the award, and is recognized as an expense, net of actual forfeitures, over the requisite service period with a corresponding increase in additional paid-in capital. Stock-based compensation expense is amortized on a straight-line basis over the requisite service period for the entire award, which is generally the vesting period of the award. Any consideration received on exercise of stock options is credited to share capital.

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(l) Liability classified stock options:

Stock option awards accounted for under Accounting Standards Codification (“ASC”) 718 - Compensation - Stock Options (“ASC 718”) that provide for an exercise price that is not denominated in: (a) the currency of the market in which a substantial portion of the Company’s equity securities trade, (b) the currency in which the optionee’s pay is denominated, or (c) the Company’s functional currency, are classified as liabilities. Following the change in functional currency on January 1, 2015, described in (m) below, options granted to members of the Company’s board of directors and certain consultants with exercise prices denominated in Canadian dollars were subject to liability accounting, resulting in a reclassification of these awards from additional paid-in capital to liability classified stock options.

In September 2015, the Company modified certain compensation arrangements to be denominated in Canadian dollars. Following this modification, options denominated in Canadian dollars that were granted to members of the Company’s board of directors and certain consultants met the criteria for equity classification with fair value at the modification date calculated using the Black-Scholes option-pricing model and reclassified from liability classified stock options back to additional paid-in capital. The modified awards are accounted for as equity awards from the date of modification.

Stock options awards accounted for under ASC 815 - Derivatives and Hedging (“ASC 815”), that provide for an exercise price which is not denominated in the Company’s functional currency are required to be classified as liabilities. Certain stock option awards with exercise prices denominated in Canadian dollars are accounted for under ASC 815 and classified as liabilities. As of December 31, 2017, such liability classified stock options totaled \$37 (2016 – \$261) and are included in the consolidated balance sheet as accounts payable and accrued expenses.

Liability classified stock options are re-measured at fair value using the Black-Scholes option-pricing model at each balance sheet date until exercised or cancelled, with changes in fair value recognized as additional paid-in capital for ASC 718 awards or general and administrative stock-based compensation expense for ASC 815 awards for the period. The Black-Scholes option pricing model uses various inputs to measure fair value, including fair value of the Company’s underlying common shares at the grant date, expected term, expected volatility, risk-free interest rate and expected dividend yield of the Company’s common shares.

(m) Foreign currency translation:

The Company’s functional and reporting currency is the U.S. dollar. The functional currency of the Company changed to U.S. dollars from Canadian dollars on January 1, 2015 based on management’s analysis of the changes in the primary economic environment in which the Company operates. The Company’s reporting currency did not change. The change in functional currency is accounted for prospectively from January 1, 2015.

For periods commencing January 1, 2015, monetary assets and liabilities denominated in foreign currencies are translated into U.S. dollars using exchange rates in effect at the balance sheet date. Opening balances related to non-monetary assets and liabilities are based on prior period translated amounts, and nonmonetary assets and nonmonetary liabilities incurred after January 1, 2015 are translated at the approximate exchange rate prevailing at the date of the transaction. Revenue and expense transactions are translated at the approximate exchange rate in effect at the time of the transaction. Foreign exchange gains and losses are included in the consolidated statement of operations and comprehensive income (loss) as foreign exchange gain (loss).

(n) Income taxes:

Deferred income taxes are recognized for the future tax consequences attributable to differences between the carrying amounts of assets and liabilities and their respective tax bases and net operating loss and credit carryforwards. Deferred income tax assets and liabilities are measured at enacted 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 income tax assets and liabilities of a change in tax rates is recognized in the consolidated statement of

operations and comprehensive income (loss) in the period that includes the enactment date. A valuation allowance is provided when realization of deferred income tax assets does not meet the more-likely-than-not criterion for recognition.

(o) Deferred tenant inducements:

Deferred tenant inducements, which include leasehold improvements paid for by the landlord and free rent, are included in the consolidated balance sheet as accounts payable and accrued expenses and recognized as a reduction of rent expense on a straight-line basis over the term of the lease.

(p) 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.

(q) Comparative figures:

Certain comparative figures have been reclassified to conform to the consolidated financial statement presentation adopted for the current year.

4. Future changes in accounting policies:

In May 2014, the Financial Accounting Standards Board (“FASB”) issued Accounting Standards Update (“ASU”) 2014-09, Revenue from Contracts with Customers (ASC 606) to clarify the principles of recognizing revenue and to develop a common revenue standard that would remove inconsistencies in revenue requirements, leading to improved comparability of revenue recognition practices across entities and industries. The standard, as subsequently amended, stipulates that an entity should recognize revenue to depict the transfer of promised goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. The new guidance will be effective for public entities for fiscal years and interim periods within those years, beginning after December 15, 2017. The Company plans to adopt the standard under the modified retrospective approach on January 1, 2018 and has identified one ongoing significant collaboration agreement with respect to revenue, the collaborative research and license agreement with Genentech, a member of the Roche Group, described in note 11b. The Company has evaluated the new guidance and does not expect a material impact on the Company’s financial statements as a result of the application of the guidance on revenue previously recognized under this agreement. In addition, application of the new guidance is also not expected to result in a material change in the amount or timing of revenues recognized, as compared to prior practice, as it relates to the milestone and royalty payments the Company is eligible to receive in future periods under this agreement.

In February 2016, the FASB issued ASU 2016-02, Leases (Topic 842): Recognition and Measurement of Financial Assets and Financial Liabilities. The update requires the recognition of lease assets and lease liabilities by lessees for those leases classified as operating leases under previous U.S. GAAP. The new guidance retains a distinction between finance leases and operating leases, with cash payments from operating leases classified within operating activities in the statement of cash flows. These amendments will be effective for public entities for fiscal years and interim periods within those years, beginning after December 15, 2018. The Company is currently evaluating the new guidance to determine the impact it will have on the Company’s consolidated financial statements.

5. Net income (loss) per common share:

Basic net income (loss) per common share is computed by dividing the net income (loss) by the weighted average number of common shares outstanding for the period. Diluted net income (loss) per common share is computed by adjusting the numerator and denominator of the basic net income (loss) per share calculation for the potential impact of dilutive securities.

For the year ended December 31, 2017, 2,172,034 stock options and warrants were excluded from the calculation of diluted net income per common share as their inclusion would be anti-dilutive. For the years ended December 31, 2016 and December 31, 2015, all stock options were anti-dilutive and were excluded from the diluted weighted average common shares outstanding for those periods.

The following is a reconciliation of the numerators and denominators of basic and diluted net loss per common share:

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| | Year Ended December 31, | | |
|---|-------------------------|-------------|-------------|
| | 2017 | 2016 | 2015 |
| Numerator: | | | |
| Net loss used to compute net loss per common share: | | | |
| Basic | \$(30,704) | \$(22,997) | \$(15,752) |
| Adjustment for change in fair value of liability classified stock options | (187) | — | — |
| Diluted | \$(30,891) | \$(22,997) | \$(15,752) |
| Denominator: | | | |
| Weighted average number of common shares: | | | |
| Basic | 17,985,061 | 15,493,474 | 14,281,837 |
| Adjustment for dilutive effect of stock options | 16,698 | — | — |
| Diluted | 18,001,759 | 15,493,474 | 14,281,837 |
| Net loss per common share - basic | \$(1.71) | \$(1.48) | \$(1.10) |
| Net loss per common share - diluted | \$(1.72) | \$(1.48) | \$(1.10) |

6. Property, plant and equipment:

Property, plant and equipment consisted of the following:

| | December 31, | |
|---|--------------|----------|
| | 2017 | 2016 |
| Research equipment | \$6,984 | \$6,789 |
| Office furniture and equipment | 1,043 | 1,045 |
| Computer equipment | 2,311 | 2,283 |
| Leasehold improvements | 6,370 | 6,370 |
| Less: accumulated depreciation and amortization | (15,638) | (15,083) |
| Net book value | \$1,070 | \$1,404 |

7. Accounts payable and accrued expenses:

Accounts payable and accrued expenses consisted of the following:

| | December 31, | |
|---|--------------|---------|
| | 2017 | 2016 |
| Trade payables | \$1,253 | \$1,463 |
| Employee compensation, benefits, and related accruals | 1,017 | 872 |
| Consulting and contracted research | 817 | 1,029 |
| Professional fees | 252 | 93 |
| Other | 44 | 129 |
| Total | \$3,383 | \$3,586 |

8. Term Loan:

On December 18, 2017, the Company entered into a Loan and Security Agreement (the "Loan Agreement") with Silicon Valley Bank (the "Bank"), pursuant to which the Bank agreed to extend term loans to the Company with an aggregate principal amount of up to \$15,000, in three tranches (the "Term Loans"). The Company borrowed an initial tranche of \$7,000, with the remaining \$8,000 available to be drawn in two separate tranches, at the Company's option, subject to the achievement of certain clinical and financial milestones.

The Loan Agreement accrues interest at a floating per annum rate of 0.5% above the prime rate, and is payable monthly commencing in January 2018. The initial tranche is interest only until September 30, 2018, followed by 30 months of equal principal and interest payments, maturing on March 31, 2021. If the second tranche is advanced, then both the first and second tranches will be interest only until March 31, 2019, followed by 24 months of equal principal and interest payments, maturing on March 31, 2021. The third tranche, if advanced, will be interest only until September 30, 2019, followed by 24 months of equal principal and interest payments, maturing on September 30, 2021. In addition, the Company is required to pay a final payment fee of 6.5% of the principal amount extended on the date of repayment of the Term Loans, which is being accreted and amortized into interest expense using the effective

interest rate method over the term of the loan.

The Company may prepay all, but not less than all, of the loaned amount subject to a prepayment fee of 3.0% of the outstanding principal if prepaid prior to the first anniversary of the effective date of the Loan Agreement, 2.0% if prepaid on or after the first anniversary, but prior to the second anniversary, or 1.0%, if prepaid on or after the second anniversary but prior to the applicable maturity date. As security for its obligations under the Loan Agreement, the Company granted the Bank a first priority security interest on substantially all of the Company's assets except its intellectual property and subject to certain other exceptions.

The Loan Agreement contains customary representations and warranties, events of default (including an event of default upon the occurrence of a material impairment on the Bank's security interest over the collateral, and a material adverse change of the Company) and affirmative and negative covenants, including, among others, covenants that limit or restrict the Company's ability to incur indebtedness, grant liens, merge or consolidate, dispose of assets, make investments, make acquisitions, enter into certain transactions with affiliates, engage in any new line of business, pay dividends or make distributions, or repurchase stock, in each case subject to certain exceptions. Upon the occurrence and during the continuance of an event of default, a default interest rate will apply that is 5.0% above the otherwise applicable interest rate.

In connection with the Loan Agreement, the Company issued a warrant to the Bank to purchase 50,411 of the Company's common shares at a price per share of \$2.43. The Bank will receive additional common shares exercisable pursuant to the warrant in connection with the second and third tranches, if and when advanced by the Bank. In no event will the number of common shares issuable pursuant to the exercise of the warrant exceed 108,023 in the aggregate. The warrant is immediately exercisable, has a 10-year term, contains a cashless exercise provision, and is classified in equity. The relative fair value of the warrant was \$100.

The initial tranche proceeds of \$7,000 were allocated based on the relative fair values of the debt instrument and the warrant instrument. The fair value of the warrant and the closing costs were recorded as debt discounts and are being amortized using the effective interest rate method over the term of the loan. The Company determined the effective interest rate on the initial tranche of the loan to be 9.25%. Amortization of the debt discount was \$11 for the year ended December 31, 2017.

Interest expense was \$24 for the year ended December 31, 2017.

The outstanding loan and unamortized debt discount balances are as follows:

| | December 31, 2017 |
|--------------------------------------|-------------------------|
| Term loan | \$ 7,000 |
| Less: unamortized discount on loan | (203) |
| Less: current portion | (700) |
| Accrued portion of final payment fee | 7 |
| Loan payable, long-term | \$ 6,104 |

Scheduled principal payments on outstanding debt, excluding the final payment fee of \$455, as of December 31, 2017, are as follows:

| | |
|-------|---------|
| 2018 | \$700 |
| 2019 | 2,800 |
| 2020 | 2,800 |
| 2021 | 700 |
| Total | \$7,000 |

9. Share capital:

(a) Financing:

On September 13, 2016, the Company completed an underwritten public offering of 3,450,000 of its common shares at a public offering price of \$7.50 per common share. The Company received approximately \$24.3 million of proceeds, net of underwriting discounts and commissions but before offering expenses.

(b) Authorized share capital:

The Company's authorized share capital consists of an unlimited number of common and preferred shares without par value.

(c) Stock-based compensation:

On June 25, 2014, the shareholders of the Company approved the 2014 Equity Incentive Plan (the “2014 Plan”) which permits the grant of stock-based compensation awards to directors, officers, employees and consultants of the Company. The Company’s pre-existing stock option plan (the “Amended and Restated Stock Option Plan”) was limited to the granting of stock options as equity incentive awards whereas the 2014 Plan also allows for the issuance of restricted shares, restricted share units, share appreciation rights and performance shares. The 2014 Plan replaced the Amended and Restated Stock Option Plan. No further options will be granted under the Company’s Amended and Restated Stock Option Plan.

The Amended and Restated Stock Option Plan provided for the grant of options for the purchase of common shares to directors, officers, employees and consultants prior to the Company’s initial public offering (“IPO”). The options granted under the Amended and Restated Stock Option Plan vest on a graduated basis over a four-year period or less and each option’s maximum term is ten years. The Amended and Restated Stock Option Plan will continue to govern the options granted thereunder.

Under the 2014 Plan, options granted generally vest on a graduated basis over a four-year period or less. The exercise price of the options is determined by the Board but must at least be equal to the fair market value of the common shares on the date of grant. Options may be exercised over a maximum term of ten years. As of December 31, 2017, a total of 30,847 stock options remain to be granted under the 2014 Plan. The number of common shares available for issuance under the 2014 Plan was increased by 700,000 in January 2018 as approved by the Board in accordance with the terms of the 2014 Plan.

Summary of stock option activity is as follows:

| | Number of Options | Weighted Average CAD \$ | Weighted Average U.S. \$ | Exercise Price | Aggregate Intrinsic Value |
|---------------------------------|----------------------|----------------------------|-----------------------------|----------------|------------------------------|
| Outstanding, January 1, 2015 | 1,484,218 | 4.88 | 4.20 | | 15,551 |
| Granted | 529,288 | 18.73 | 14.67 | | |
| Exercised | (270,254) | 4.66 | 3.65 | | 2,426 |
| Forfeited, cancelled or expired | (21,780) | 11.21 | 8.78 | | |
| Outstanding, December 31, 2015 | 1,721,472 | 9.62 | 6.95 | | 1,880 |
| Granted | 323,794 | 9.79 | 7.39 | | |
| Exercised | (121,292) | 3.67 | 2.77 | | 568 |
| Forfeited, cancelled or expired | (13,151) | 14.98 | 11.31 | | |
| Outstanding, December 31, 2016 | 1,910,823 | 9.84 | 7.32 | | 4,464 |
| Granted | 620,950 | 8.69 | 6.69 | | |
| Exercised ⁽¹⁾ | (71,006) | 3.72 | 2.86 | | 108 |
| Forfeited, cancelled or expired | (120,862) | 9.06 | 6.98 | | |
| Outstanding, December 31, 2017 | 2,339,905 | 9.32 | 7.41 | | 159 |
| Exercisable, December 31, 2017 | 1,439,301 | 8.91 | 7.08 | | 159 |

(1) During the year ended December 31, 2017, 63,425 (2016 – 47,413) stock options were exercised for the same number of common shares in exchange for cash. In the same period, the Company issued 4,405 (2016 – 47,841) common shares for the cashless exercise of 7,581 (2016 – 73,879) stock options.

The following table summarizes the stock options outstanding and exercisable at December 31, 2017:

| Range of Exercise Prices | Options Outstanding | | Options Exercisable | |
|--------------------------|----------------------|---|----------------------|------------------------------------|
| | Number of Options | Weighted Average Contractual Life | Number of Options | Weighted Average Exercise Price |
| | | | | |

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| U.S. \$ | | (years) | CAD \$ | U.S. \$ | | CAD \$ | U.S. \$ |
|-------------------|-----------|---------|--------|---------|-----------|--------|---------|
| \$2.12 - \$2.95 | 227,725 | 5.05 | 2.67 | 2.13 | 226,675 | 2.67 | 2.12 |
| \$2.96 - \$3.04 | 514,021 | 2.22 | 3.74 | 2.97 | 514,021 | 3.74 | 2.97 |
| \$3.05 - \$7.44 | 273,400 | 9.36 | 5.25 | 4.18 | 30,515 | 8.73 | 6.94 |
| \$7.45 - \$7.73 | 310,825 | 8.09 | 9.52 | 7.57 | 158,605 | 9.53 | 7.58 |
| \$7.74 - \$8.49 | 458,936 | 8.83 | 10.46 | 8.32 | 52,106 | 9.84 | 7.82 |
| \$8.50 - \$17.70 | 226,608 | 6.44 | 12.11 | 9.63 | 210,494 | 11.81 | 9.39 |
| \$17.71 - \$21.82 | 328,390 | 7.21 | 22.34 | 17.77 | 246,885 | 22.34 | 17.77 |
| | 2,339,905 | 6.51 | 9.32 | 7.41 | 1,439,301 | 8.91 | 7.08 |

At December 31, 2017, there were 1,439,301 options exercisable with a weighted average remaining contractual life as at December 31, 2017 of 5.04 years.

A summary of the Company's non-vested stock option activity and related information for the year ended December 31, 2017 is as follows:

| | Number of Options | Weighted Average Grant Date Fair Value | |
|-------------------------------|-------------------|--|--------|
| | | CAD \$ | USD \$ |
| Non-vested, January 1, 2017 | 618,811 | 9.58 | 7.13 |
| Granted | 620,950 | 6.51 | 5.02 |
| Vested | (274,580) | 9.68 | 7.45 |
| Forfeited and cancelled | (64,577) | 7.46 | 5.74 |
| Non-vested, December 31, 2017 | 900,604 | 7.12 | 5.66 |

The aggregate fair value of options vested during the year ended December 31, 2017 was \$2,047 (2016 – \$3,220, 2015 – \$999).

The fair value of stock options at the date of grant is estimated using the Black-Scholes option-pricing model which requires multiple subjective inputs. 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. Prior to the Company's IPO in November 2014, the Company's shares did not have a readily available market; therefore, the Company lacks company-specific historical and implied volatility information. Consequently, the expected volatility of stock options was estimated based on a combination of the Company's available historical volatility information and historical volatility analysis of peers that were similar to the Company with respect to industry, stage of life cycle, size, and financial leverage. Expected life assumptions are based on the Company's historical data. The dividend yield is based on the fact that the Company has never paid cash dividends and has no present intention to pay cash dividends. Forfeitures are recognized as they occur.

The weighted-average option pricing assumptions are as follows:

| | Years ended December 31 | | |
|--|-------------------------|--------|--------|
| | 2017 | 2016 | 2015 |
| Average risk-free interest rate | 2.35% | 1.58% | 1.75% |
| Expected volatility | 80 % | 75 % | 75 % |
| Average expected term (in years) | 7.37 | 6.22 | 6.23 |
| Expected dividend yield | 0.00% | 0.00% | 0.00% |
| Weighted average fair value of options granted | \$5.02 | \$4.94 | \$9.83 |

Stock-based compensation expense is classified in the consolidated statements of operations and comprehensive income (loss) as follows:

Years ended December 31,

| | 2017 | 2016 | 2015 |
|----------------------------|---------|---------|---------|
| Research and development | \$985 | \$874 | \$624 |
| General and administrative | 1,251 | 1,287 | 3,105 |
| | \$2,236 | \$2,161 | \$3,729 |

As of December 31, 2017, the unrecognized stock-based compensation cost related to the non-vested stock options was \$4,251, which is expected to be recognized over a weighted-average period of 2.37 years.

10. Concentrations of market risk:

(a) Foreign currency risk:

At December 31, 2017, the Company had U.S. dollar denominated cash and cash equivalents and marketable securities of \$28,028 (December 31, 2016 – \$35,859) and Canadian denominated cash and cash equivalents and marketable securities of CAD\$19,619 (December 31, 2016 – CAD\$37,980).

The Company faces foreign currency exchange rate risk in part, as a result of entering into transactions denominated in currencies other than U.S. dollars, particularly those denominated in Canadian dollars. The Company also holds non-U.S. dollar denominated cash and cash equivalents, marketable securities, accounts receivable and accounts payable, which are denominated in Canadian 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 with the Canadian dollar, as a majority of non-U.S. dollar denominated expenses are denominated in Canadian dollars and a significant portion of cash and cash equivalents and marketable securities are held in Canadian dollars. To limit the Company's exposure to volatility in currency markets, management estimates anticipated expenses that will be denominated in Canadian and U.S. dollars and then purchases a corresponding amount of Canadian or U.S. dollars at the current spot rate. Once these estimated expense amounts are acquired, the Company does not hedge its exposure and thus assumes the risk of future gains or losses on the amounts of Canadian dollars held.

(b) Interest Rate Risk:

At December 31, 2017, the Company had cash and cash equivalents and marketable securities of \$43,667. The Company's interest rate risk is primarily attributable to its cash and cash equivalents and marketable securities. 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 cash and cash equivalents and marketable securities. The Company does not enter into investments for trading or speculative purposes and has not used any derivative financial instruments to manage interest rate exposure.

The Company had a total outstanding loan balance of \$7,000 as of December 31, 2017, of which \$700 was due within 12 months. The interest rate on borrowings under the Loan Agreement with the Bank accrues at a floating per annum rate of 0.5% above the prime rate.

11. 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 non-refundable 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.

Commercialization milestone payments may include payments triggered by annual product sales that achieve pre-specified thresholds.

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(a)Teva Pharmaceutical Industries Ltd. (“Teva Pharmaceutical”) collaborative development and license agreement: In December 2012, the Company entered into a collaborative development and license agreement with Teva Pharmaceutical, through its subsidiary, Ivax International GmbH, pursuant to which the Company granted Teva Pharmaceutical an exclusive worldwide license to develop and commercialize certain products, including TV-45070 (formerly XEN402). On March 7, 2018, the Company entered into an agreement to terminate the collaborative development and license agreement, see subsequent event note 16. Under the terms of the original agreement, Teva Pharmaceutical paid the Company an upfront fee of \$41,000. Teva Pharmaceutical funded all development costs with respect to the licensed products. In addition, Teva Pharmaceutical provided funding to the Company for certain of the Company’s full-time equivalents (“FTEs”) performing the research collaboration plan. The Company identified several deliverables under the agreement with Teva Pharmaceutical, 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 Pharmaceutical. The Company concluded that the licenses did not have stand-alone value to Teva Pharmaceutical without the Company’s technical expertise and joint steering committee participation during the initial three-year period; therefore, the Company recognized the upfront payment as revenue ratably over the three-year period ended December 31, 2015.

(b)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 that selectively inhibit the Nav1.7 sodium channel and companion diagnostics for the potential treatment of pain. Pursuant to this agreement, the Company granted Genentech a worldwide exclusive license to develop and commercialize compounds directed to Nav1.7 and products incorporating such compounds for all uses. The Company 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 the Company an upfront fee of \$10,000. Genentech provided funding to the Company for certain of the Company’s FTEs performing the research collaboration plan. 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 recognized the upfront payment as revenue ratably over the three-year period ended December 22, 2014.

The Company is eligible to receive pre-commercial and commercial milestone payments with respect to the licensed products totaling up to an additional \$613,000, comprised of up to \$45,500 in pre-clinical 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 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 until the date that is ten years after first commercial sale on a country-by-country basis, plus a low single-digit percentage for large-molecule inhibitors of Nav1.7 for a period of ten years from first commercial sale on a country-by-country basis. The Company believes that the potential milestone payments for pre-clinical, 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. In the year ended December 31, 2017, no milestone payments have been recognized (2016 – \$nil; 2015 – \$nil).

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. To date, no such milestone payments have been recognized.

In March 2014, the Company entered into a new agreement with Genentech for pain genetics, with a focus on identifying genetic targets associated with rare phenotypes where individuals have an inability to perceive pain or where individuals have non-precipitated spontaneous severe pain. Pursuant to the terms of this agreement, any intellectual property arising out of the collaboration is jointly owned by the Company and Genentech. The Company also granted Genentech a time-limited, exclusive right of first negotiation on a target-by-target basis to form joint drug discovery collaborations. Under the terms of this agreement, Genentech paid an upfront payment of \$1,500. The Company is eligible to receive additional milestone payments totaling up to \$1,500.

The Company identified several deliverables under this agreement with Genentech, including non-exclusive licenses to certain intellectual property controlled by the Company, a commitment to participate in a joint steering committee and collaborative research services to be performed by the Company. 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 two year period; therefore, the Company recognized the upfront payment as revenue ratably over the two-year period ended March 18, 2016.

The Company believes that the potential milestone payments 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. In the year ended December 31, 2017, a \$250 milestone payment has been recognized (2016 – \$nil; 2015 – \$250).

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 certain milestone payments, a single-digit percentage of net sales for pain products the Company sells directly and a single-digit percentage of royalties received for sales of pain products by Genentech.

The following table is a summary of the revenue recognized from the Company's collaborations for each of the years ended December 31, 2017, 2016 and 2015.

| | Year Ended December | | |
|--------------------------------|---------------------|---------|----------|
| | 31, | 2016 | 2015 |
| | 2017 | 2016 | 2015 |
| Teva: | | | |
| Recognition of upfront payment | \$— | \$— | \$10,897 |
| Research funding | 59 | 116 | 112 |
| Genentech: | | | |
| Recognition of upfront payment | — | 157 | 725 |
| Research funding | — | 1,494 | 3,589 |
| Milestone payments | 250 | — | 250 |
| Total collaboration revenue | \$309 | \$1,767 | \$15,573 |

12. 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 is amortized over the term of the lease.

Lease expense for the year ended December 31, 2017 was \$1,079 (2016 – \$936, 2015 – \$917). Future minimum annual lease payments under existing operating lease commitments are as follows:

Year ending December 31:

| | |
|-------|---------|
| 2018 | 1,225 |
| 2019 | 1,227 |
| 2020 | 1,229 |
| 2021 | 1,162 |
| 2022 | 279 |
| Total | \$5,122 |

(b) Priority access agreement with Medpace Inc. (“Medpace”):

In August 2015, the Company entered into a priority access agreement with Medpace for the provision of certain clinical development services. Under the terms of the agreement, the Company has committed to using Medpace non-exclusively for clinical development services over the five year term of the agreement. In consideration for priority access to Medpace resources and preferred service rates, the Company has committed to \$7,000 of services over the term of the agreement, \$3,000 of which was paid in the year ended December 31, 2015. Of the amounts paid by the Company in 2015 in connection with the priority access agreement, an aggregate of \$2,770 has been recorded as expenses to date for services rendered, \$nil has been classified as current prepaid expenses (2016 – \$392) and \$230 has been classified as long-term prepaid expenses (2016 – \$408) for the provision of future services as at December 31, 2017.

(c) License, manufacture and supply agreement:

In March 2017, the Company entered into a license, manufacture and supply agreement with a pharmaceutical contract manufacturing organization for the access and use of certain regulatory documents as well as for the manufacture and supply of clinical and commercial drug product to support the development of XEN007. Under the terms of the agreement, the Company paid an upfront fee of \$500 CAD and will be required to pay a low single-digit percentage royalty on net sales of any products developed and commercialized under the agreement.

(d) Asset purchase agreement with 1st Order Pharmaceuticals, Inc. (“1st Order”):

In April 2017, the Company acquired XEN1101 (previously known as 1OP2198) from 1st Order pursuant to an asset purchase agreement. 1st Order previously acquired 1OP2198 from an affiliate of Valeant Pharmaceuticals International, Inc. (“Valeant”), and the Company has assumed certain financial responsibilities under that agreement. Under the terms of the agreement, the Company paid an upfront fee of \$350 and milestone payments in 2017 totaling \$700, which was expensed as research and development. Future potential payments to both 1st Order and Valeant include \$1,000 in clinical development milestones, up to \$13,000 in regulatory milestones, and up to approximately \$33,600 in sales-based and other milestones, which includes a \$1,500 milestone that may be payable pre-commercially, plus a mid-to-high single-digit percentage royalty on commercial sales.

(e) License agreement

In July 2017, the Company entered into a license agreement with a pharmaceutical company for the access and use of certain regulatory documents to support the development of XEN007. Under the terms of the agreement, the Company paid an upfront fee of \$1,000, which was expensed as research and development. Future potential payments include \$2,000 in clinical development milestones, up to \$7,000 in regulatory milestones, plus a low-to-mid single-digit percentage royalty on net sales of any products developed and commercialized under the agreement.

(f) Guarantees and indemnifications:

The Company has entered into license and research agreements with third parties that include indemnification provisions that are customary in the industry. These indemnification provisions generally require the Company to compensate the other party for certain damages and costs incurred as a result of third party claims or damages arising from these transactions.

The maximum amount of potential future indemnification is unlimited; however, the Company currently holds commercial and product liability insurance. This insurance limits the Company’s exposure and may enable it to recover a portion of any future amounts paid. Historically, the Company has not made any indemnification payments under such agreements and 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.

13. Income taxes:

Income tax (recovery) expense varies from the amounts that would be computed by applying the expected Canadian and provincial statutory income tax rate of 26% (2016 – 26%, 2015 – 26%) to loss before income taxes as shown in the following table:

| | 2017 | 2016 | 2015 |
|---|-----------|-----------|-----------|
| Computed recoveries at Canadian federal and | \$(8,000) | \$(5,980) | \$(4,095) |

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| | | | |
|---------------------------------|---------|---------|---------|
| provincial tax rates | | | |
| Change in valuation allowance | 9,210 | 6,897 | 2,482 |
| Investment tax credits earned | (1,393) | (1,500) | (1,220) |
| Tax attributes expired/utilized | 683 | 617 | 2,851 |
| Non-deductible expenditures | 594 | 569 | 977 |
| Financing fees in equity | — | (531) | — |
| Effect of tax rate increases | (1,444) | — | — |
| Other | 350 | (72) | (995) |
| Income tax (recovery) expense | \$— | \$— | \$— |

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 Company's net deferred income tax assets are as follows:

| | 2017 | 2016 |
|---|----------|----------|
| Deferred income tax assets | | |
| Scientific research and experimental development pool | \$25,056 | \$22,823 |
| Investment tax credits | 22,872 | 22,483 |
| Non-capital losses | 13,645 | 7,800 |
| Depreciable assets | 5,360 | 4,163 |
| Deferred financing fees | 578 | 1,020 |
| Other | 114 | 126 |
| Less - valuation allowance | (67,625) | (58,415) |
| Net deferred income tax assets | \$— | \$— |

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. A full valuation allowance continues to be applied against deferred income tax assets as the Company has assessed that the realization of such assets does not meet the "more likely than not" criteria.

At December 31, 2017, the Company has unclaimed tax deductions for scientific research and experimental development expenditures of \$92,799 (2016 – \$87,781) with no expiry.

At December 31, 2017, the Company has \$21,066 (2016 – \$20,160) of investment tax credits available to offset federal taxes payable and \$7,560 (2016 – \$7,624) of provincial tax credits available to offset provincial taxes payable in the future.

At December 31, 2017, the Company has non-capital losses, net of uncertain tax positions, carried forward for tax purposes, which are available to reduce taxable income of future years of approximately \$50,536 (2016 – \$29,999).

The investment tax credits and loss carry forwards expire over various years to 2037.

As of December 31, 2017, the total amount of the Company's unrecognized tax benefits of uncertain tax positions were \$6,350 (2016 – \$6,350). If recognized in future periods, the unrecognized tax benefits would affect the Company's effective tax rate. 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, 2017 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.

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 files income tax returns in Canada and the United States, the jurisdictions in which the Company believes that 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. Tax years ranging from 2002 to 2016 remain subject to Canadian income tax examinations.

14. Related Parties:

Dr. August J. Troendle, an officer and director of Medpace, which provides clinical development services to the Company, was a beneficial owner of more than 5% of the Company's common shares during a portion of 2016. The Company incurred \$3,097 of clinical development service fees under its priority access agreement and a master services agreement with Medpace for the year ended December 31, 2016 (2015 – \$922). Additionally, the Company has recorded \$1,010 of prepaid expenses as of December 31, 2016 (December 31, 2015 – \$2,314) for future clinical development services under such agreements with Medpace.

15. Selected quarterly consolidated financial data (unaudited):

The following table presents certain unaudited quarterly consolidated financial information for the years ended December 31, 2017 and 2016 (in thousands of U.S. dollars except per share amounts). This information reflects all normal recurring adjustments, which are, in the opinion of management, necessary for a fair statement of the results of the interim periods.

| | Three Months Ended | | | |
|-----------------------------------|--------------------|-------------|------------------|-----------------|
| | March 31, | June 30, | September 30, | December 31, |
| | 2017 | 2017 | 2017 | 2017 |
| Revenue | \$16 | \$15 | \$ 264 | \$ 16 |
| Loss from operations | (7,987) | (7,893) | (8,644) | (8,051) |
| Net loss | (7,517) | (7,380) | (7,742) | (8,065) |
| Basic net loss per common share | \$(0.42) | \$(0.41) | \$(0.43) | \$(0.45) |
| Diluted net loss per common share | \$(0.43) | \$(0.41) | \$(0.43) | \$(0.45) |

| | Three Months Ended | | | |
|---|--------------------|-------------|------------------|-----------------|
| | March 31, | June 30, | September 30, | December 31, |
| | 2016 | 2016 | 2016 | 2016 |
| Revenue | \$601 | \$413 | \$ 413 | \$ 376 |
| Loss from operations | (5,658) | (6,366) | (7,331) | (5,462) |
| Net loss | (3,263) | (6,016) | (7,714) | (6,004) |
| Basic and diluted net loss per common share | \$(0.23) | \$(0.42) | \$(0.51) | \$(0.34) |

16. Subsequent event:

On March 7, 2018, the Company and Teva Pharmaceuticals International GmbH and Teva Canada Limited (together "Teva"), entered into a termination agreement terminating by mutual agreement the collaborative development and license agreement dated December 7, 2012, as amended.

Pursuant to the termination agreement and subject to receipt by us of an order from the Ontario Securities Commission (“OSC”), Teva has agreed to transfer and assign 1,000,000 common shares of the Company held by Teva Canada Limited to the Company for cancellation. Teva will also return, license or assign to the Company certain intellectual property including certain patent rights. The termination agreement requires the Company to pay a low single-digit percentage royalty to Teva based on net sales of approved products, if any, resulting from any continued development and commercialization of TV-45070 by the Company during the period that assigned or licensed patents cover such products. Teva will also transfer regulatory filings related to TV-45070 to the Company.

The termination agreement will become effective on the date specified by the Company in a written notice to Teva. The effective date will be after the date that the Company receives the OSC order granting the Company exemptive relief from the requirements related to issuer bids under applicable Canadian securities laws in connection with the transfer and assignment to the Company by Teva Canada of the 1,000,000 common shares and not earlier than 10 business days from the date that a press release announcing the termination agreement is issued by the Company. The Company has made an application to the OSC for the OSC order and expects the effective date to be on or about March 22, 2018.

Item 9. Changes in and Disagreements With Accountants on Accounting and Financial Disclosure
None.

Item 9A. Controls and Procedures

Evaluation of disclosure controls and procedures. Our management, with the participation of our Chief Executive Officer and our Chief Financial Officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2017. The term “disclosure controls and procedures,” as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC’s rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company’s management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure.

Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of December 31, 2017, our Chief Executive Officer and our Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were, in design and operation, effective at the reasonable assurance level.

Management’s Annual Report on Internal Control over Financial Reporting. Our management, with the participation of our Chief Executive Officer and our Chief Financial Officer, is responsible for establishing and maintaining adequate internal control over our financial reporting, as such term is defined in Rule 13a-15(f) and Rule 15d-15(f) of the Securities Exchange Act of 1934. Our internal control over financial reporting is a process to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. Our internal control over financial reporting includes those policies and procedures that:

- (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of our assets;
- (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that our receipts and expenditures are being made only in accordance with authorizations of our management and directors; and
- (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on the financial statements.

The effectiveness of any system of internal control over financial reporting, including ours, is subject to inherent limitations, including the exercise of judgment in designing, implementing, operating, and evaluating the controls and procedures, and the inability to eliminate misconduct completely. Accordingly, any system of internal control over financial reporting, including ours, no matter how well designed and operated, can only provide reasonable, not absolute, assurances. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions or that the degree of compliance with the policies or procedures may deteriorate. Management has assessed the effectiveness of our internal control over financial reporting as at December 31, 2017. In making its assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in Internal Control – Integrated Framework (2013) to evaluate the effectiveness of our internal control over financial reporting. Based on this assessment using those criteria, management has concluded that our internal control over financial reporting was effective as of December 31, 2017.

Changes in internal control over financial reporting. There was no change in our internal control over financial reporting identified in connection with the evaluation required by Rule 13a-15(d) and 15d-15(d) of the Exchange Act

that occurred during the three months ended December 31, 2017 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

We have a written code of conduct that applies to all of our directors, officers and employees. A copy of the most up-to-date version of our code of conduct is available within the “Investors” section on our company website located at <http://www.xenon-pharma.com> and on SEDAR at www.sedar.com.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

The information required by Item 10 of Form 10-K is incorporated by reference to our Proxy Statement for the 2018 Annual Meeting of Shareholders to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2017.

Item 11. Executive Compensation

The information required by Item 11 of Form 10-K is incorporated by reference to our Proxy Statement for the 2018 Annual Meeting of Shareholders to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2017.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Shareholder Matters

The information required by Item 12 of Form 10-K is incorporated by reference to our Proxy Statement for the 2018 Annual Meeting of Shareholders to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2017.

Item 13. Certain Relationships and Related Transactions, and Director Independence

The information required by Item 13 of Form 10-K is incorporated by reference to our Proxy Statement for the 2018 Annual Meeting of Shareholders to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2017.

Item 14. Principal Accounting Fees and Services

The information required by Item 14 of Form 10-K is incorporated by reference to our Proxy Statement for the 2018 Annual Meeting of Shareholders to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2017.

PART IV

Item 15. Exhibits, Financial Statement Schedules

(a)(1) Financial Statements — The financial statements included in Item 8 are filed as part of this Annual Report on Form 10-K.

(a)(2) Financial Statement Schedules — All schedules have been omitted because they are not applicable or required, or the information required to be set forth therein is included in the consolidated Financial Statements or notes thereto included in Item 8 of this Annual Report on Form 10-K.

(a)(3) Exhibits — The exhibits required by Item 601 of Regulation S-K are listed in paragraph (b) below.

(b) Exhibits — The exhibits listed on the Exhibit Index (following the Signatures section of this report) are filed herewith or are incorporated by reference to exhibits previously filed with the SEC.

Item 16. Form 10-K Summary

Not applicable.

EXHIBIT INDEX

| Exhibit Number | Description of Document | Incorporated by Reference | | | |
|----------------|--|---------------------------|------------|---------|-------------------|
| | | Form | File No. | Exhibit | Filing Date |
| 3.1 | <u>Articles of the Company.</u> | 10-Q | 001-36687 | 3.1 | December 15, 2014 |
| 3.2 | <u>Amended and Restated By-laws of the Company.</u> | 10-Q | 001-36687 | 3.2 | December 15, 2014 |
| 4.1 | <u>Form of Common Share Certificate.</u> | S-1/A | 333-198666 | 4.1 | October 6, 2014 |
| 4.2 | <u>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, as amended.</u> | S-1/A | 333-198666 | 4.2 | October 6, 2014 |
| 4.3 | <u>Warrant to Purchase Shares, dated December 18, 2017, by and between Xenon Pharmaceuticals Inc. and Silicon Valley Bank</u> | 8-K | 001-36687 | 4.1 | December 18, 2017 |
| 10.1† | <u>Exclusive Collaborative Research and Option Agreement, dated June 10, 2009, by and between the Company and Merck Sharp & Dohme Research Ltd, as amended.</u> | S-1/A | 333-198666 | 10.1 | October 6, 2014 |
| 10.2† | <u>Collaborative Research and License Agreement, dated December 22, 2011, by and among the Company, Genentech, Inc. and F.</u> | S-1/A | 333-198666 | 10.3 | October 6, 2014 |

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Hoffmann-La Roche Ltd, as amended.

| | | | | | |
|--------|---|-------|------------|-------|--------------------|
| 10.3† | <u>Collaborative Development and License Agreement, dated December 7, 2012, by and between the Company and Ivax International GmbH, as amended.</u> | S-1/A | 333-198666 | 10.4 | October 6, 2014 |
| 10.4# | <u>Stock Option Plan, as amended, and form of option agreement thereunder.</u> | S-1/A | 333-198666 | 10.7 | October 6, 2014 |
| 10.5# | <u>2014 Equity Incentive Plan.</u> | S-1 | 333-198666 | 10.8 | September 10, 2014 |
| 10.5A# | <u>Form of Share Option Agreement, as amended, under the 2014 Equity Incentive Plan.</u> | 10-K | 001-36687 | 10.8A | March 8, 2017 |

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| Exhibit Number | Description of Document | Incorporated by Reference | | | |
|----------------|--|---------------------------|------------|---------|--------------------|
| | | Form | File No. | Exhibit | Filing Date |
| 10.6# | <u>Offer Letter, dated October 3, 2014, by and between the Company and Simon Pimstone.</u> | S-1/A | 333-198666 | 10.9 | October 6, 2014 |
| 10.7# | <u>Offer Letter, dated October 3, 2014, by and between the Company and Paul Goldberg.</u> | S-1/A | 333-198666 | 10.10 | October 6, 2014 |
| 10.8# | <u>Offer Letter, dated October 3, 2014, by and between the Company and Ian Mortimer.</u> | S-1/A | 333-198666 | 10.11 | October 6, 2014 |
| 10.9# | <u>Offer Letter, dated October 3, 2014, by and between the Company and Robin Sherrington.</u> | S-1/A | 333-198666 | 10.13 | October 6, 2014 |
| 10.10 | <u>Lease, dated as of 2001, by and between the Company and Discovery Parks Incorporated, as amended through July 1, 2014.</u> | S-1 | 333-198666 | 10.14 | September 10, 2014 |
| 10.11# | <u>Form of Director and Executive Officer Indemnification Agreement.</u> | S-1/A | 333-198666 | 10.15 | October 6, 2014 |
| 10.12† | <u>Amendment #4, dated May 13, 2015, to the Collaborative Research and License Agreement, dated December 22, 2011, by and among the Company, Genentech, Inc. and F. Hoffman-La Roche Ltd, as amended.</u> | 10-Q | 001-36687 | 10.1 | August 13, 2015 |
| 10.13 | <u>Lease Modification Agreement, effective July 1, 2015, by and between the Company and Redstone Enterprises Ltd.</u> | 10-Q | 001-36687 | 10.1 | November 10, 2015 |
| 10.14 | <u>Lease Modification Agreement, effective December 1, 2015, by and between the Company and Redstone Enterprises Ltd.</u> | 10-K | 001-36687 | 10.19 | March 8, 2016 |
| 10.15† | <u>Amendment #5, dated November 19, 2015, to the Collaborative Research and License Agreement, dated December 22, 2011, by and among the Company, Genentech, Inc. and F. Hoffman-La Roche Ltd, as amended.</u> | 10-K | 001-36687 | 10.20 | March 8, 2016 |
| 10.16† | <u>Amendment #6, dated March 9, 2016, to the Collaborative Research and License Agreement, dated December 22, 2011, by and among the Company, Genentech, Inc. and F. Hoffman-La Roche Ltd, as amended.</u> | 10-Q | 001-36687 | 10.1 | May 10, 2016 |
| 10.17# | <u>Offer letter, effective January 1, 2017, by and between Xenon Pharmaceuticals USA Inc. and James Empfield.</u> | 10-K | 001-36687 | 10.20 | March 8, 2017 |
| 10.18† | <u>Letter Agreement to Amendment #4, dated May 8, 2017, to the Collaborative Research and License Agreement, dated December 22, 2011, by and among the Company, Genentech, Inc. and F. Hoffman-La Roche Ltd, as amended.</u> | 10-Q | 001-36687 | 10.1 | August 3, 2017 |

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| | | | | | |
|--------|--|------|-----------|------|-------------------|
| 10.19† | <u>Asset Purchase Agreement, dated April 25, 2017, by and between the Company and 1st Order Pharmaceuticals, Inc.</u> | 10-Q | 001-36687 | 10.2 | August 3, 2017 |
| 10.20 | <u>Loan and Security Agreement, dated December 18, 2017, by and among Xenon Pharmaceuticals Inc., Xenon Pharmaceuticals USA Inc. and Silicon Valley Bank</u> | 8-K | 001-36687 | 10.1 | December 18, 2017 |
| 21.1 | <u>List of Subsidiaries of the Company.</u> | 10-K | 001-36687 | 21.1 | March 8, 2017 |
| 23.1 | <u>Consent of KPMG LLP, Independent Registered Public Accounting Firm.</u> | | | | |
| 24.1 | <u>Powers of Attorney (contained on signature page).</u> | | | | |
| 31.1 | <u>Rule 13a-14(a) / 15d-14(a) Certification of Principal Executive Officer</u> | | | | |

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| Exhibit Number | Description of Document | Incorporated by Reference | | |
|-------------------|--|---------------------------|----------|---------------------|
| | | Form | File No. | Exhibit Filing Date |
| 31.2 | <u>Rule 13a-14(a) / 15d-14(a) Certification of Principal Financial Officer</u> | | | |
| 32.1* | <u>Section 1350 Certification of Principal Executive Officer</u> | | | |
| 32.2* | <u>Section 1350 Certification of Principal Financial Officer</u> | | | |
| 101.INS | XBRL Instance Document | | | |
| 101.SCH | XBRL Taxonomy Extension Schema Document | | | |
| 101.CAL | XBRL Taxonomy Extension Calculation Linkbase Document | | | |
| 101.DEF | XBRL Taxonomy Extension Definition Linkbase Document | | | |
| 101.LAB | XBRL Taxonomy Extension Label Linkbase Document | | | |
| 101.PRE | XBRL Taxonomy Extension Presentation Linkbase Document | | | |

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.

*The Certifications attached as Exhibits 32.1 and 32.2 that accompany this Annual Report on Form 10-K are not deemed filed with the Securities and Exchange Commission and are not to be incorporated by reference into any filing of Xenon Pharmaceuticals Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of this Form 10-K, irrespective of any general incorporation language contained in such filing.

Item 16. Form 10-K Summary

Not applicable.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Dated: March 7, 2018 XENON PHARMACEUTICALS INC.

By: /s/ Simon Pimstone
Simon Pimstone
President and Chief Executive Officer

POWER OF ATTORNEY

Each person whose signature appears below hereby constitutes and appoints Simon Pimstone and Ian Mortimer, and each of them severally, as his or her true and lawful attorneys-in-fact and agents, with full power to act without the other and 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 and all amendments and supplements to this report, and any and all other instruments necessary or incidental in connection herewith, and to file the same, with all exhibits thereto, and all other documents in connection therewith, with the Commission.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the Registrant and in the capacities and on the dates indicated.

| Signature | Title | Date |
|--------------------|---|------------------|
| /s/ Simon Pimstone | | March 7, 2018 |
| Simon Pimstone | President, Chief Executive Officer and Director (Principal Executive Officer) | |
| /s/ Ian Mortimer | | March 7, 2018 |
| Ian Mortimer | Chief Financial Officer and Chief Operating Officer (Principal Financial and Accounting Officer) Chair of the Board of Directors | March 7, 2018 |
| /s/ Michael Tarnow | | |

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Michael Tarnow

/s/ Mohammad Azab

March
7, 2018

Mohammad Azab Director

/s/ Steven Gannon

March
7, 2018

Steven Gannon Director

/s/ Michael Hayden

March
7, 2018

Michael Hayden Director

/s/ Frank Holler

March
7, 2018

Frank Holler Director

/s/ Gary Patou

March
7, 2018

Gary Patou Director

/s/ Richard Scheller

March
7, 2018

Richard Scheller Director

/s/ Dawn Svoronos

March
7, 2018

Dawn Svoronos Director

