KIMBERLY CLARK CORP
Form 10-Q
November 06, 2009

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 10-Q

(Mark One)

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

For the quarterly period ended September 30, 2009

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 1-225

KIMBERLY-CLARK CORPORATION
(Exact name of registrant as specified in its charter)

Delaware	39-0394230
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)

P. O. Box 619100
Dallas, Texas
75261-9100
(Address of principal executive offices)
(Zip Code)

(972) 281-1200
(Registrant’s telephone number, including area code)

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 x 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 x No ¨

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

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

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act).

Yes ¨ No x

As of October 30, 2009, there were 415,379,458 shares of the Corporation’s common stock outstanding.

PART I – FINANCIAL INFORMATION

Item 1. Financial Statements.

KIMBERLY-CLARK CORPORATION AND SUBSIDIARIES
CONSOLIDATED INCOME STATEMENT
(Unaudited)

(Millions of dollars, except per share amounts)	Three Months Ended September 30		Nine Months Ended September 30	
	2009	2008	2009	2008
Net Sales	$ 4,913	$ 4,998	$ 14,133	$
Cost of products sold	3,186	3,535	9,379	
Gross Profit	1,727	1,463	4,754	
Marketing, research and general expenses	852	848	2,524	
Other (income) and expense, net	4	5	122	
Operating Profit	871	610	2,108	
Interest income	7	15	21	
Interest expense	(67)	(76)	(211)	
Income Before Income Taxes, Equity Interests and Extraordinary Loss	811	549	1,918	
Provision for income taxes	(240)	(154)	(562)	
Income Before Equity Interests and Extraordinary Loss	571	395	1,356	
Share of net income of equity companies	40	53	116	
	-	-	-	

Extraordinary loss, net of income taxes, attributable to Kimberly-Clark Corporation			
Net Income	611	448	1,472
Net income attributable to noncontrolling interests	(29)	(35)	(80)
Net Income Attributable to Kimberly-Clark Corporation	$ 582	$ 413	$ 1,392
Per Share Basis:			
Basic			
Before extraordinary loss	$ 1.40	$ .99	$ 3.35
Extraordinary loss	-	-	-
Net Income Attributable to Kimberly-Clark Corporation	$ 1.40	$ .99	$ 3.35
Diluted			
Before extraordinary loss	$ 1.40	$ .99	$ 3.35
Extraordinary loss	-	-	-
Net Income Attributable to Kimberly-Clark Corporation	$ 1.40	$ .99	$ 3.35
Cash Dividends Declared	$ .60	$ .58	$ 1.80

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

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 and its affiliate, F. Hoffman-La Roche Ltd, or Roche, to discover and develop selec inhibitors of Nav1.7 for the treatment of pain. For a more detailed description of th agreement with Genentech, see "—Collaborations, Commercial and License Agree on our discovery of Nav1.7 deficiency underlying the rare human disease called co indifference to pain, or CIP, where individuals with CIP are unable to feel pain, we Nav1.7 is a highly-validated target for the treatment of pain. Our Genentech collab on discovering and developing oral drugs that selectively target Nav1.7.

Chronic pain conditions, such as severe cancer pain and neuropathic pain, are gene as unmet medical needs providing potential commercial opportunities for a new ora Currently available pain drugs often have either a lack of meaningful pain relief or effects for many patients. An orally administered, selective Nav1.7 inhibitor could mechanism for the treatment of moderate to severe pain as a single agent or in com existing analgesics that work through different mechanisms. We believe that the se of Nav1.7 may lower the potential for dose-limiting central nervous system side-ef for an improved side-effect profile for oral administration of such an inhibitor, whi potentially allow for the treatment of pain that has a central or deep tissue compone cancer pain and neuropathic pain.

Genentech had been focused on the development of GDC-0310, but after completin additional pre-clinical studies with GDC-0310 and reviewing the totality of data av Genentech decided to discontinue further clinical development of GDC-0310 and e future Nav1.7 development efforts on back-up molecules.

Additional Collaborative Work with Genentech

We formed a second collaboration with Genentech in March 2014 for pain genetics rare phenotypes where individuals have an inability to perceive pain or where indiv non-precipitated spontaneous severe pain. We believe these phenotypes may unloc molecular regulators of pain signaling in humans, which we will seek to validate as pain drugs. In March 2017, the research term for this second collaboration agreeme until March 2018. Under that agreement, Genentech has paid us a $1.5 million upfr two $0.25 million milestone payments related to the identification of novel pain tar 2015 and July 2017. For a more detailed description of the terms of our collaborati Genentech, see "—Collaborations, Commercial and License Agreements" below.

Selective Small-Molecule Inhibitors of Targets for the Treatment of Cardiovascula

We entered into a collaborative research and option agreement with Merck in June
novel targets and compounds for the treatment of cardiovascular disease. For a mo
description of the terms of our agreement with Merck, see "—Collaborations, Com
Agreements" below. In 2012, Merck exercised its option to obtain an exclusive lic
cardiovascular disease and compound inhibitors that were discovered during the re
collaboration. The target, when inhibited, is predicted to provide a beneficial lipid
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 Pharma
1st Order, pursuant to which we acquired all rights with respect to XEN1101 (prev
1OP2198). 1st Order previously acquired 1OP2198 from Valeant Pharmaceuticals
S.a.r.l., an indirect subsidiary of Bausch Health Companies Inc., together with Val
Pharmaceuticals Ireland Limited, Bausch Health, and assumed certain obligations,
potential milestone and royalty payments. Under the terms of the asset purchase ag
1st Order an upfront fee of approximately $0.4 million and a $0.7 million mileston
achieving a clinical development milestone.

In September 2018, we signed an agreement with Bausch Health to buy out all futu
payments and royalties owed to Bausch Health with respect to XEN1101, includin
million in potential clinical development, regulatory and sales-based milestones an
single digit percentage royalty on commercial sales in exchange for a one-time pay
million. We remain responsible for future potential payments to 1st Order of $0.5 m
development milestones, up to $6.0 million in regulatory milestones for multiple in
$1.5 million in other milestones, which may be payable pre-commercially. There a
obligations to 1st Order.

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

In December 2011, we entered into a collaborative research and license agreement
and its affiliate, Roche, to discover and develop small and large molecules that sele
Nav1.7 sodium channel and companion diagnostics for the potential treatment of p
this agreement, we granted Genentech a worldwide exclusive license to develop an
compounds directed to Nav1.7 and products incorporating such compounds for all
granted Genentech a worldwide non-exclusive license to diagnostic products for th
developing or commercializing such compounds.

Under the terms of the agreement, Genentech paid us an upfront fee of $10.0 millio
milestone payment for the selection of a compound for development and an $8.0 m
payment upon the approval by Health Canada of a CTA. Genentech provided fundi
certain of our full-time equivalents, or FTEs, performing the research collaboration
concluded in December 2016. We are eligible to receive pre-commercial and comm
payments with respect to the licensed products totaling up to an additional $613.0 m
comprised of up to $45.5 million in pre-clinical and clinical milestone payments, u

$387.5 million in regulatory milestone payments, and up to $180.0 million in sales-
payments for multiple products and indications. In addition, we are eligible to recei
based on net sales of the licensed products, which range from a mid single-digit per
percent for small-molecule inhibitors for the timeframe that such products are cove
licensed patents and a low single-digit percentage thereafter until the date that is ten
commercial sale on a country-by-country basis, plus a low single-digit percentage f
inhibitors of Nav1.7 for a period of ten years from first commercial sale on a count
basis. Our pre-commercial and commercial milestone payments and royalties may
reductions based on the period in which the compound that is selected for developm
commercialization was initially conceived.

Our agreement with Genentech expires on the date of the expiration of all payment
under the agreement. Genentech may terminate the agreement with three months ad
anytime on or after the third anniversary of the effective date of the agreement, and
terminate the agreement in the event of a material breach by the other party that rem
after 90 days. In the event that Genentech terminates the agreement due to our brea
retains its licenses and its payment obligations to us are reduced. In the event that w
agreement due to Genentech's breach, the rights and licenses granted to Genentech
subject to certain rights to make and use certain large-molecule product candidates
by Genentech, and Genentech is obligated to assign certain regulatory approvals an
licenses to us to enable us to develop and commercialize certain terminated produc
collaboration.

Our collaborative research and license agreement with Genentech has been amende
in May 2015, November 2015, March 2016, May 2017, July 2018 and September 2
extend the term of the research program or to provide us with greater flexibility in
compounds that target Nav1.6. Pursuant to the current amendment, we have obtain
non-exclusive, irrevocable, perpetual, world-wide, sublicensable license under the
forming part of the Genentech intellectual property developed under the Nav1.7 co
necessary or useful to make, use, sell, offer for sale, and import compounds from o
program that are above a certain potency threshold on Nav1.7 and products contain
compounds. Our license from Genentech includes commercialization rights but we
from developing or commercializing our Nav1.6 compounds below a certain poten
the field of epilepsy and any of our Nav1.6 compounds, regardless of their potency
field of pain. In exchange for the rights granted to us under this amendment, Genen
receive a low single-digit percentage, tiered royalty on net sales of our Nav1.6 com
including XEN901, for a period of ten years from first commercial sale on a countr
basis. Pursuant to the amendment, we granted Genentech a royalty-free, non-exclus
license under our Nav1.6 intellectual property to make, use, sell, offer for sale and
compounds below a certain potency on Nav1.7 and products containing those comp
uses and indications except epilepsy.

In March 2014, we entered into an additional agreement with Genentech for pain g
focused on identifying genetic targets associated with rare phenotypes where indivi
inability to perceive pain or where individuals have non-precipitated spontaneous s
Pursuant to the terms of this agreement, any intellectual property arising out of the
be jointly owned by us and Genentech. We also granted Genentech a time-limited,
first negotiation on a target-by-target basis to form joint drug discovery collaborati
terms of this agreement, Genentech paid us an upfront payment of $1.5 million and
million milestone payments related to the identification of novel pain targets in Sep
July 2017. Genentech's time-limited, exclusive right of first negotiation, which was
throughout the research term, expired at the same time as the agreement in March 2
such termination, we remain eligible for up to an additional $1.5 million in milesto

Agreement with Merck for Cardiovascular Disease

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

Under the terms of the agreement, Merck had the option to obtain an exclusive lice
intellectual property controlled by us to develop and commercialize compounds and
directed to targets in the research program, which has now expired. In June 2012, M
its option and paid us $2.0 million to obtain such a worldwide exclusive license to
commercialize compound inhibitors of a target that was identified using our discov
Through December 31, 2018, we have received milestone payments and an option
million, and we are eligible for further research, development and regulatory milest
up to $64.0 million, comprised of $21.0 million in pre-clinical and clinical milestor
up to $43.0 million in regulatory milestone payments for products directed to the li

well as royalties from the mid to high single-digit range in countries where such pr
covered by a valid composition or method of use claim of a Xenon or Merck patent
covered by such claims, royalties in the mid single-digit range for ten years after fi
sale of such products.

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

Our agreement with Merck expires on the date of the expiration of all royalty paym
us under the agreement. Merck has the right to terminate the agreement upon provi
notices to us. Each party may terminate the agreement in the event of a material bre
party that remains uncured for 90 days after notice of such breach. In the event that
terminates the agreement due to our breach, the licenses granted to Merck survive a
paid up. In the event that we terminate the agreement due to Merck's breach, the lic
Merck terminate.

Termination Agreement with Teva

On March 7, 2018, we and Teva Pharmaceuticals International GmbH and Teva Ca together Teva, entered into a termination agreement terminating by mutual agreeme collaborative development and license agreement dated December 7, 2012, as amer subsequently closed on March 27, 2018. In connection with the termination, Teva r cancelled 1,000,000 of our common shares that were owned by Teva. Pursuant to t termination agreement, Teva has also returned, licensed or assigned to us certain in property, including certain patent rights and transferred regulatory filings related to termination agreement requires us to pay a low single digit percentage royalty to Te sales of approved products, if any, resulting from any continued development and c of TV-45070 by us or a sublicensee during the period that assigned or licensed pate products. To date, no such sales have occurred.

Intellectual Property

As part of our business strategy, we generally file patent applications disclosing an targets and their novel uses, novel compositions that modulate such targets, methoc using such compositions and various therapeutic formulations of such composition product candidates. In some cases, we also file claims on screening assays as well a and methods for use in diagnosing certain diseases. We generally file applications i Canada, the European Union, or EU, and other commercially significant foreign ju also rely on trade secrets, internal know-how, technological innovations and agreen parties to develop, maintain and protect our competitive position. Our ability to be depend on the success of this strategy.

As of December 31, 2018, we owned, co-owned or licensed 30 issued U.S. patents approximately 18 pending U.S. patent applications, including provisional and non-p filings. We also owned, co-owned or licensed an additional 106 pending and grante applications worldwide, including 24 country-specific validations of four European

As of December 31, 2018, we owned two issued U.S. patents and one U.S. provisio application related to XEN1101, and methods of making and using XEN1101 and c compounds. The issued patents are expected to expire between 2028 and 2029 (abs extensions of term). In addition, we have 13 foreign issued patents (exclusive of Eu national validations) and have six pending corresponding applications in various fo jurisdictions relating to XEN1101 and certain related compounds.

As of December 31, 2018, we have filed a PCT international patent application and U.S. non-provisional patent application directed to XEN901 and methods of makin XEN901 and certain related compounds. Any patents issuing from these applicatio expire in 2037 (absent any extensions of term).

As of December 31, 2018, we have filed a PCT international patent application, a U non-provisional patent application and three U.S. provisional patent applications di of our selective inhibitors of Nav1.6 (exclusive of XEN901), as well as methods of using the same. Any patents issuing from these applications are expected to expire and 2039 (absent any extensions of term).

As of December 31, 2018, we, together with Genentech, co-owned four issued U.S
pending U.S. patent applications, two foreign issued patents (exclusive of Europea
validations) and have filed 43 pending counterpart patent applications in various ju
directed to Nav1.7 inhibitors, as well as methods of making and using the same. Th
as well as any patents issuing from these applications are expected to expire betwe
(absent any extensions of term).

As provided for in our termination agreement with Teva, Teva assigned to us one is
two pending U.S. patent applications (one of which has since issued as a U.S. pate
two pending PCT international patent applications related to TV-45070 (one of wh
entered national phase in Australia, Canada, China, Europe, Japan, Israel and New
issued U.S. patent assigned to us is expected to expire in 2036 (absent any extensio
any patents issuing from the assigned applications are expected to expire in 2037 (a
extensions of term). For a more detailed description of the terms of our termination
Teva, see "—Collaborations, Commercial and License Agreements" above. Exclud
included in the terms of the termination agreement, as of December 31, 2018, we o
U.S. patents related to TV-45070, and methods of making and using TV-45070 and
compounds. The issued patents are expected to expire between 2026 and 2033 (abs
extensions of term). In addition, we have nine foreign issued patents (exclusive of
national validations) and have filed two pending corresponding foreign application
TV-45070 and certain related compounds.

Competition

The biotechnology and pharmaceutical industries are highly competitive and are ch
rapidly advancing technologies and a strong emphasis on proprietary products. Wh
that our technology, development experience, scientific knowledge and drug discov
provide us with certain advantages, we face potential competition in our discovery
development efforts from many different approaches and sources, including pharm
biotechnology companies, academic institutions and governmental agencies and pu
research institutions. Any product candidates or products that we or our collaborato
develop and commercialize will compete with existing products and new products
available in the future.

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

Our commercial opportunities could be reduced or eliminated if our competitors de
commercialize products or therapies that are safer, more effective, have fewer or le
effects, are more convenient or are less expensive than any products that we may d
competitors also may obtain FDA, European Medicines Agency, or EMA, Health C
regulatory approval for their products more rapidly than we may obtain approval fo
could result in our competitors establishing a strong market position before we are
market. In addition, our ability to compete may be affected in many cases by insure
party payers.

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

The key competitive factors affecting the success of all of our product candidates, i
likely to be their efficacy, safety, convenience, price, the effectiveness of alternativ
level of competition and the availability of coverage, and adequate reimbursement
and other third party payers. Our product candidates that are in clinical developmen
with various therapies and drugs, both in the marketplace and currently under deve

XEN496, XEN1101, and XEN901 for the Treatment of Epilepsy

If more than one of XEN496, XEN1101, or XEN901 were approved for the treatme
we anticipate that they could potentially compete with each other and other AEDs,
can be categorized into four classes by AED mechanism: modulation of voltage-ga
enhancement of GABA-mediated inhibitory neurotransmission, reduction of glutam
excitatory neurotransmission, and SV2A modulation. Commonly used AEDs inclu
levetiracetam, carbamazepine, clobazam, lamotrigine, valproate, oxcarbazepine, to

lacosamide, perampanel and cannabidiol. There are currently no FDA-approved tre
specifically indicated for the early infantile epileptic encephalopathies KCNQ2-EE
however, a number of different AEDs are currently used in these patient population
aware of other companies that are developing selective Nav1.6 inhibitors for the tre
epilepsy. There are other AEDs in development that could potentially compete with
XEN1101 or XEN901, including products in development from UCB, Inc., Zogeni
Therapeutics, Marinus Pharmaceuticals, Inc., Inc., Knopp Biosciences LLC, Upshe
Laboratories, Inc., Insys Therapeutics Inc., Supernus Pharmaceuticals Inc., Eisai C
Therapeutics Inc., Sunovion Pharmaceuticals Inc., and Takeda Pharmaceutical Con

Selective Inhibitors of Nav1.7 for the Treatment of Pain

Drug discovery and development for various pain applications is intensely competi
large number of approved products for neuropathic pain, inflammatory pain and oth
indications. These approved products include capsaicin, celecoxib, lidocaine, narco
gabapentin, and pregabalin. We are also aware of development programs at several
and biotechnology companies that are developing Nav1.7 inhibitors or other sodiun
inhibitors for the treatment of pain, including Amgen Inc., AstraZeneca PLC, Biog
Bristol-Myers Squibb Company, Dainippon Sumitomo Co., Ltd., Eli Lilly and Con
NeuroQuest Inc., Newron Pharmaceuticals SpA, Vertex Pharmaceuticals Inc., Voy
Therapeutics, Inc. and Chromocell Corporation in collaboration with its partner As
Moreover, we are aware of various other product candidates in development that ta
mechanisms of action to treat various pain indications, including calcium channel i
growth factor inhibitors, and Nav1.8 inhibitors.

Government Regulation

We are developing small-molecule product candidates, which are regulated as drug
equivalent regulatory authorities outside the U.S. Within the FDA, the Center for D
and Research, or CDER, regulates drugs. Drugs are subject to regulation under the
Drug, and Cosmetic Act, or FD&C Act, and other federal, provincial, state, local ar
and regulations. The FD&C Act and corresponding regulations govern, among othe
testing, manufacturing, safety, efficacy, labeling, packaging, storage, record keepin
import, export, reporting, advertising and other promotional practices involving dru
approval must be obtained before clinical testing of drugs is initiated, and each clin
protocol for such product candidates is reviewed by the FDA prior to initiation in th
approval also must be obtained before marketing of drugs in the U.S. The process o
regulatory approvals and the subsequent compliance with appropriate federal, prov
and foreign statutes and regulations require the expenditure of substantial time and
resources and we may not be able to obtain the required regulatory approvals.

U.S. Drug Development Process

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

- completion of nonclinical laboratory tests and animal studies according to good la
  practices, or GLPs, and applicable requirements for the humane use of laboratory
  applicable regulations;
- submission to the FDA of an application for an IND, which must become effective
  clinical studies may begin;
- performance of adequate and well-controlled human clinical studies according to t
  regulations commonly referred to as good clinical practices, or GCPs, and any add
  requirements for the protection of human research subjects and their health inform
  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 i
  substantial evidence of safety and efficacy based on large scale phase 3 clinical stu
    - satisfactory completion of an FDA inspection of the manufacturing faci
      where the product is produced to assess compliance with good manufac
      or GMP, to assure that the facilities, methods and controls are adequate
      manufacture the product pursuant to regulatory requirements;
- potential FDA audit of the nonclinical and clinical study sites that generated the da
  the NDA; and
- FDA review and approval of the NDA.

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

- Phase 1. The drug is initially introduced into healthy human subjects and tested fo
  case of some products for severe or life-threatening diseases, especially when the
  too inherently toxic to ethically administer to healthy volunteers, the initial human
  conducted in patients that have the condition or disease being studied.
    - Phase 2. The drug is evaluated in a limited patient population to identify
      effects and safety risks, to preliminarily evaluate the efficacy of the prod
      targeted diseases and to determine a dose range and dosing schedule.

- Phase 3. Clinical studies are undertaken to further evaluate dosing and c
  clinical efficacy, and safety in an expanded patient population at geogra
  dispersed clinical study sites. These clinical studies are intended to esta
  risk/benefit ratio of the product and provide an adequate basis for produ

Post-approval clinical studies, sometimes referred to as Phase 4 clinical studies, ma
after initial marketing approval. These clinical studies are used to gain additional e
the treatment of patients in the intended therapeutic indication, particularly for long
follow-up. During all phases of clinical development, regulatory agencies require e
monitoring and auditing of all clinical activities, clinical data, and clinical study inv

Concurrent with clinical studies, companies usually complete additional animal stu
also develop additional information about the physical characteristics of the drug as
a process for manufacturing the product in commercial quantities in accordance wi
requirements. The manufacturing process must be capable of consistently producin
of the product candidate and, among other requirements, the sponsor must develop
ensuring the quality of the final drug. Additionally, appropriate packaging must be
tested and stability studies must be conducted to demonstrate that the drug candidat
undergo unacceptable deterioration over its labeled shelf life.

U.S. Review and Approval Processes

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

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

Within 60 days following submission of the application, the FDA reviews the NDA
is substantially complete before the agency accepts it for filing. The FDA may refu
marketing application that it deems incomplete or not properly reviewable at the tim
and may request additional information, including additional clinical data. In this e
must be resubmitted with the additional information. The resubmitted application a
review before the FDA accepts it for filing. Once the submission is accepted for fil
begins an in-depth substantive review of the NDA. The FDA reviews the applicatio
among other things, whether the proposed product is safe and effective for its inten
whether the product is being manufactured in accordance with GMPs. The FDA ma
applications for novel products or products that present difficult questions of safety
advisory committee, typically a panel that includes clinicians and other experts, for
evaluation and a recommendation as to whether the application should be approved
conditions. The FDA is not bound by the recommendations of an advisory committ
considers such recommendations carefully when making decisions. During the proc
process, the FDA also will determine whether a Risk Evaluation and Mitigation Str
is necessary to assure the safe use of the product. If the FDA concludes a REMS is
sponsor of the NDA must submit a proposed REMS; the FDA will not approve the
without a REMS, if required.

Notwithstanding the submission of relevant data and information, the FDA may ult
that the NDA does not satisfy its regulatory criteria for approval and deny approval
from clinical studies are not always conclusive and the FDA may interpret data diff
interpret the same data. If the agency decides not to approve the marketing applicat
issue a Complete Response letter that usually describes all of the specific deficienc
application identified by the FDA. The deficiencies identified may be minor, for ex
labeling changes, or major, for example, requiring additional clinical studies. Addit
Complete Response letter may include recommended actions that the applicant mig

the application in a condition for approval. If a Complete Response letter is issued, may either resubmit the NDA, addressing all of the deficiencies identified in the let the application.

If a product receives regulatory approval, the approval will be limited to the specifi dosages studied in clinical trials or the indications for use may otherwise be limited restrict the commercial value of the product. Further, the FDA may require that cer contraindications, warnings or precautions be included in the product labeling. The impose restrictions and conditions on product distribution, prescribing, or dispensi 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 comple 90% of standard NDAs within ten months from filing and 90% of priority NDAs w from filing, whereupon a review decision is to be made. The FDA does not always goal dates and its review goals are subject to change from time to time. The review PDUFA goal date may be extended by three months if the FDA requests or the app otherwise provides additional information or clarification regarding information alr 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 exped
the development and review of drugs. Even if a drug qualifies for one or more of th
FDA may later decide that the drug no longer meets the conditions for qualification
drugs that are eligible for these programs are those for serious or life-threatening co
with the potential to address unmet medical needs, and those that offer meaningful
existing treatments. For example, Fast Track is a process designed to expedite the
drugs that treat serious or life-threatening diseases or conditions and fill unmet me
the Fast Track process, drugs that offer major advances in treatment or provide a tr
adequate therapy exists, may also receive priority review by the FDA, or review wi
of the filing of an NDA compared to a traditional review time of ten months. Altho
and priority review do not affect the standards for approval of a drug, and may not
approval, if approval is granted, for Fast Track designated drugs, the FDA will also
facilitate early and frequent meetings with a sponsor of a Fast Track designated dru
such drug's review and development.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug inten
disease or condition, which is generally a disease or condition that affects fewer tha
individuals in the U.S., or more than 200,000 individuals in the U.S. and for which
reasonable expectation that the cost of developing and making a drug available in t
type of disease or condition will be recovered from sales of the product. We have re
drug designation from the FDA for XEN007 (active ingredient flunarizine), a drug
internally for the potential treatment of HM and AHC. Orphan product designation
requested before submitting an NDA. After the FDA grants orphan product designa
of the therapeutic agent and its potential orphan use are disclosed publicly by the F
product designation does not convey any advantage in or shorten the duration of the
review and approval process.

Orphan drug products may also be eligible for RPD designation if greater than 50%
living with the disease are under age 19 and the condition affects fewer than 200,00
the U.S. A priority review voucher will be given to the sponsor of a product with an
designation at the time of product approval that is transferable to another company.
received RPD designation from the FDA for XEN007 for the treatment of AHC. Th
assurance we will receive a RPD priority review voucher or that it will result in a fa
process, review or approval for a subsequent marketing application. Further, it is po
if we obtain approval for XEN007 and qualify for such a priority review voucher, t
no longer be in effect at the time of approval. Although priority review vouchers m
transferred to third parties, there is no guaranty that we will be able to realize any v
to sell a priority review voucher.

If a product that has orphan designation subsequently receives the first FDA approv
for the disease or condition for which it has such designation, the product is entitled
product exclusivity, which means that the FDA may not approve any other applicat
the same drug for the same indication for seven years, except in limited circumstan
showing of clinical superiority to the product with orphan exclusivity. Competitors
receive approval of different products for the indication for which the orphan produ

or obtain approval for the same product but for a different indication for which the
has exclusivity. Orphan product exclusivity also could block the approval of one of
seven years if a competitor obtains approval of the same product as defined by the
product candidate is determined to be contained within the competitor's product for
indication or disease. If a drug designated as an orphan product receives marketing
indication broader than what is designated, it may not be entitled to orphan product
Orphan drug status in the EU has similar, but not identical, benefits, including up to
exclusivity.

Post-Approval Requirements

Rigorous and extensive FDA regulation of drug continues after approval, particular
GMP. We will rely, and expect to continue to rely, on third parties for the productio
commercial quantities of any products that we may commercialize. Manufacturers
are required to comply with applicable requirements in the GMP regulations, inclu
control and quality assurance and maintenance of records and documentation. Othe
requirements applicable to drug manufacturers, include reporting of GMP deviation
the safety, efficacy or quality of a distributed product, record-keeping requirements
adverse effects, reporting updated safety and efficacy information, and complying
record and signature requirements.

We also must comply with the FDA's advertising and promotion requirements, suc
to direct-to-consumer advertising, the prohibition on promoting products for uses o
populations that are not described in the product's approved labeling (known as "of
industry-sponsored scientific and educational activities. Discovery of previously un
or the failure to comply with the applicable regulatory requirements may result in r
marketing of a product or withdrawal of the product from the market as well as pos
criminal sanctions. Failure to comply with the applicable U.S. requirements at any
product development process, approval process or after approval, may subject an ap
manufacturer to administrative or judicial civil or criminal sanctions and adverse pu
sanctions could include refusal to approve pending applications, withdrawal of an a
hold, warning or untitled letters, product recalls, product seizures, total or partial su
production or distribution, injunctions, fines, refusals of government contracts, mar
advertising or communications with doctors, debarment, restitution, disgorgement o
or criminal penalties. Any agency or judicial enforcement action could have a mate
effect on us.

Drug manufacturers and other entities involved in the manufacture and distribution
drugs are required to register their establishments with the FDA and certain state ag
subject to periodic unannounced inspections by the FDA and certain state agencies
with GMPs and other laws. Accordingly, manufacturers must continue to expend ti
effort in the area of production and quality control to maintain GMP compliance. D
problems with a product after approval may result in restrictions on a product, man
holder of an approved NDA, including withdrawal of the product from the market.
changes to the manufacturing process or facility generally require prior FDA appro
implemented and other types of changes to the approved product, such as adding ne
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
candidates, some of our U.S. patents may be eligible for limited patent term extensi
Drug Price Competition and Patent Term Restoration Act of 1984, commonly refer
Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent re
up to five years as compensation for patent term lost during product development a
regulatory review process. However, patent term restoration cannot extend the rem
patent beyond a total of 14 years from the product's approval date. Only one patent
approved product is eligible for the extension and the application for the extension
submitted prior to the expiration of the patent. The U.S. Patent and Trademark Offi
consultation with the FDA, reviews and approves the application for any patent ter
restoration.

Under the Hatch-Waxman Amendments, a drug product containing a new chemical
active ingredient is entitled to five years of market exclusivity, and a product whose
ingredient was previously FDA approved, and for which the sponsor is required to
clinical data is entitled to three years of market exclusivity. A drug can also obtain
exclusivity in the U.S. and, if granted, adds six months to existing exclusivity perio
terms. This six-month exclusivity, which runs from the end of other exclusivity pro
term, may be granted based on the timely, voluntary, and as-agreed upon completio
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 re
environmental protection and hazardous substances affect our business. These and
our use, handling and disposal of various biological, chemical and radioactive subs
and wastes generated by, our operations. If our operations result in contamination o
environment or expose individuals to hazardous substances, we could be liable for
governmental fines. We believe that we are in material compliance with applicable
laws and that continued compliance therewith will not have a material adverse effe
business. We cannot predict, however, how changes in these laws may affect our fu

Global Anti-Corruption Laws

The U.S. Foreign Corrupt Practices Act and the Canadian Corruption of Foreign Pu
Act, the U.S. Travel Act, the OECD Anti-Bribery Convention, Title 18 United Stat
201, and any other applicable domestic or foreign anti-corruption or anti-bribery la
are subject prohibit corporations and individuals from engaging in certain activities
retain business or to influence a person working in an official capacity. It is illegal
pay or authorize the payment of anything of value to any foreign government offici
staff member, political party or political candidate in an attempt to obtain or retain
otherwise influence a person working in an official capacity. We may also be held
of our third party agents under the U.S. Foreign Corrupt Practices Act, Canadian C
Foreign Public Officials Act, and other applicable anti-corruption and anti-bribery
Noncompliance with these laws could subject us to investigations, sanctions, settle
prosecution, other enforcement actions, disgorgement of profits, significant fines, d
civil and criminal penalties or injunctions, suspension or debarment from contracti
persons, the loss of export privileges, whistleblower complaints, reputational harm,
coverage, and other collateral consequences. Any investigations, actions or sanctio
previously mentioned harm could have a material negative effect on our business, c
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
jurisdictions governing, among other things, research, development, testing, manuf
control, approval, labeling, packaging, storage, record-keeping, promotion, adverti
post-approval monitoring and reporting, marketing and export and import of drugs,
reimbursement requirements. Generally, before a new drug can be marketed, consi
demonstrating its quality, safety and efficacy must be obtained, organized into a fo
each regulatory authority, submitted for review and approved by the regulatory aut
or not we obtain FDA approval for a product, we must obtain the requisite approva
authorities in foreign countries prior to the commencement of clinical studies or ma
product in those countries. Certain countries outside of the U.S. have a similar proc
the submission of a clinical study application much like the IND prior to the comm
human clinical studies. In the EU, for example, a CTA must be submitted to each c
health authority and an independent ethics committee, much like the FDA and the I
Once the CTA is approved in accordance with a country's requirements, clinical st
may proceed. Similar requirements regarding a CTA and ethics approval exist in C

The requirements and process governing the conduct of clinical studies, product lic
pricing and reimbursement vary from country to country. In all cases, the clinical s
conducted in accordance with GCP and the applicable regulatory requirements and
principles that have their origin in the Declaration of Helsinki. The EU clinical trial
currently is undergoing a transition process mainly aimed at harmonizing and strea
clinical-trial authorization, simplifying adverse-event reporting procedures, improv
supervision of clinical trials and increasing their transparency. Recently enacted Cl
Regulation EU No 536/2014 is intended to ensure that the rules for conducting clin
EU are identical; however, it has not yet been fully implemented.

To obtain regulatory approval of an investigational drug under EU regulatory syste
submit a marketing authorization application, or MAA. The application used to file
U.S. is similar to that required in the EU, with the exception of, among other things
document requirements. Reimbursement approval for the drug by regulatory author
required before a drug may be commercialized. The EU also provides opportunities
exclusivity. For example, in the EU, upon receiving marketing authorization, new c
generally receive eight years of data exclusivity and an additional two years of mar
granted, data exclusivity prevents regulatory authorities in the EU from referencing
data to assess a generic application. During the additional two-year period of marke
generic marketing authorization can be submitted, and the innovator's data may be
generic product can be marketed until the expiration of the market exclusivity. Hov
guarantee that a product will be considered by the EU's regulatory authorities to be
entity, and products may not qualify for data exclusivity. Products receiving orphan
the EU can receive ten years of market exclusivity, during which time no similar m
for the same indication may be placed on the market. An orphan product can also o
additional two years of market exclusivity in the EU for pediatric studies. No exten
supplementary protection certificate can be granted on the basis of pediatric studies
indications.

The criteria for designating an “orphan medicinal product” in the EU are similar in in the U.S. Under Article 3 of Regulation (EC) 141/2000, a medicinal product may orphan if (1) it is intended for the diagnosis, prevention or treatment of a life-threat chronically debilitating condition; (2) either (a) such condition affects no more than persons in the EU when the application is made, or (b) the product, without the ben from orphan status, would not generate sufficient return in the EU to justify investm there exists no satisfactory method of diagnosis, prevention or treatment of such co authorized for marketing in the EU, or if such a method exists, the product will be benefit to those affected by the condition, as defined in Regulation (EC) 847/2000. medicinal products are eligible for financial incentives such as reduction of fees or are, upon grant of a marketing authorization, entitled to ten years of market exclusi approved therapeutic indication. The application for orphan drug designation must before the application for marketing authorization. The applicant will receive a fee marketing authorization application if the orphan drug designation has been granted designation is still pending at the time the marketing authorization is submitted. Or designation does not convey any advantage in, or shorten the duration of, the regula approval process.

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

- the second applicant can establish that its product, although similar, is safer, more 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 Canada and countries in Eastern Eur America or Asia, the requirements governing the conduct of clinical studies, produ establishment licensing, coverage, data protection, pricing and reimbursement vary country. In all cases, again, the clinical studies are conducted in accordance with G applicable regulatory requirements and the ethical principles that have their origin i of Helsinki.

If we fail to comply with applicable foreign regulatory requirements, we may be su other things, fines, suspension or withdrawal of regulatory approvals, product recal import or export, seizure of products, operating restrictions and criminal prosecutio

Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any p for which we obtain regulatory approval. In the U.S. and markets in other countries products for which we receive regulatory approval for commercial sale will depend availability of coverage and adequate reimbursement from third-party payers. Third include government programs such as Medicare or Medicaid, managed care plans, insurers, and other organizations. These third-party payers may deny coverage or re a product or therapy in whole or in part if they determine that the product or therap medically appropriate or necessary. Third-party payers may attempt to control cost

coverage to specific drug products on an approved list, or formulary, which might r
the FDA-approved drug products for a particular indication, and by limiting the am
reimbursement for particular procedures or drug treatments.

The cost of pharmaceuticals continues to generate substantial governmental and thi
interest. We expect that the pharmaceutical industry will experience pricing pressur
trend toward managed healthcare, the increasing influence of managed care organiz
additional legislative proposals. Third-party payers are increasingly challenging the
examining the medical necessity and cost-effectiveness of medical products and se
to their safety and efficacy. We may need to conduct expensive pharmacoeconomic
to demonstrate the medical necessity and cost-effectiveness of our products, in add
required to obtain the FDA approvals. Our product candidates may not be considere
necessary or cost-effective. A payer's decision to provide coverage for a drug prod
that an adequate reimbursement rate will be approved. Adequate third-party reimbu
be available to enable us to maintain price levels sufficient to realize an appropriate
investment in product development.

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

In international markets, reimbursement and healthcare payment systems vary sign
country, and many countries have instituted price ceilings on specific products and
can be no assurance that our products will be considered medically reasonable and
specific indication, that our products will be considered cost-effective by third-part
coverage or an adequate level of reimbursement will be available or that the third-p
reimbursement policies will not adversely affect our ability to sell our products pro

In addition, in many foreign countries, the proposed pricing for a drug must be app
may be lawfully marketed. The requirements governing drug pricing and reimburse
from country to country. For example, the EU provides options for its member state
range of medicinal products for which their national health insurance systems provi
reimbursement and to control the prices of medicinal products for human use. A me
approve a specific price for the medicinal product or it may instead adopt a system
indirect controls on the profitability of the company placing the medicinal product
There can be no assurance that any country that has price controls or reimbursemen
pharmaceutical products will allow favorable reimbursement and pricing arrangem
our products. Historically, products launched in the EU do not follow price structur
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 re
to the healthcare system that could affect our future results of operations. In particu
been and continue to be a number of initiatives at the U.S. federal and state levels t
healthcare costs.

In the U.S., the Medicare Prescription Drug, Improvement, and Modernization Act
Medicare Modernization Act, changed the way Medicare covers and pays for pharm
products. The Medicare Modernization Act expanded Medicare coverage for drug p
elderly by establishing Medicare Part D and introduced a new reimbursement meth
average sales prices for physician administered drugs under Medicare Part B. In ad
legislation provided authority for limiting the number of drugs that will be covered
therapeutic class under the new Medicare Part D program. Cost reduction initiative
provisions of this legislation could decrease the coverage and reimbursement rate th
receive for any of our approved products. While the Medicare Modernization Act a
drug benefits for Medicare beneficiaries, private payers often follow Medicare cove
payment limitations in setting their own reimbursement rates. Therefore, any reduc
reimbursement that results from the Medicare Modernization Act may result in a si
payments from private payers.

Enacted in March 2010, the Patient Protection and Affordable Care Act, as amende
a sweeping law intended to broaden access to health insurance, reduce or constrain
healthcare spending, enhance remedies against healthcare fraud and abuse, add new
requirements for healthcare and health insurance industries, impose new taxes and
pharmaceutical and medical device manufacturers and impose additional health pol
Among other things, PPACA revises the definition of “average manufacturer price”
purposes, which could increase the amount of Medicaid drug rebates to states. Furt
imposes a significant annual fee on companies that manufacture or import branded
products. Substantial new provisions affecting compliance have also been enacted,

our business practices with healthcare practitioners and a significant number of pro
yet, or have only recently become, effective. PPACA may continue to place downw
pharmaceutical pricing, especially under the Medicare program, and may also incre
regulatory burdens and operating costs.

In addition, other legislative changes have been proposed and adopted since PPAC
These new laws may result in reductions in Medicare and other healthcare funding,
have a material adverse effect on our customers and accordingly, our financial oper

We expect that PPACA, as well as other healthcare reform measures that have beer
adopted in the future, may result in more rigorous coverage criteria and in additiona
pressure on the price that we receive for any approved product, and could seriously
revenue. Any reduction in reimbursement from Medicare or other government prog
in a similar reduction in payments from private payers. The implementation of cost
measures or other healthcare reforms may prevent us from being able to generate re
profitability, or commercialize our products.

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

In addition, different pricing and reimbursement schemes exist in other countries. I
Community, governments influence the price of pharmaceutical products through t
reimbursement rules and control of national healthcare systems that fund a large pa
those products to consumers. Some jurisdictions operate positive and negative list s
which products may be marketed only once a reimbursement price has been agreed
these countries may require, as condition of obtaining reimbursement or pricing app
completion of clinical trials that compare the cost-effectiveness of a particular prod
currently available therapies. Other member states allow companies to fix their own
medicines, but monitor and control company profits. The downward pressure on he
general, particularly prescription drugs, has become very intense. As a result, increa
barriers are being erected to the entry of new products. In addition, in some countri
imports from low-priced markets exert a commercial pressure on pricing within a c

Other Healthcare Laws and Compliance Requirements

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

The federal Anti-Kickback Statute prohibits any person, including a prescription dr
(or a party acting on its behalf), from knowingly and willfully soliciting, receiving,
providing remuneration, directly or indirectly, to induce or reward either the referra
individual, or the furnishing, recommending, or arranging for a good or service, for
may be made under a federal healthcare program such as the Medicare and Medica
statute has been interpreted to apply to arrangements between pharmaceutical manu
hand and prescribers, purchasers, and formulary managers on the other. The term “
not defined in the federal Anti-Kickback Statute and has been broadly interpreted t
anything of value, including for example, gifts, discounts, the furnishing of supplie
credit arrangements, payments of cash, waivers of payments, ownership interests a

anything at less than its fair market value. Although there are a number of statutory
regulatory safe harbors protecting certain business arrangements from prosecution,
and safe harbors are drawn narrowly, and practices that involve remuneration inten
prescribing, purchasing or recommending may be subject to scrutiny if they do not
exemption or safe harbor. Our practices may not in all cases meet all of the criteria
protection from federal Anti-Kickback Statute liability. The reach of the Anti-Kick
broadened by PPACA, which, among other things, amends the intent requirement o
Anti-Kickback Statute such that a person or entity no longer needs to have actual k
statute or specific intent to violate it in order to have committed a violation. In addi
provides that the government may assert that a claim including items or services re
violation of the federal Anti-Kickback Statute constitutes a false or fraudulent clain
the federal False Claims Act (discussed below) or the civil monetary penalties statu
imposes fines against any person who is determined to have presented or caused to
claims to a federal healthcare program that the person knows or should know is for
service that was not provided as claimed or is false or fraudulent. Additionally, ma
adopted laws similar to the federal Anti-Kickback Statute, and some of these state p
to referral of patients for healthcare items or services reimbursed by any third-party
the Medicare and Medicaid programs in at least some cases, and do not contain safe

The federal False Claims Act imposes liability on any person or entity that, among
knowingly presents, or causes to be presented, a false or fraudulent claim for paym
healthcare program. The qui tam provisions of the False Claims Act allow a private
bring civil actions on behalf of the federal government alleging that the defendant h
false claim to the federal government, and to share in any monetary recovery. In re
number of suits brought by private individuals has increased dramatically. In additi
have enacted false claims laws analogous to the False Claims Act. Many of these st
where a claim is submitted to any third-party payer and not merely a federal healthc
There are many potential bases for liability under the False Claims Act. Liability ar
when an entity knowingly submits, or causes another to submit, a false claim for re
the federal government. The False Claims Act has been used to assert liability on th
inadequate care, kickbacks and other improper referrals, improperly reported gover
metrics such as Best Price or Average Manufacturer Price, improper use of Medica
detailing the provider of services, improper promotion of off-label uses (i.e., uses n
approved by FDA in a drug's label), and allegations as to misrepresentations with r
services rendered. Our future activities relating to the reporting of discount and reb
and other information affecting federal, provincial, state and third party reimburser
products, and the sale and marketing of our products and our service arrangements
purchases, among other activities, may be subject to scrutiny under these laws. We
predict whether we would be subject to actions under the False Claims Act or a sim
the impact of such actions. However, the cost of defending such claims, as well as a
imposed, could adversely affect our financial performance. Also, the Health Insura
and Accountability Act of 1996, or HIPAA, created several new federal crimes, inc
fraud, and false statements relating to healthcare matters. The healthcare fraud statu
knowingly and willfully executing a scheme to defraud any healthcare benefit prog
private third-party payers. The false statements statute prohibits knowingly and wil
concealing or covering up a material fact or making any materially false, fictitious
statement in connection with the delivery of or payment for healthcare benefits, ite

In addition, we may be subject to, or our marketing activities may be limited by, da
security regulation in the U.S. and foreign jurisdictions in which we conduct our bu
jurisdictions in which we conduct our clinical trials. For example, HIPAA and its im
regulations established uniform federal standards for certain "covered entities" (hea
health plans and healthcare clearinghouses) governing the conduct of certain electr
transactions and protecting the security and privacy of protected health information
Recovery and Reinvestment Act of 2009 included expansion of HIPAA's privacy a
standards called the Health Information Technology for Economic and Clinical Hea
HITECH. Among other things, HITECH makes HIPAA's privacy and security stan
applicable to "business associates"—independent contractors or agents of covered
receive, maintain, or transmit protected health information in connection with prov
or on behalf of a covered entity. HITECH also increased the civil and criminal pena
imposed against covered entities, business associates and possibly other persons, an
attorneys general new authority to file civil actions for damages or injunctions in fe
enforce the federal HIPAA laws and seek attorney's fees and costs associated with
civil actions. In addition, in May 2016, the EU formally adopted the General Data P
Regulation, or GDPR, which applies to all EU member states from May 25, 2018 a
European Union Data Protection Directive. The GDPR has imposed many new or a
requirements including, but not limited to, obtaining consent of the individuals to w
data relates, the nature and scope of notifications provided to the individuals, the se

confidentiality of the personal data, data breach notification and using third party p
connection with the processing of the personal data. Failure to comply with the GD
us to regulatory sanctions, delays in clinical trials, criminal prosecution and/or civil
penalties. Additionally, GDPR creates a direct cause of action by individual data su
GDPR is a complex law and the regulatory guidance is still evolving, including wit
the GDPR should be applied in the context of clinical trials or other transactions fro
gain access to personal data. These changes in the law will increase our costs of co
result in greater legal risks. Other countries maintain different privacy laws that we

There are also an increasing number of federal, state and provincial “sunshine” law
manufacturers to make reports to states on pricing and marketing information. Seve
enacted legislation requiring pharmaceutical companies to, among other things, est
compliance programs, file periodic reports with the state, make periodic public disc
marketing, pricing, clinical trials and other activities, and/or register their sales repr
well as to prohibit pharmacies and other healthcare entities from providing certain
prescribing data to pharmaceutical companies for use in sales and marketing, and to
other sales and marketing practices. In addition, pursuant to a similar federal requir
manufacturers must track and report to the federal government certain payments an
of value made to physicians and other healthcare professionals and teaching hospita
or investment interests held by physicians and their immediate family members. Th
government discloses the reported information on a publicly available website. The
affect our sales, marketing, and other promotional activities by imposing administra
compliance burdens on us. If we fail to track and report as required by these laws o
comply with these laws, we could be subject to the penalty provisions of the pertine
federal authorities.

Because of the breadth of these laws and the narrowness of available statutory and exemptions, it is possible that some of our business activities could be subject to ch one or more of such laws. If our operations are found to be in violation of any of th state laws described above or any other governmental regulations that apply to us, subject to penalties, including criminal and significant civil monetary penalties, dar imprisonment, exclusion from participation in government healthcare programs, in or seizure of products, total or partial suspension of production, denial or withdraw pre-marketing product approvals, private qui tam actions brought by individual wh the name of the government or refusal to allow us to enter into supply contracts, inc government contracts, and the curtailment or restructuring of our operations, any of adversely affect our ability to operate our business and our results of operations. To any of our products are sold in a foreign country, we may be subject to similar fore regulations, which may include, for instance, applicable post-approval requirement safety surveillance, anti-fraud and abuse laws, and implementation of corporate co programs and reporting of payments or transfers of value to healthcare professional

Environmental Matters

Our operations require the use of hazardous materials (including biological materia us to a variety of federal, provincial and local environmental and safety laws and re of the regulations under the current regulatory structure provide for strict liability, l potentially liable without regard to fault or negligence. We could be held liable for fines as a result of our, or someone else's, business operations should contaminatio environment or individual exposure to hazardous substances occur. We cannot prec in laws or development of new regulations will affect our business operations or th compliance.

Employees

As of December 31, 2018, we had 92 employees, including 89 full-time employees employees, 57 were primarily engaged in research and development, 24 of whom h M.D. (or equivalent) degree. None of our employees are represented by a labor uni experienced any work stoppages, and we consider our relations with our employees

Research and Development

We have committed, and expect to continue to commit, significant resources to dev product candidates. We have assembled an experienced research and development scientific and clinical development personnel. Our research and development exper ended December 31, 2018 and 2017 were $23.6 million and $25.6 million, respecti

Manufacturing

We currently rely, and expect to continue to rely, on third parties and our collabora manufacture of our product candidates for pre-clinical and clinical testing, as well a manufacture if our product candidates receive marketing approval. Accordingly, w internally developed any manufacturing facilities or hired related personnel.

To date, we have obtained materials for our product candidates from multiple third
manufacturers. We believe that all of the materials required for the manufacture of
candidates can be obtained from more than one source. However, the manufacturin
each of our product candidates vary and sourcing adequate supplies may be made r
depending on the type of product candidate involved. Our product candidates gener
manufactured in reliable and reproducible synthetic processes from readily availabl
materials. This chemistry generally is amenable to scale-up and does not require un
in the manufacturing process.

Corporate Information

We were incorporated in the Province of British Columbia on November 5, 1996 u
predecessor to the Business Corporations Act (British Columbia) under the name "
Inc." We continued from British Columbia to the federal jurisdiction pursuant to Se
Canada Business Corporations Act, or the CBCA, on May 17, 2000 and concurrent
name to "Xenon Genetics Inc." We registered as an extra-provincial company in Br
July 10, 2000 and changed our name to "Xenon Pharmaceuticals Inc." on August 2
one wholly-owned subsidiary as at December 31, 2018, Xenon Pharmaceuticals US
was incorporated in Delaware on December 2, 2016. Our principal executive office
200 – 3650 Gilmore Way, Burnaby, British Columbia, Canada V5G 4W8, and our
is (604) 484-3300. We are a reporting issuer in British Columbia, Alberta and Onta
shares are not listed on any recognized Canadian stock exchange. Our common sha
NASDAQ Global Market under the symbol "XENE."

Where You Can Find Additional Information

We make available free of charge through our investor relations website, http://investor.xenon-pharma.com, our annual reports, quarterly reports, current rep statements and all amendments to those reports as soon as reasonably practicable a is electronically filed or furnished with the U.S. Securities and Exchange Commiss These reports may also be obtained without charge by contacting Investor Relation Pharmaceuticals Inc., 200 – 3650 Gilmore Way, Burnaby, British Columbia, Canad e-mail: investors@xenon-pharma.com. Our website and the information contained incorporated therein are not intended to be incorporated into this Annual Report on addition, the public may read and copy any materials we file or furnish with the SE Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549 or may obta on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0 the SEC maintains a website that contains reports, proxy and information statement information regarding reports that we file or furnish electronically with them at ww Additional information related to Xenon is also available on SEDAR at www.sedar

Item 1A. Risk Factors

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

Risks Related to Our Financial Condition and Capital Requirements

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

We are a clinical stage biotechnology company and, other than the years ended Dec and 2013, we have recorded net losses in each annual reporting period since incepti we do not expect to have sustained profitability for the foreseeable future. We had n $34.5 million for the year ended December 31, 2018 and an accumulated deficit of of December 31, 2018, which were driven by expenses incurred in connection with development programs and from general and administrative costs associated with o

We have devoted most of our financial resources to research and development, incl and pre-clinical development activities. To date, we have financed our operations th equity securities, funding received from our licensees and collaborators, debt financ lesser extent, government funding. We have not generated any significant revenue f sales and our product candidates will require substantial additional investment befo provide us with any revenue.

We expect to incur significant expenses and increasing operating losses for the fore
we:

- continue our research and pre-clinical and clinical development of our product can
- expand the scope of our clinical studies for our current and prospective product ca
- initiate additional pre-clinical, clinical or other studies for our product candidates;
- change or add additional manufacturers or suppliers and manufacture drug supply
for clinical trials and commercialization;
- seek regulatory and marketing approvals for any of our product candidates that su
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, inclu
limitation, payments to Memorial University of Newfoundland, 1st Order Pharma
other third parties;
- maintain, protect and expand our intellectual property portfolio;
- establish a sales, marketing and distribution infrastructure to commercia
for which we may obtain marketing approval;

- create additional infrastructure to support our operations and our product develop
  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, includin
required by the U.S. Food and Drug Administration, or FDA, the European Medici
EMA, Health Canada, or other regulatory agencies, domestic or foreign, to perfor
other studies in addition to those that we currently anticipate. Our prior losses, com
expected future losses, have had and will continue to have an adverse effect on our
equity.

We have not generated any significant royalty revenue from product sales and may
profitable on a U.S. GAAP basis.

Our ability to generate meaningful revenue and achieve profitability on a U.S. GA
on our ability, alone or with strategic collaborators, to successfully complete the de
and obtain the regulatory approvals necessary to commercialize, our product candi
Substantially all of our revenue since inception has consisted of upfront and milest
associated with our collaboration and license agreements. Revenue from these agre
dependent on successful development of our product candidates by us or our collab
not generated any significant royalty revenue from product sales, and do not otherv
generating revenue from product sales for the foreseeable future, if ever. If any of
candidates fail in clinical trials or do not gain regulatory approval, or if any of our f
any, once approved, fail to achieve market acceptance or adequate market share, w
become profitable. Although we were profitable for the years ended December 31,
we have not been profitable since that time and may not become profitable in subse
Our ability to generate future revenue from product sales depends heavily on our su
success of our collaborators, in:

- completing research, pre-clinical and clinical development of our product candida
- seeking and obtaining regulatory and marketing approvals for product candidates
  complete clinical studies;
- commercializing products for which we obtain regulatory and marketing approval
  collaborator or, if launched independently, by establishing sales, marketing and di
  infrastructure;
- negotiating favorable terms in any collaboration, licensing or other arrangements i
  may enter;
- obtaining market acceptance of products for which we obtain regulatory and mark
  therapies;
- addressing any competing technological and market developments;
- establishing and maintaining supply and manufacturing relationships with third pa
  provide adequate (in amount and quality) products and services to support clinical
  the market demand for any approved products in the future;
- developing sustainable, scalable, reproducible, and transferable manufacturing pro
  our products approved in the future;
- maintaining, protecting, expanding and enforcing our portfolio of intellectual prop
  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 w
candidates receive approval and the availability of insurance coverage and the avai
amount of reimbursement from third-party payers for future products, if any. If we
achieve sufficient revenue to become profitable and remain so, our financial condit
results will be negatively impacted, and the market price of our common shares mi
impacted.

We will likely need to raise additional funding, which may not be available on acce
all. Failure to obtain this necessary capital when needed may force us to delay, limi
product development efforts or other operations.

Since our inception, we have dedicated most of our resources to the discovery and
our proprietary pre-clinical and clinical product candidates, and we expect to conti
substantial resources doing so for the foreseeable future. These expenditures will in
associated with research and development, potential milestone payments and royalt
parties, manufacturing of product candidates and products approved for sale, condu
experiments and clinical trials and obtaining and maintaining regulatory approvals,
commercializing any products later approved for sale. During the year ended Decer
we incurred approximately $23.6 million of costs associated with research and dev
exclusive of costs incurred by our collaborators in developing our product candidat

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

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

We are unable to estimate the funds we will actually require to complete research a
of our product candidates or the funds required to commercialize any resulting proc

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

Our operating plan may change as a result of many factors currently unknown to us
need to seek additional funds sooner than planned, through public or private equity
financings, government or other third-party funding, marketing and distribution arr

other collaborations, strategic alliances and licensing arrangements or a combinatio
approaches. Raising funds in the future may present additional challenges and futu
not be available in sufficient amounts or on terms acceptable to us, if at all.

We may allocate our limited resources to pursue a particular drug candidate or indi
capitalize on other drug candidates or indications that may be more profitable or fo
greater likelihood of success.

Because we have limited financial and management resources, we focus on a limite
research programs and drug candidates. As a result, we may forgo or delay pursuit
with other drug candidates or for other indications that later prove to have greater c
potential. Our resource allocation decisions may cause us to fail to capitalize on via
drugs or profitable market opportunities. Our spend on current and future research
programs and drug candidates for specific indications may not yield any commerci
If we do not accurately evaluate the commercial potential or target market for a par
candidate, we may relinquish valuable rights to that drug candidate through collabo
or other arrangements in cases in which it would have been more advantageous for
development and commercialization rights.

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

In December 2017, we entered into a loan and security agreement with Silicon Vall
to which we borrowed an aggregate principal amount of $12 million. In August 20
into an amended and restated loan and security agreement with Silicon Valley Bank
term loan to us with an aggregate principal amount of $15.5 million, which amount
August 2018. Proceeds from the principal amount borrowed in August 2018 were u
refinance the amounts borrowed under the December 2017 loan and security agreem
$0.5 million final payment fee to Silicon Valley Bank in connection with the refina
December 2017 loan and security agreement.

Borrowings under our amended and restated loan and security agreement are secure
substantially all of our assets except intellectual property and subject to certain othe
loan and security agreement restricts our ability, among other things, to:

- sell, transfer or otherwise dispose of any of our business assets or property, subjec
  exceptions;
- make material changes to our business;
- enter into transactions resulting in significant changes to the voting control of our
- 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 di
  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 amended and restated loan agreement and se
to comply with various affirmative covenants. The covenants and restrictions and c
amended and restated loan and security agreement, as well as any future financing
we may enter into, may restrict our ability to finance our operations, engage in busi
expand or fully pursue our business strategies. Our ability to comply with these cov

affected by events beyond our control, and we may not be able to meet those coven
any of these covenants could result in a default under the amended and restated loa
agreement, which could cause all of the outstanding indebtedness under the facility
immediately due and payable.

If we are unable to generate sufficient cash available to repay our debt obligations
become due and payable, either when they mature, or in the event of a default, we
obtain additional debt or equity financing on favorable terms, if at all, which may
our business operations and financial condition.

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

The terms of any financing arrangements we enter into may adversely affect the ho
rights of our shareholders and the issuance of additional securities, whether equity
the possibility of such issuance, may cause the market price of our common shares
sale of additional equity or convertible securities also would dilute all of our shareh
example, in May 2018, we entered into a sales agreement with Stifel, Nicolaus & C
Incorporated, or Stifel, to sell up to $30.0 million of our common shares, from time
an "at-the-market" equity offering program under which Stifel would act as sales a
aggregate of 3,440,000 common shares under the May 2018 sales agreement for pr
approximately $29.2 million, net of commissions paid, but excluding estimated tra
expenses, before its termination by mutual agreement between us and Stifel in July
connection with our entry into the July 2018 sales agreement with Jefferies LLC, o
Stifel on the same date. Pursuant to the July 2018 sales agreement, Jefferies and Sti
sales agents to sell our common shares having aggregate gross proceeds of up to $5
sold an aggregate of 1,600,000 common shares under the July 2018 sales agreemen
approximately $14.8 million, net of commissions paid, but excluding estimated tra
expenses, before its termination by mutual agreement between us, Jefferies and Stif
2018. In September 2018, we completed an underwritten public offering of 4,500,0
common shares at a public offering price of $14.00 per share for net proceeds of $5
of underwriting discounts and commissions, but before other offering expenses. We
an amended and restated loan and security agreement with Silicon Valley Bank pur
we have borrowed an aggregate principal amount of $15.5 million. Our loan pursua
amended and restated loan and security agreement is secured by substantially all of
intellectual property and the agreement requires us to comply with various affirmat
covenants. The incurrence of additional indebtedness would result in increased fixe
obligations and, potentially, the imposition of additional restrictive covenants. Such
covenants could include limitations on our ability to incur additional debt, limitatio
to acquire, sell or license intellectual property rights and other operating restriction
adversely impact our ability to conduct our business. We could also be required to
through arrangements with collaborators or otherwise at an earlier stage than otherw
desirable resulting in the loss of rights to some of our product candidates or other u
any of which may have a material adverse effect on our business, operating results
addition, any additional fundraising efforts may divert our management from their
activities, which may adversely affect our ability to develop and commercialize our
candidates.

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

Global credit and financial markets experienced extreme disruptions at various poi
decade, characterized by diminished liquidity and credit availability, declines in co
confidence, declines in economic growth, increases in unemployment rates, and un
economic stability. If another such disruption in credit and financial markets and de
confidence in economic conditions occurs, our business may be adversely affected.
credit markets were to deteriorate significantly in the future, it may make any neces
equity financing more difficult to complete, more costly, and more dilutive. Failure
necessary financing in a timely manner and on favorable terms could have a materi

on our growth strategy, financial performance and the market price of our common
require us to delay or abandon development or commercialization plans. In addition
that one or more of our current collaborators, service providers, manufacturers and
would not survive or be able to meet their commitments to us under such circumsta
could directly affect our ability to attain our operating goals on schedule and on bu

We are subject to risks associated with currency fluctuations which could impact o
operations.

As of December 31, 2018, approximately 7% of our cash and cash equivalents and
securities were denominated in Canadian dollars. We incur significant expenses in
in connection with our operations in Canada. We do not currently engage in foreig
hedging arrangements for our Canadian dollar expenditures, and, consequently, for
fluctuations may adversely affect our earnings; however, in the future, we may eng
rate hedging activities in an effort to mitigate the impact of exchange rate fluctuati
technique we implement may fail to be effective. If our hedging activities are not e
in currency exchange rates may have a more significant impact on the market price
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 and XEN901, along with
candidates we expect to enter clinical development, which include XEN496 and XE
pre-clinical compounds, are in varying stages of development and will require subs
development, testing and regulatory approval prior to commercialization. It may be
years before these product candidates or any of our other product candidates receiv
approval, if ever. If any of our product candidates fail to become approved product
growth prospects, operating results and financial condition may be adversely affect
in the market price of our common shares could result.

We and our collaborators face substantial competition in the markets for our produ
which may result in others discovering, developing or commercializing products be
so more successfully than we or our collaborators do.

The biotechnology and pharmaceutical industries are characterized by rapidly adva
technologies, intense competition and a strong emphasis on proprietary products. W
competition in target discovery and product development from many different appr
sources, including major pharmaceutical, specialty pharmaceutical and biotechnolo
academic institutions, governmental agencies, as well as public and private researc
Any product candidates that we or our collaborators successfully develop and comm
compete with existing products and any new products that may become available in

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

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

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

To the extent that we are unable to compete effectively against one or more of our c
these areas, our business will not grow and our financial condition, results of opera

market price of our common shares may suffer.

If XEN496, XEN1101 or XEN901 were approved for the treatment of epilepsy, we they could potentially compete with each other and other anti-epileptic drugs, or Al used AEDs include phenytoin, levetiracetam, carbamazepine, clobazam, lamotrigin oxcarbazepine, topiramate, lacosamide, perampanel and cannabidiol, among others currently no FDA-approved treatments indicated for KCNQ2 epileptic encephalopa known as KCNQ2-EE or EIEE7) or for SCN8A epileptic encephalopathy (otherwis SCN8A-EE or EIEE13), an early infantile epileptic encephalopathy due to gain-of- mutations in the SCN8A gene that encodes the Nav1.6 sodium channel. We are not companies that are developing selective Nav1.6 inhibitors for the treatment of epile other AEDs in development that could potentially compete with XEN496, XEN110 including products in development from UCB, Inc., Zogenix, Inc., Sage Therapeuti Pharmaceuticals, Inc., SciFluor Lifesciences, Inc., Knopp Biosciences LLC, and Up Laboratories, Inc.

Drug discovery and development for various pain applications is intensely competi
large number of approved products for neuropathic pain, inflammatory pain and oth
indications. These approved products include capsaicin, celecoxib, lidocaine, narco
gabapentin, and pregabalin. We are also aware of development programs at several
and biotechnology companies that are developing Nav1.7 inhibitors or other sodium
inhibitors for the treatment of pain, including Amgen Inc., AstraZeneca PLC, Biog
Bristol-Myers Squibb Company, Dainippon Sumitomo Co., Ltd., Eli Lilly and Com
NeuroQuest Inc., Newron Pharmaceuticals SpA, Vertex Pharmaceuticals Inc., Voy
Therapeutics, Inc. and Chromocell Corporation in collaboration with its partner As
Moreover, we are aware of various other product candidates in development that ta
mechanisms of action to treat various pain indications, including calcium channel i
growth factor inhibitors, and Nav1.8 inhibitors.

We have no marketed proprietary products and have not yet advanced a product ca
Phase 2 clinical trials, which makes it difficult to assess our ability to develop our f
candidates and commercialize any resulting products independently.

As a company, we have no experience in Phase 3 and later stage clinical developme
regulatory requirements or the commercialization of products. We have not yet dem
ability to independently and repeatedly conduct clinical development after Phase 2,
conduct an international multi-center clinical trial, conduct a pivotal clinical trial, o
approval, manufacture drug product on a commercial scale or arrange for a third pa
our behalf, and commercialize therapeutic products. We will need to develop such
to execute on our business strategy to develop and independently commercialize pr
for orphan and niche indications. To execute on our business plan for the developm
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 w
  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, regulato
  commercialization activities.

If we are unsuccessful in accomplishing these objectives, we will not be able to dev
commercialize any future product candidates independently and could fail to realiz
advantages of doing so.

If we are not successful in discovering, acquiring or in-licensing product candidates
XEN496, XEN1101, XEN901, and XEN007, our ability to expand our business and
strategic objectives may be impaired.

We have built a product development pipeline by identifying product candidates ei
internal research efforts or though acquiring or in-licensing other product candidate
internal discovery efforts have yielded multiple development candidates, including
our internal discovery efforts and our assessment of potential acquisition or in-licen
opportunities require substantial technical, financial and human resources, regardle
identify any viable product candidates.

If we are unable to identify additional product candidates suitable for clinical devel
commercialization either from our internal research efforts or though acquiring or i
product candidates or technologies, we may not be able to obtain product revenue i
which likely would result in significant harm to our financial position and adversel
market price of our common shares.

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

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

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

If our discovery activities fail to identify novel targets for drug discovery, or such t
unsuitable for treating human disease, or we are unable to develop product candida
specificity and selectivity for such targets, we will fail to develop viable products.
develop and commercialize viable products, we will not achieve commercial succe

If we fail to attract and retain senior management and key personnel, we may be un
successfully develop our product candidates, perform our obligations under our col
agreements, conduct our clinical trials and commercialize our product candidates.

Our success depends in part on our continued ability to attract, retain and motivate
management, clinical and scientific personnel.

We could experience difficulties attracting and retaining qualified employees as co
qualified personnel in the biotechnology and pharmaceutical field is intense. We ar
dependent upon our senior management, particularly Dr. Simon Pimstone, our Chie
Officer, and Mr. Ian Mortimer, our President and Chief Financial Officer, as well a
employees. The loss of services of either of these individuals or one or more of our
of senior management could materially delay or even prevent the successful develo
product candidates.

In addition, we will need to hire additional personnel as we expand our clinical dev
activities and develop commercial capabilities, including a sales infrastructure to su
independent commercialization efforts. We may not be able to attract and retain pe
acceptable terms given the competition among numerous pharmaceutical and biote
companies for individuals with similar skill sets. The inability to recruit or loss of t
executive or key employee may impede the progress of our research, development
commercialization objectives.

Our employees, collaborators and other personnel may engage in misconduct or oth
activities, including non-compliance with regulatory standards and requirements ar

We are exposed to the risk of fraud or other misconduct by our employees, collabo
principal investigators, consultants and commercial partners. Misconduct by these
include intentional failures to comply with the regulations of the FDA, EMA, Healt
other regulators, provide accurate information to the FDA, EMA, Health Canada ar
regulators, comply with data privacy and security and healthcare fraud and abuse la
regulations in the U.S. and abroad, report financial information or data accurately c
unauthorized activities to us. In particular, sales, marketing and business arrangeme
healthcare industry are subject to extensive laws and regulations intended to preven
misconduct, kickbacks, self-dealing and other abusive practices. Additionally, laws
privacy and security, including the federal Health Insurance Portability and Accoun
1996, or HIPAA, as amended by the Health Information Technology for Economic
Health Act of 2009, or HITECH, the General Data Protection Regulation (EU) 201
and the Personal Information Protection and Electronic Documents Act, or PIPEDA
comparable laws in other jurisdictions, may impose obligations with respect to safe
privacy, use, security and transmission of individually identifiable health informati
material or information we have obtained through our direct-to-patient web-based r
approach for identifying patients with rare or extreme phenotypes or patients identi
trials.

Various laws and regulations may restrict or prohibit a wide range of pricing, disco
and promotion, sales commission, customer incentive programs and other business
Any misconduct could also involve the improper use of information obtained in the
clinical studies, which could result in regulatory sanctions and cause serious harm t
We have adopted a code of conduct applicable to all of our employees, officers, dir
representatives, including consultants, but it is not always possible to identify and d
and the precautions we take to detect and prevent misconduct may not be effective
unknown or unmanaged risks or losses or in protecting us from governmental inves
actions or lawsuits stemming from a failure to comply with these laws and regulati
actions are instituted against us, and we are not successful in defending ourselves o
rights, those actions could have a significant impact on our business, including the
significant fines or other sanctions, exclusion from participation in government hea
or the curtailment or restructuring of our operations.

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

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

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

Dr. Simon Pimstone devotes a small amount of his time to clinical work outside of
company, conducting, generally, one outpatient clinic per week on average. Future
impose significant added responsibilities on members of management, and our mar
need to divert a disproportionate amount of its attention away from our day-to-day
devote a substantial amount of time to managing these growth activities.

If we are unable to effectively manage our growth, our expenses may increase mor
our ability to generate and grow revenue could be reduced, and we may not be able
business strategy. Our future financial performance and our ability to commercializ
candidates and compete effectively will depend, in part, on our ability to effectively
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 da
malware, unauthorized access, terrorism, war, or natural disasters could interrupt o
partner operations. For example, the loss of pre-clinical trial data, data from comple
clinical trials for our product candidates or other confidential information could res
our regulatory filings and development efforts, significantly increase our costs and
adverse impacts to our business. To the extent that any disruption or cybersecurity
result in a loss of or damage to our data, or inappropriate disclosure of confidential
information, we could incur liability and other remediation costs, and the developm
product candidates could be delayed. While we have implemented security measure
have not detected a cybersecurity breach of our systems nor experienced a material
our internal computer systems and the external systems and services used by our th
manufacturers, or CMOs, third-party contract research organizations, or CROs, or
consultants, directors and partners remain potentially vulnerable to damage from th

A variety of risks associated with international operations could materially adverse
business.

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

- different regulatory requirements for initiating clinical trials and maintaining appr
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 pa
economies and markets;
    - differing and multiple payor reimbursement regimes, government payo
    self-pay systems;
- compliance with tax, employment, immigration and labor laws for employees livi
abroad;

- foreign currency fluctuations, which could result in increased operating e
  reduced revenue, and other obligations of doing business in another coun
- workforce uncertainty in countries where labor unrest is more common than in No
- likelihood of potential or actual violations of domestic and internationa
  laws, such as the U.S. Foreign Corrupt Practices Act and the U.K. Brib
  U.S. and international import, export and re-export control and sanctio
  regulations, which likelihood may increase with an increase of operatio
  jurisdictions;
- tighter restrictions on privacy and the collection and use of data, including clinical
  material, may apply in jurisdictions outside of North America; and
- business interruptions resulting from geopolitical actions, including war and terro
  disasters including earthquakes, typhoons, floods and fires.

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

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

Generally, for any taxable year in which 75% or more of our gross income is passiv
least 50% of the average quarterly value of our assets (which may be determined in
market value of our common shares, which is subject to change) are held for the pr
produce, passive income, we would be characterized as a passive foreign investmer
PFIC, for U.S. federal income tax purposes. Based on the price of our common sha
composition of our gross income and gross assets, we believe that we may be deem
taxable years ended December 31, 2018 and 2017, and we could be a PFIC in subs
status as a PFIC is a fact-intensive determination made on an annual basis, and we
any assurance regarding our PFIC status for the taxable years ending December 31,
or for future taxable years.

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

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

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

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

There is a risk that we may become subject to income tax in jurisdictions outside o
United States, if under the laws of any such jurisdiction, we are considered to be ca
or business there or earn income that is considered to be sourced there and we do n
exemption. In jurisdictions where we do not believe we are subject to tax, we can p
certainty that tax authorities in those jurisdictions will not subject one or more tax y
examination. Tax examinations are often complex as tax authorities may disagree w
of items reported by us, the result of which could have a material adverse effect on
results and financial condition.

Acquisitions or joint ventures could disrupt our business, cause dilution to our shar
otherwise harm our business.

We actively evaluate various strategic transactions on an ongoing basis and may ac
businesses, products or technologies as well as pursue strategic alliances, joint vent
investments in complementary businesses. Any of these transactions could be mate
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
- unanticipated liabilities related to acquired companies;
- difficulties integrating acquired personnel, technologies and operations into our ex
- retention of key employees;

- diversion of management time and focus from operating our business to
  strategic alliances or joint ventures or acquisition integration challenges;
- increases in our expenses and reductions in our cash available for operations and
- possible write-offs or impairment charges relating to acquired businesses.

Foreign acquisitions involve unique risks in addition to those mentioned above, inc
related to integration of operations across different cultures and languages, currenc
particular economic, political and regulatory risks associated with specific countrie

Also, the anticipated benefit of any strategic alliance, joint venture or acquisition m
materialize. Future acquisitions or dispositions could result in potentially dilutive is
equity securities, the incurrence of debt, contingent liabilities or amortization exper
of goodwill, any of which could harm our financial condition. We cannot predict th
or size of future joint ventures or acquisitions, or the effect that any such transactio
our operating results.

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

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

The regulatory approval process is expensive and the time required to obtain appro
FDA, EMA, Health Canada or other regulatory authorities in other jurisdictions to
is uncertain and may take years. Whether regulatory approval will be granted is unp
depends upon numerous factors, including the substantial discretion of the regulato
Approval policies, regulations, or the type and amount of pre-clinical and clinical d
gain approval may change during the course of a product candidate's clinical devel
vary among jurisdictions. Moreover, pre-clinical and clinical data are often suscept
interpretations and analyses, and even if the pre-clinical studies show promising res
trials are successfully completed, we cannot guarantee that the FDA, EMA, Health
regulatory authorities in other jurisdictions will interpret the results as we do, and m
manufacturing-related studies or non-clinical studies could be required before we s
candidates for approval. Many companies that have believed their product candidat
satisfactorily in pre-clinical studies and clinical trials have nonetheless failed to obt
approval of their products. To the extent that the results of our studies and trials are
to the FDA, EMA, Health Canada or other regulatory authorities in other jurisdictio
a marketing application, approval of our product candidates may be significantly de
be required to expend significant additional resources, which may not be available
additional trials in support of potential approval of our product candidates. It is also
none of our existing product candidates or any of our future product candidates wil
regulatory approval, even if we expend substantial time and resources seeking such

Our product candidates could fail to receive regulatory approval for many reasons,
following:

- the FDA, EMA, Health Canada or other regulatory authorities may disagree with t
  implementation of our or our collaborators' clinical trials;

- we or our collaborators may be unable to demonstrate to the satisfaction of the FD Canada or other regulatory authorities that a product candidate is safe and effectiv indication;
  - the results of clinical trials may not meet the level of statistical significan FDA, EMA, Health Canada or other regulatory authorities for approval;
- we, or our collaborators, may be unable to demonstrate that a product candidate's benefits outweigh its safety risks;
- the FDA, EMA, Health Canada or other regulatory authorities may disagree with collaborators' interpretation of data from pre-clinical studies or clinical trials;
  - the data collected from clinical trials of our product candidates may not b support the submission of a New Drug Application, or NDA, or other sub obtain regulatory approval in the U.S. or elsewhere;
- the FDA, EMA, Health Canada or other regulatory authorities may fail to approve manufacturing processes, controls or facilities of third-party manufacturers with w collaborators contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA, EMA, Health Canada or other reg authorities may significantly change in a manner rendering our or our collaborator insufficient for approval.

Even if we, or our collaborators, obtain approval for a particular product, regulatory
grant approval contingent on the performance of costly post-approval clinical trials
a product with a label that does not include the labeling claims necessary or desirab
successful commercialization of that product.

In addition, because there may be approved treatments for some of the diseases for
seek approval, in order to receive regulatory approval, we may need to demonstrate
that the product candidates we develop to treat those diseases are not only safe and
may need to be compared to existing products, which may make it more difficult fo
candidates to receive regulatory approval or adequate reimbursement.

Clinical drug development involves a lengthy and expensive process with uncertain
uncertain outcomes. If clinical trials are prolonged, delayed or not completed, we, o
collaborators, may be unable to commercialize our product candidates on a timely b

Clinical testing of product candidates is expensive and, depending on the stage of d
take a substantial period of time to complete. Clinical trial outcomes are inherently
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 rela

- side effects or adverse events in study participants presenting an unacceptable safe
- inability to reach agreement with prospective CROs and clinical trial sites, or the l
  agreements;
- failure of third-party contractors, such as CROs, or investigators to comply with re
  requirements, including GCPs;
    - delay or failure in obtaining the necessary approvals from regulators or in
      review boards, or IRBs, in order to commence a clinical trial at a prospec
      their suspension or termination of a clinical trial once commenced;
- a requirement to undertake and complete additional pre-clinical studies to generate
  support the continued clinical development of a product candidate or submission o
- inability to enroll sufficient patients to complete a protocol, particularly in orphan
- 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, stability and distribution;
- our inability to add new or additional clinical trial sites;
- our inability to manufacture, or obtain from third parties, adequate supply of drug
  product sufficient to complete our pre-clinical studies and clinical trials; and
- governmental or regulatory delays and changes in regulatory requirements, policy

The results of any Phase 3 or other pivotal clinical trial may not be adequate to sup
approval. These clinical trials are lengthy and, with respect to non-orphan indicatio
involve many hundreds to thousands of patients. In addition, if the FDA, EMA, He
another regulator disagrees with our or our collaborator's choice of the key testing
primary endpoint, the results for the primary endpoint are not robust or significant
control group of patients not receiving the experimental therapy, or our statistical a
inconclusive, such regulator may refuse to approve our product candidate in the reg
has jurisdiction. The FDA, EMA, Health Canada or other regulators also may requi
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, collaborators, by the IRBs of the institutions in which such trial is being conducted Safety Monitoring Board for such trial, or by the FDA, EMA, Health Canada or oth authorities. Such authorities may impose such a suspension or termination due to a factors, including failure to conduct the clinical trial in accordance with regulatory our clinical protocols, inspection of the clinical trial operations or trial site by the F Health Canada or other regulatory authorities resulting in the imposition of a clinic candidate manufacturing problems, unforeseen safety issues or adverse side effects demonstrate a benefit from using a drug, changes in governmental regulations or ac actions or lack of adequate funding to continue the clinical trial. In addition, delays safety concerns arising from trials or other clinical data regarding another company candidate in the same compound class as one of ours.

Additionally, changes in applicable regulatory requirements and guidance may occ need to amend clinical trial protocols to reflect these changes or to include addition could yield important scientific information critical to our overall development stra protocol amendment process often requires review and approval by several review regulatory agencies and scientific, regulatory and ethics boards and IRBs. These pr amendments may not be accepted by the review bodies in the form submitted, or at impact costs, timing or successful completion of a clinical trial.

If we or our collaborators experience delays in the completion of, or termination of of one of our product candidates, the commercial prospects of the product candidat could shorten the period during which we may have the exclusive right to commerc products under patent protection, and our or our collaborators' ability to commence generate product revenue from the product will be delayed. In addition, any delays clinical trials will increase our costs and slow down our product candidate develop approval process. Any of these occurrences may harm our business, financial condi prospects significantly. In addition, many of the factors that cause, or lead to, a dela commencement or completion of clinical trials may also ultimately lead to the deni approval of our product candidates.

XEN496 targets an ultra-orphan indication of KCNQ-EE and the FDA has indicate pivotal trial in approximately 20 patients may be sufficient to demonstrate effective in KCNQ2-EE provided that no new or unexpected safety issues arise during drug Even though we believe the safety and efficacy profile of ezogabine, the active ingr XEN496, in pediatric patients with KCNQ-EE generated to date by others appears on published clinical case reports, the clinical development of XEN496 may not be the FDA or other regulatory authorities may require additional data in more patient be able to generate sufficient data for approval in this patient population.

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

Before obtaining regulatory approvals for the commercial sale of our products, we through lengthy, complex and expensive pre-clinical testing and clinical trials that candidate is both safe and effective for use in each target indication. Clinical trials demonstrate safety and efficacy of the product candidate studied for the target indic 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 which there is relatively limited clinical experience, and our clinical trials may use and measurement methodologies or subjective patient feedback, which adds a layer our clinical trials and may delay regulatory approval. In addition, our focus on orph markets may cause us to select target indications that are in more challenging thera Related to our collaboration with Genentech, clinical trials for pain are inherently d conduct. The primary measure of pain is based on subjective patient feedback, whi influenced by factors outside of our control and can vary widely from day to day fo patient, from patient to patient, and from site to site within a clinical study. The pla 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 tria
able to obtain regulatory approval or commercialize these product candidates and p
case, we would need to develop other compounds and conduct associated pre-clinic
clinical trials, as well as potentially seek additional financing, all of which would h
adverse effect on our business, growth prospects, operating results, financial condit
operations.

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

We may not be able to identify, recruit and enroll a sufficient number of patients, o
required or desired characteristics to achieve diversity in a study, to complete our c
a timely manner. Patient enrollment for clinical trials for ultra-orphan, orphan and r
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 ultra-orphan, orphan and niche indications, such SCN8A-EE, other early infantile epileptic encephalopathies, or EIEEs, AHC and H significant recruitment challenges for clinical trials and a full understanding of the populations is still relatively unknown. Many of these patients may not be suitable participate in our clinical trials. This means that we or our collaborators generally v multi-site and potentially multi-national trials, which can be expensive and require coordination and supervision. If we experience delays in completing our clinical tri could result in increased costs, delays in advancing our product development, delay effectiveness of our product candidates or termination of the clinical studies altoget are successful in receiving regulatory approval, the limited patient populations in u orphan and niche indications may impact the successful commercialization of our p and reimbursement rates, which could impact revenue and our ability to achieve pr

ACH, KCNQ2-EE and SCN8A-EE have no FDA-approved treatments, and the clin required to obtain approval are not well defined.

Given the nature of some of the rare diseases we are seeking to treat, we may have clinical endpoints to be tested in our studies, which can lead to some subjectivity in study results and could result in regulatory agencies not agreeing with the validity o or our interpretation of the clinical data, and therefore denying approval. In post-Ph the illness of the subjects in our studies and the nature of their rare diseases, we ma or choose to conduct certain studies on an open-label basis. Additionally, we may e interim clinical data at multiple time points during the studies, which could introdu study results, or result in statistical penalties being applied to the data, and potentia denial of approval.

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

Although we may file new intellectual property to protect XEN496 and XEN007, t candidates are not currently covered by any patent and we may have to rely solely o designation to gain market exclusivity for these drug candidates. Currently, this des market exclusivity in the U.S. and the EU for seven years and ten years, respectivel the first such product approved for such orphan indication. This market exclusivity however, pertain to indications other than those for which the drug was specifically approval, nor does it prevent other types of drugs from receiving orphan designatio these same indications. Further, even after an orphan drug is approved, the FDA ca approve a drug with similar chemical structure for the same condition if the FDA c 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 sati designation criteria or can be lost altogether if the marketing authorization holder c second orphan drug application or cannot supply enough drug, or when a second ap demonstrates its drug is “clinically superior” to the original orphan drug. XEN007, evaluating for the potential treatment of HM or AHC, has received orphan drug des FDA for each indication we are developing. We have also received orphan drug de

the FDA for XEN496, a drug we are evaluating for the treatment of KCNQ2-EE. If
drug designations for other indications or in other jurisdictions, we may fail to rece
drug designations and, even if we succeed, such orphan drug designations may fail
maintain orphan drug exclusivity upon approval, which would harm our competitiv
Further, not all jurisdictions, such as Canada, have orphan drug designations. Neith
designation, nor rare pediatric disease, or RPD, designation gives the drug any adva
regulatory review or approval process.

The FDA has granted RPD designation to XEN007 for treatment of AHC; however able to realize any value from such designation.

Our product candidate XEN007 has received RPD designation from the FDA for th AHC. The FDA defines a "rare pediatric disease" as a disease that affects fewer tha individuals in the U.S. primarily under the age of 18 years old. Under the FDA's RP review voucher program, upon the approval of a new drug application, NDA, or a b application, BLA, for the treatment of an RPD, the sponsor of such application wou a priority review voucher that can be used to obtain priority review for a subsequen There is no assurance we will receive a RPD priority review voucher or that use of review voucher will result in a faster review or approval for a subsequent marketing Further, this program has been subject to criticism, including by the FDA, and it is even if we obtain approval for XEN007 and qualify for such a priority review vouc may no longer be in effect at the time of XEN007 approval. Also, although priority may be freely sold or transferred to third parties, there is no guarantee that we will any value if we were to sell a priority review voucher to a third party.

Results of pre-clinical studies may not be predictive of clinical trial results and resu clinical trials may not be predictive of the results of later-stage clinical trials and th clinical trials may not satisfy the requirements of the FDA, EMA, Health Canada o regulatory authorities.

The results of pre-clinical studies, either generated by us, such as for XEN901, or b by other third parties from which we have in-licensed or acquired a drug candidate, XEN1101, may not be predictive of results in clinical testing. Moreover, pre-clinica often be difficult to compare across different studies for a variety of reasons, includ experimental protocols and techniques, personnel, equipment and other factors, wh pre-clinical results less reliable and predictive of clinical trial results. In addition, p data or case reports from third parties or early clinical trial data of our product cand predictive of the results of later-stage clinical trials. Interpretation of results from e smaller, studies that suggest a clinically meaningful response in some patients, requ Results from later stages of clinical trials enrolling more patients may fail to show t and efficacy results or otherwise fail to be consistent with the results of earlier trial product candidate. Later clinical trial results may not replicate earlier clinical trials reasons, including differences in trial design, different trial endpoints (or lack of tri exploratory studies), patient population, number of patients, patient selection criter drug dosage and formulation and lack of statistical power in the earlier studies. The are enhanced where the diseases under study lack established clinical endpoints, va of efficacy, as is often the case with orphan diseases for which no drugs have been previously and where the product candidates target novel mechanisms. For example knowledge, XEN901 is the first selective Nav1.6 sodium channel inhibitor being de treatment of epilepsy and therefore standard pre-clinical studies may not be adequa efficacy in a clinical trial due to its novel molecular mechanism.

Further, our product candidates may not be approved even if they achieve their prin our Phase 3 clinical trials. The FDA, EMA, Health Canada or foreign regulatory au disagree with our trial design and our interpretation of data from pre-clinical studie trials. In addition, any of these regulatory authorities may change its requirements f of a product candidate even after reviewing and providing comments or advice on a

pivotal clinical trial that, if successful, would potentially form the basis for an appli
approval by the FDA, EMA, Health Canada or another regulatory authority. Furthe
these regulatory authorities may also approve our product candidates for a narrowe
we request or may grant approval contingent on the performance of costly post-ma
trials.

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

As product candidates are developed through pre-clinical to late stage clinical trials
approval and commercialization, it is common that various aspects of the developm
such as manufacturing methods and formulation, are altered along the way in an ef
products, processes and results. Such changes carry the risk that they will not achie
objectives. Any of these changes could cause our product candidates to perform dif
affect the results of planned clinical trials or other future clinical trials conducted w
materials. This could delay completion of clinical trials, require the conduct of brid
trials or the repetition of one or more clinical trials, increase clinical trial costs, dela
product candidates and/or jeopardize our or our collaborators' ability to commence
generate revenue.

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

Sales of our approved products, if any, will be subject to the regulatory requiremen marketing approval in the countries in which we obtain regulatory approval, and w regulatory approval to commercialize our product candidates in North America, the additional foreign countries. Clinical trials conducted in one country may not be ac regulatory authorities in other countries and regulatory approval in one country doe approval in any other country, while a failure or delay in obtaining regulatory appro country may have a negative effect on the regulatory approval process in others. Fo approval in the U.S. by the FDA does not ensure approval by regulatory authorities countries or jurisdictions, and approval by one foreign regulatory authority does no by the FDA, EMA, Health Canada or regulatory authorities in other countries. App vary among jurisdictions and can be lengthy and expensive, and involve requireme administrative review periods different from, and greater than, those in the U.S., in pre-clinical studies or clinical trials. Even if our product candidates are approved, r approval for any product may be withdrawn by the regulatory authorities in a partic

Even if a product is approved, the FDA, EMA, Health Canada, or another applicabl authority, as the case may be, may limit the indications for which the product may require extensive warnings on the product labeling or require expensive and time-c trials or reporting as conditions of approval. In many countries outside the U.S., a p must be approved for reimbursement before it can be approved for sale in that coun 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 o for approval of product candidates with which we must comply prior to marketing Obtaining foreign regulatory approvals and compliance with such foreign regulator could result in significant delays, difficulties and costs for us and could delay or pr introduction of our current and any future products, in certain countries.

If we fail to receive applicable marketing approvals or comply with the regulatory international markets, our target market will be reduced and our ability to realize th potential of our product candidates will be harmed and our business will be adverse

We work with outside scientists and their institutions in executing our business stra developing product candidates. These scientists may have other commitments or co which could limit our access to their expertise and harm our ability to develop viab candidates.

We work with scientific advisors and collaborators at academic institutions and oth institutions. These scientists and collaborators are not our employees; rather, they s independent contractors or the primary investigators under research collaboration a we have with their sponsoring academic or research institution. Such scientists and may have other commitments that would limit their availability to us. Although our advisors generally agree not to do competing work, if an actual or potential conflict between their work for us and their work for another entity arises, we may lose thei also possible that some of our valuable proprietary knowledge may become publicl

these scientific advisors if they breach their confidentiality agreements with us, wh
competitive harm to our business.

Risks Related to Commercialization

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

We do not have a sales or marketing infrastructure and, as a company, have no sale
distribution experience. Our strategy involves, in part, building our own commercia
selectively commercialize future products in niche or orphan indications. Where we
involvement would advance our business, we seek to retain the right to participate
development and commercialization of such products.

To develop internal sales, distribution and marketing capabilities, we will have to i
amounts of financial and management resources, some of which will need to be co
any confirmation that any of our proprietary product candidates will be approved. F
products for which we decide to perform sales, marketing and distribution function
could face a number of additional risks, including:

- our inability to recruit and retain adequate numbers of qualified sales and marketi
develop alternative sales channels;

- the inability of sales personnel to obtain access to physicians or an inadequate nu physicians to prescribe any future products;
- the lack of complementary products to be offered by sales personnel, which may p competitive disadvantage relative to companies with more extensive product lines
- unforeseen costs and expenses associated with creating and maintaining sales and marketing organization.

Where and when appropriate, we may elect to utilize contract sales forces or distrib assist in the commercialization of our product candidates. If we enter into arrangem parties to perform sales, marketing and distribution services for a product, the resul the profitability from this revenue to us is likely to be lower than if we had sold, ma distributed that product ourselves. In addition, we may not be successful in enterin arrangements with third parties to sell, market, and distribute our product candidate unable to do so on terms that are favorable to us. We likely will have little control o parties, and any of these third parties may fail to devote the necessary resources an market, and distribute our current or any future products effectively.

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

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

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

- restrictions on the marketing or manufacturing of the product, withdrawal of the p market or voluntary or mandatory product recalls;
- fines, warning letters or holds on any post-approval clinical trials;
- refusal by the FDA, EMA, Health Canada or another applicable regulatory author pending applications or supplements to approved applications filed by us or our co suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of pr 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 results of operations.

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

Some of our product candidates focus on treatments for rare and ultra-rare diseases
number of patients who have some of the diseases that we are targeting, our profita
depend on successfully identifying patients with these rare and ultra-rare diseases.
reported estimates of the prevalence of these diseases are based on studies of small
population in specific geographic areas, which are then extrapolated to estimate the
the diseases in the U.S. or elsewhere. Our projections of both the number of people
diseases, as well as the subset of people with these diseases who have the potential
treatment with our product candidates, are based on our internal estimates. These
been derived from a variety of sources, including scientific literature, surveys of cli
foundations, and market research, and may prove to be incorrect. Further, new stud
the estimated incidence or prevalence of these diseases, and, as a result, the numbe
these diseases may turn out to be lower than expected. Our effort to identify patien
we seek to treat is in early stages, and we cannot accurately predict the number of p
treatment might be possible. Additionally, the potentially addressable patient popu
our product candidates may be limited or may not be amenable to treatment with ou
candidates, and new patients may become increasingly difficult to identify or gain a
would adversely affect our results of operations and our business. Finally, even if
significant market share for our product candidates, because the potential target pop
small, we may never achieve profitability despite obtaining such significant market

Even if we or our collaborators receive approval to commercialize our products, un
regulations and challenging third-party coverage and reimbursement practices coul
business.

Our or any collaborators' ability to commercialize any products successfully will d
the extent to which coverage and reimbursement for these products and related trea
available from government healthcare programs, private health insurers, managed c
other organizations. Government authorities and third-party payers, such as private
and health maintenance organizations, decide which medications they will pay for a
reimbursement levels. A primary trend in the U.S. healthcare industry is cost conta
Government authorities and third-party payers have attempted to control costs by li
and the amount of reimbursement for particular medications. Increasingly, third-pa
requiring that drug companies provide them with predetermined discounts from list
challenging the prices charged for medical products. We cannot be sure that covera
reimbursement will be available for any product that we or any collaborator comme
reimbursement is available, the level of reimbursement. In addition, coverage and r
may impact the demand for, or the price of, any product candidate for which we or
obtains marketing approval. If coverage and reimbursement are not available or rei
available only to limited levels, we or our collaborators may not be able to successf
commercialize any product candidate for which marketing approval is obtained.

There may be significant delays in obtaining coverage and reimbursement for newl
and coverage may be more limited than the purposes for which the drug is approve
EMA, Health Canada or other regulatory authorities. Moreover, eligibility for cove

reimbursement does not imply that a drug will be paid for in all cases or at a rate th
costs, including research, development, manufacture, sale and distribution expense
reimbursement levels for new drugs, if applicable, may also be insufficient to cove
collaborator's costs and may not be made permanent. Reimbursement rates may va
use of the drug and the clinical setting in which it is used, may be based on reimbu
already set for lower cost drugs and may be incorporated into existing payments fo
Net prices for drugs may be reduced by mandatory discounts or rebates required by
healthcare programs or private payers and by any future relaxation of laws that pres
imports of drugs from countries where they may be sold at lower prices than in the
payers often rely upon Medicare coverage policy and payment limitations in setting
reimbursement policies. Our or any collaborator's inability to promptly obtain cove
profitable payment rates from both government-funded and private payers for any a
that we or our collaborators develop could have a material adverse effect on our op
our ability to raise capital needed to commercialize products and our overall financ

Our target patient populations in orphan and niche indications, such as KCNQ2-EE
AHC, are relatively small. In order for therapies that are designed to treat smaller p
to be commercially viable, the pricing, coverage and reimbursement for such therap
higher, on a relative basis, to account for the lack of volume. Accordingly, we will
implement pricing, coverage and reimbursement strategies for any approved produc
for the smaller potential market size. If we are unable to establish or sustain covera
reimbursement for our current and any future products from third party payers or th
the adoption of those products and sales revenue will be adversely affected, which,
adversely affect the ability to market or sell those products.

Recently enacted and future legislation may increase the difficulty and cost for us t
any products that we or our collaborators develop and affect the prices we may obt

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

For example, in 2010, the Patient Protection and Affordable Care Act, as amended
Care and Education Reconciliation Act of 2010, collectively, the PPACA, was enac
measures that have significantly changed, or will significantly change, the way hea
financed by both governmental and private insurers. The Trump administration and
through legislation, executive orders and other measures, has taken action to repeal
certain provisions of the PPACA. The impact of any such changes on us and the ph
industry as a whole is currently unknown. In addition, there has been heightened go
scrutiny over the manner in which manufacturers set prices for their marketed prod
resulted in several Congressional inquiries and proposed and enacted federal and st
designed to, among other things, bring more transparency to product pricing, reviev
between pricing and manufacturer patient programs, and reform government progra
reimbursement methodologies for pharmaceutical products. Congress and the Trum
have each indicated that it will continue to seek new legislative and/or administrati
control drug costs. These and other health reform measures that are implemented m
material adverse effect on our result of operations.

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

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

We cannot predict the likelihood, nature or extent of government regulation that ma
future legislation or administrative action, either in the U.S. or abroad. If we or our
slow or unable to adapt to changes in existing requirements or the adoption of new

policies, or if we or our collaborators are not able to maintain regulatory compliance candidates may lose any marketing approval that may have been obtained and we n or sustain profitability, which would adversely affect our business.

Foreign governments tend to impose strict price controls, which may adversely affe profitability.

In most foreign countries, particularly those in the EU, prescription drug pricing an reimbursement is subject to governmental control. In those countries that impose pr pricing negotiations with governmental authorities can take considerable time after marketing approval for a product. To obtain reimbursement or pricing approval in s 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 markete countries, the pricing review period begins after marketing or product licensing app In some foreign markets, prescription pharmaceutical pricing remains subject to co governmental control even after initial approval is granted. As a result, we or our co might obtain marketing approval for a product in a particular country, but then be s regulations that delay commercial launch of the product, possibly for lengthy time negatively impact the revenue that is generated from the sale of the product in that reimbursement of such products is unavailable or limited in scope or amount, or if unsatisfactory levels, or if there is competition from lower priced cross-border sales will be negatively affected.

Risks Related to Our Dependence on Third Parties

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

We have no control over the resources, time and effort that our collaborators may d
programs and limited access to information regarding or resulting from such progra
dependent on our collaborators, including Genentech and Merck, to fund and condu
and any clinical development of product candidates under our collaboration with ea
for the successful regulatory approval, marketing and commercialization of one or
products or product candidates. Such success will be subject to significant uncertai

Our ability to recognize revenue from successful collaborations may be impaired b
including:

- a collaborator may shift its priorities and resources away from our programs due t
business strategies, or a merger, acquisition, sale or downsizing of its company or
- a collaborator may cease development in therapeutic areas which are the subject o
alliances;
- a collaborator may change the success criteria for a particular program or product
delaying or ceasing development of such program or candidate;
- a significant delay in initiation of certain development activities by a collaborator
payment of milestones tied to such activities, thereby impacting our ability to func
activities;
- a collaborator could develop a product that competes, either directly or indirectly,
or future products, if any;
- a collaborator with commercialization obligations may not commit su
or human resources to the marketing, distribution or sale of a product
- a collaborator with manufacturing responsibilities may encounter regulatory, reso
issues and be unable to meet demand requirements;
- a collaborator may exercise its rights under the agreement to terminate our collabo
- a dispute may arise between us and a collaborator concerning the research or deve
product candidate, commercialization of a product or payment of royalties or mile
any of which could result in a delay in milestones, royalty payments or terminatio
and possibly resulting in costly litigation or arbitration which may divert manage
resources;
- a collaborator may not adequately protect the intellectual property rights associate
or product candidate; and
- a collaborator may use our proprietary information or intellectual property in such
invite litigation from a third party.

If our collaborators do not perform in the manner we expect or fulfill their responsi
timely manner, or at all, the clinical development, regulatory approval and commer
could be delayed, terminated or be commercially unsuccessful. Conflicts between u
collaborators may arise. In the event of termination of one or more of our collabora
it may become necessary for us to assume the responsibility of any terminated proc
candidates at our own expense or seek new collaborators. In that event, we would l
to limit the size and scope of one or more of our independent programs or increase
and seek additional funding which may not be available on acceptable terms or at a

business would be materially and adversely affected.

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

In the ordinary course, we engage with other biotechnology and pharmaceutical co
discuss potential in-licensing, out-licensing, alliances and other strategic transactio
to enter into these types of transactions to enhance and accelerate the development
product candidates and the commercialization of any resulting products. We face si
competition in seeking appropriate collaborators and the negotiation process is time
complex. Moreover, we may not be successful in our efforts to establish other colla
other alternative arrangements for any future product candidates because our resear
development pipeline may be insufficient, our product candidates may be deemed t
of a stage of development for collaboration effort and/or third parties may view our
candidates as lacking the requisite potential to demonstrate safety and efficacy. Eve
successful in our efforts to establish collaborations, the terms that we agree upon m
favorable to us and we may not be able to maintain such collaborations if, for exam
or approval of a product candidate is delayed or sales of an approved product are di

If any of our existing collaboration agreements is terminated, or if we determine tha
other product collaborations is in our best interest but we either fail to enter into, de
into or fail to maintain such collaborations:

- the development of certain of our current or future product candidates may be term
  delayed;
- our cash expenditures related to development of our product candidates would inc
  significantly and we may need to seek additional financing sooner than expected;
- we may be required to hire additional employees or otherwise develop expertise, s
  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 candida
- the competitiveness of any product that is commercialized could be reduced.

We intend to rely on third-party manufacturers to produce our clinical product cand
Any failure by a third-party manufacturer to produce acceptable supplies for us ma
our ability to initiate or complete our clinical trials or commercialize approved proc

We do not currently own or operate any manufacturing facilities nor do we have sig
manufacturing experience or personnel. We rely on our collaborators to manufactu
candidates licensed to them or work with multiple CMOs to produce sufficient qua
materials required for the manufacture of our product candidates for pre-clinical tes
trials and intend to do so for the commercial manufacture of our products. If we are
arrange for such third-party manufacturing sources, or fail to do so on commerciall
terms, we may not be able to successfully produce sufficient supply of product can
be delayed in doing so. Such failure or substantial delay could materially harm our

Reliance on third-party manufacturers entails risks to which we would not be subje
manufactured product candidates ourselves, including reliance on the third party fo
compliance and quality control and assurance, volume production, the possibility o
manufacturing agreement by the third party because of factors beyond our control (
failure to synthesize and manufacture our product candidates in accordance with ou
specifications) and the possibility of termination or nonrenewal of the agreement by

at a time that is costly or damaging to us. In addition, the FDA, EMA, Health Cana
regulatory authorities require that our product candidates be manufactured accordin
similar foreign standards. Pharmaceutical manufacturers and their subcontractors a
register their facilities and/or products manufactured at the time of submission of th
application and then annually thereafter with the FDA, EMA, Health Canada and o
agencies. They are also subject to periodic unannounced inspections by the FDA, E
Canada and other regulatory agencies. Any subsequent discovery of problems with
manufacturing or laboratory facility used by us or our collaborators, may result in r
product or on the manufacturing or laboratory facility, including product recall, sus
manufacturing, product seizure or a voluntary withdrawal of the drug from the mar
by our third-party manufacturers to comply with cGMP or any failure to deliver su
of product candidates in a timely manner, could lead to a delay in, or failure to obta
approval of any of our product candidates.

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

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

If we are unable to maintain or enter into agreements with these third parties on acc
if any such engagement is terminated prematurely, we may be unable to enroll patie
basis or otherwise conduct our trials in the manner we anticipate. In addition, there
that these third parties will devote adequate time and resources to our studies or per
by our contract or in accordance with regulatory requirements, including maintenan
trial information regarding our product candidates. If these third parties fail to meet
deadlines, fail to transfer to us any regulatory information in a timely manner, fail t
protocols or fail to act in accordance with regulatory requirements or our agreemen
they otherwise perform in a substandard manner or in a way that compromises the
accuracy of their activities or the data they obtain, then clinical trials of our future p
candidates may be extended or delayed with additional costs incurred, or our data m
by the FDA, EMA, Health Canada or other regulatory agencies.

Ultimately, we are responsible for ensuring that each of our clinical trials is conduc
with the applicable protocol, legal, regulatory and scientific standards, and our relia
parties does not relieve us of our regulatory responsibilities.

We and our CROs are required to comply with current good laboratory practices, o
and cGMP regulations and guidelines enforced by the FDA, Health Canada, the co
authorities of the member states of the European Economic Area and comparable fo
authorities for products in clinical development. Regulatory authorities enforce thes
through periodic inspections of clinical trial sponsors, principal investigators, clinic
manufacturing facilities, nonclinical testing facilities and other contractors. If we or
CROs fail to comply with these applicable regulations, the clinical data generated i
studies and clinical trials may be deemed unreliable and our submission of marketi
may be delayed or the FDA, EMA, Health Canada or another regulatory authority m
perform additional clinical trials before approving our marketing applications. Upo
FDA, EMA, Health Canada or another regulatory authority could determine that an
trials fail or have failed to comply with applicable cGCP regulations. In addition, o
must be conducted with product produced under the cGMP regulations enforced by
Health Canada and other regulatory authorities, and our clinical trials may require a
test subjects. Our failure to comply with cGLP, cGCP and cGMP regulations may r
repeat clinical trials, which would delay the regulatory approval process and increa
Moreover, our business may be implicated if any of our CROs violates federal or st
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 lo
information on patients enrolled in our ongoing clinical trials unless we are able to
of those patients to another qualified clinical trial site. Further, if our relationship w
CROs is terminated, we may be unable to enter into arrangements with alternative
commercially reasonable terms, or at all.

Switching or adding CROs or other suppliers can involve substantial cost and requi
management time and focus. In addition, there is a natural transition period when a
supplier commences work. As a result, delays may occur, which can materially imp
meet our desired clinical development timelines. If we are required to seek alternat
arrangements, the resulting delays and potential inability to find a suitable replacem
materially and adversely impact our business.

Risks Related to Intellectual Property

We could be unsuccessful in obtaining or maintaining adequate patent protection fo
our products or product candidates.

Our commercial success will depend, in large part, on our ability to obtain and mai
other intellectual property protection with respect to our product candidates. We ev
patent portfolio in the ordinary course of business to enhance patent protection in a
strategic focus and in key markets for our potential products and abandon existing
applications related to terminated development programs or areas of low strategic i
Patents might not be issued or granted with respect to our patent applications that a
pending, and issued or granted patents might later be found to be invalid or unenfo
interpreted in a manner that does not adequately protect our current product or any
or fail to otherwise provide us with any competitive advantage. The patent position
and pharmaceutical companies is generally uncertain because it involves complex l
considerations. The standards applied by the U.S. Patent and Trademark Office, or
foreign patent offices in granting patents are not always applied uniformly or predi
example, there is no uniform worldwide policy regarding patentable subject matter
claims allowable in biotechnology and pharmaceutical patents. Consequently, pate
from our pending patent applications. As such, we do not know the degree of future
we will have on our proprietary products and technology, if any, and a failure to ob
intellectual property protection with respect to our product candidates and proprieta
could have a material adverse impact on our business.

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

Our intellectual property rights will not necessarily provide us with competitive ad

The degree of future protection afforded by our intellectual property rights is uncer
intellectual property rights have limitations, and may not adequately protect our bu
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
covered by the claims of the patents that we or our collaborators own or have excl
-

others may independently develop similar or alternative technologies without infri
intellectual property rights;

- issued patents that we own or have exclusively licensed may not provide us with a
advantages, or may be held invalid or unenforceable, as a result of legal challenge
competitors;
- we may obtain patents for certain compounds many years before we obtain marke
products containing such compounds, and because patents have a limited life, whi
run out prior to the commercial sale of the related product, the commercial value o
be limited;
- our competitors might conduct research and development activities in countries w
have patent rights and then use the information learned from such activities to dev
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 righ
extent as the laws of the U.S., or we may fail to apply for or obtain adequate intell
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 p
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 mate
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 thr
world would be prohibitively expensive, and our intellectual property rights in som
outside the U.S. can be less extensive than those in the U.S. In addition, the laws of
countries do not protect intellectual property rights to the same extent as federal an
U.S. Consequently, we may not be able to prevent third parties from practicing our
countries outside the U.S., or from selling or importing products made using our in
into the U.S. or other jurisdictions. Competitors may use our technologies in jurisdi
have not obtained patent protection to develop their own products and further, may
infringing products to territories where we have patent protection, but enforcement
as that in the U.S. These products may compete with our current or future products
patents or other intellectual property rights may not be effective or sufficient to pre
competing.

Many companies have encountered significant problems in protecting and defendin
property rights in foreign jurisdictions. The legal systems of certain countries, parti
developing countries, do not favor the enforcement of patents, trade secrets and oth
property protection, particularly those relating to biotechnology products, which co
difficult for us to stop the infringement of our patents or marketing of competing pr
violation of our proprietary rights generally. Proceedings to enforce our patent righ
jurisdictions could result in substantial costs and divert our efforts and attention fro
of our business, could put our patents at risk of being invalidated or interpreted nar
patent applications at risk of not issuing and could provoke third parties to assert cl
We may not prevail in any lawsuits that we initiate and the damages or other remed
any, may not be commercially meaningful. Accordingly, our efforts to enforce our
property rights around the world may be inadequate to obtain a significant commer
from the intellectual property that we develop or license.

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

Any of our intellectual property rights could be challenged or invalidated despite m
to obtain patent and other intellectual property protection with respect to our produ
proprietary technology. For example, if we were to initiate legal proceedings again
enforce a patent covering one of our product candidates, the defendant could counte
patent is invalid and/or unenforceable. In patent litigation in the U.S. and in some o
defendant counterclaims alleging invalidity and/or unenforceability are commonpla
validity challenge could be an alleged failure to meet any of several statutory requi
example, lack of novelty, obviousness or non-enablement. Grounds for an unenforc
could be an allegation that someone connected with prosecution of the patent withh
information from the USPTO or the applicable foreign counterpart, or made a misle
during prosecution. A litigant or the USPTO itself could challenge our patents on th
we believe that we have conducted our patent prosecution in accordance with the d
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 b
prior art, of which we and the patent examiner were unaware during prosecution. If
to prevail on a legal assertion of invalidity and/or unenforceability, we would lose a
perhaps all, of the patent protection on a product candidate. Even if a defendant doe
legal assertion of invalidity and/or unenforceability, our patent claims may be cons
that would limit our ability to enforce such claims against the defendant and others
defending such a challenge, particularly in a foreign jurisdiction, and any resulting
protection could have a material adverse impact on one or more of our product can
business.

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

Patent protection and patent prosecution for some of our product candidates is depe
ability to assert patents and defend them against claims of invalidity is maintained b

There have been and may be times in the future when certain patents that relate to o
candidates or any approved products are controlled by our licensees or licensors. A
under such arrangements, have rights to consult with our collaborators on actions ta
back-up rights of prosecution and enforcement, we have in the past and may in the
rights to prosecute and maintain patents and patent applications within our portfolio
ability to assert such patents against infringers. For example, currently some of the
the patent portfolio for novel Nav1.7 inhibitors are held by Genentech.

If any current or future licensee or licensor with rights to prosecute, assert or defen
to our product candidates fails to appropriately prosecute and maintain patent prote
covering any of our product candidates, or if patents covering any of our product ca
asserted against infringers or defended against claims of invalidity or unenforceabil
which adversely affects such coverage, our ability to develop and commercialize an
candidate may be adversely affected and we may not be able to prevent competitor
using and selling competing products.

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

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

Interference proceedings, derivation proceedings, entitlement proceedings, ex parte
inter partes reexamination, inter partes review, post-grant review, and opposition pr
provoked by third parties or brought by the USPTO or any foreign patent authority
challenge inventorship, ownership, claim scope, or validity of our patent applicatio
unfavorable outcome could require us to cease using the related technology or to at
rights to it from the prevailing party. Our business could be harmed if the prevailing
offer us a license on commercially reasonable terms, if any license is offered at all.
interference proceedings may fail and, even if successful, may result in substantial
our management and other employees.

We may not be able to prevent, alone or with our licensors, misappropriation of our
confidential information, particularly in countries where the laws may not protect th
fully as in the U.S. Furthermore, because of the substantial amount of discovery req
connection with intellectual property litigation, there is a risk that some of our conf
information could be compromised by disclosure during this type of litigation. In a
could be public announcements of the results of hearings, motions or other interim
developments. If securities analysts or investors perceive these results to be negativ
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
other intellectual property rights of third parties could result in costly litigation or c
substantial time and money to resolve, even if litigation is avoided.

Our commercial success depends upon our ability to develop product candidates an
products that may be approved in the future, using our proprietary technology with
intellectual property rights of others. Our product or product candidates or any uses
now and in the future infringe third-party patents or other intellectual property righ
might allege that we or our collaborators are infringing their patent rights or that we
misappropriated their trade secrets, or that we are otherwise violating their intellect

rights, whether with respect to the manner in which we have conducted our researc
composition, use or manufacture of the compounds we have developed or are deve
collaborators. Such third parties might resort to litigation against us or other parties
to indemnify, which litigation could be based on either existing intellectual propert
property that arises in the future.

It is possible that relevant patents or patent applications held by third parties will co
candidates at the time of launch and we may also fail to identify, relevant patents o
applications held by third parties that cover our product candidates. For example, a
before November 29, 2000, and certain applications filed after that date that will no
the U.S. remain confidential until patents issue. Other patent applications in the U.S
other jurisdictions are published approximately 18 months after the earliest filing fo
is claimed, with such earliest filing date being commonly referred to as the priority
Furthermore, publication of discoveries in the scientific or patent literature often la
discoveries. Therefore, we cannot be certain that we or our collaborators were the f
the first to file patent applications on, our product candidates or for their uses, or th
candidates will not infringe patents that are currently issued or that are issued in the
event that a third party has also filed a patent application covering one of our produ
similar invention, we may have to participate in an adversarial proceeding, known a
declared by the USPTO or its foreign counterpart to determine priority of invention
pending patent applications and patents which have been published can, subject to c
limitations, be later amended in a manner that could cover our current or future pro
their use.

Defending against claims of patent infringement, misappropriation of trade secrets violations of intellectual property rights could be costly and time consuming, regar outcome. Thus, even if we were to ultimately prevail, or to settle at an early stage, could burden us with substantial unanticipated costs. In addition, litigation or threa could result in significant demands on the time and attention of our management te them from the pursuit of other company business. Claims that our product candidat use of our future products infringe, misappropriate or otherwise violate third-party 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 finan They are, therefore, likely to be able to sustain the costs of complex intellectual pro longer than we could. In addition, the uncertainties associated with litigation could adverse effect on our ability to raise the funds necessary to conduct our clinical tria internal research programs, in-license needed technology, or enter into strategic co would help us bring our product candidates to market.

In addition, any future intellectual property litigation, interference or other adminis proceedings will result in additional expense and distraction of our personnel. An a in such litigation or proceedings may expose us or any future strategic collaborator proprietary position, expose us to significant liabilities, or require us to seek licens available on commercially acceptable terms, if at all, each of which could have a m effect on our business.

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

If third parties successfully assert their intellectual property rights against us, we m from using certain aspects of our technology or barred from developing and comm products. Prohibitions against using certain technologies, or prohibitions against co certain products, could be imposed by a court or by a settlement agreement betwee plaintiff. In addition, if we are unsuccessful in defending against allegations that w misappropriated or otherwise violated patent or other intellectual property rights of be forced to pay substantial damage awards to the plaintiff. There is inevitable unc intellectual property litigation and we could lose, even if the case against us is wea litigation leads to an outcome unfavorable to us, we may be required to obtain a lic intellectual property owner in order to continue our research and development prog any resulting product. It is possible that the necessary license will not be available commercially acceptable terms, or at all. Alternatively, we may be required to mod our current or future products, if any, in order to avoid infringing or otherwise viol intellectual property rights. This may not be technically or commercially feasible, products less competitive, or may delay or prevent the entry of those products to th the foregoing could limit our research and development activities, our ability to co or more product candidates, or both.

In order to avoid or settle potential claims with respect to any patent or other intell rights of third parties, we may choose or be required to seek a license from a third required to pay license fees or royalties or both, which could be substantial. These be available on acceptable terms, or at all. Even if we or any future collaborators w a license, the rights may be nonexclusive, which could result in our competitors ga

same intellectual property. Ultimately, we could be prevented from commercializin
forced, by court order or otherwise, to cease some or all aspects of our business ope
result of actual or threatened patent or other intellectual property claims, we are un
licenses on acceptable terms. Further, we could be found liable for significant mon
a result of claims of intellectual property infringement. In the future, we may receiv
license and demands to license from third parties claiming that we are infringing th
property or owe license fees and, even if such claims are without merit, we could fa
avoid or settle such claims.

If Genentech, Merck or other collaborators license or otherwise acquire rights to in
property controlled by a third party in various circumstances, for example, where a
not be legally developed or commercialized in a country without the third-party int
right or, where it is decided that it would be useful to acquire such third-party right
commercialize the product, they are eligible under our collaboration agreements to
payments payable to us on a product-by-product basis and, in certain cases, on a co
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 a
commercialization rights to our product candidates or technology from third parties
license rights that are important to our business.

Under our existing license and other agreements, including those associated with o
XEN007 programs, we are subject to various obligations, including diligence oblig
development and commercialization obligations, as well as potential milestone pay
obligations. If we fail to comply with any of these obligations or otherwise breach
agreements, our licensing partners may have the right to terminate the applicable li
in part. Generally, the loss of any one of our current licenses, or any other license w
the future, could materially harm our business, prospects, financial condition and re
operations.

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

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

Recent court decisions could increase the uncertainties and costs surrounding the p
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 P
Myriad Genetics, Inc., held that isolated DNA sequences are not patentable. In Dec
USPTO issued its Interim Guidance on Patent Subject Matter Eligibility, in which i
Myriad's "marked difference" standard for patent subject matter eligibility to all po
products. This standard applies to patent claims that recite not only nucleic acids (s
Myriad), but also other subject matter that could be considered a natural product, su
proteins, extracts, organisms, antibodies, chemicals, and minerals. As a consequenc
decision and the USPTO’s Interim Guidance, if any of our future product candidate
DNA, peptides, proteins or the like, we will not be able to obtain patents in the U.S
novel gene targets that we discover, which could limit our ability to prevent third p
developing drugs directed against such targets.

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

Depending upon the timing, duration and specifics of FDA marketing approval of o
candidates, if any, one or more U.S. patents may be eligible for limited patent term
the Hatch-Waxman Act. The Hatch-Waxman Act permits a patent restoration term

years as compensation for patent term lost during clinical testing of the product and FDA regulatory review process. However, we may not be granted an extension bec example, failing to apply within applicable deadlines, failing to apply prior to expir patents or otherwise failing to satisfy applicable requirements. Moreover, the applic 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 su less than we request, the period during which we will have the right to exclusively product will be shortened and our competitors may obtain approval of competing p 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 ma to secure those registrations could adversely affect our business.

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

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

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

Risks Related to Our Industry

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

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

We currently carry product liability insurance of $10,000,000 per occurrence and $
aggregate limit. We believe our product liability insurance coverage is appropriate
current clinical programs; however, we may not be able to maintain insurance cove
reasonable cost or in sufficient amounts to protect us against losses due to liability.
obtain marketing approval for product candidates, we intend to expand our insuran
include the sale of commercial products; however, we may then be unable to obtai
insurance on commercially reasonable terms or in adequate amounts. On occasion,
have been awarded in class action lawsuits based on drugs or medical treatments th
unanticipated adverse effects. A successful product liability claim or series of clai

us could cause the market price of our common shares to decline and, if judgments
insurance coverage, could adversely affect our future results of operations and busi

Patients with certain of the diseases targeted by our product candidates are often al
and advanced stages of disease and have both known and unknown significant pre-
potentially life-threatening conditions. During the course of treatment, patients may
events, including death, for reasons that may be related to our product candidates. S
subject us to costly litigation, require us to pay substantial amounts of money to inj
delay, negatively impact or end our opportunity to receive or maintain regulatory a
those product candidates, or require us to suspend or abandon our commercializatio
a circumstance in which we do not believe that an adverse event is related to our pr
investigation into the circumstance may be time-consuming or inconclusive. These
may interrupt our sales efforts, delay our regulatory approval process in other coun
and limit the type of regulatory approvals our product candidates receive or mainta
these factors, a product liability claim, even if successfully defended, could have a
effect on our business, financial condition or results of operations.

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

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

- the federal Anti-Kickback Statute, which prohibits, among other things, persons fr
and willfully soliciting, offering, receiving or providing remuneration, directly or
or in kind, to induce or reward either the referral of an individual for, or the purch
recommendation of, any good or service for which payment may be made under fe
healthcare programs such as Medicare and Medicaid;
- federal civil and criminal false claims laws and civil monetary penalty laws, inclu
False Claims Act, which impose criminal and civil penalties, including civil whist
tam actions, against individuals or entities for knowingly presenting, or causing to
the federal government, including the Medicare and Medicaid programs, or other
claims for payment that are false or fraudulent or making a false statement to avoi
conceal an obligation to pay money to the federal government;
    - HIPAA, which imposes criminal and civil liability for executing a scheme
    healthcare benefit program and making false statements relating to healthc
- the federal Open Payments program; and
- analogous state and foreign laws and regulations, such as state anti-kickback and f
which may apply to sales or marketing arrangements and claims involving healthc
services reimbursed by non-governmental third-party payers, including private ins
foreign laws that require pharmaceutical companies to comply with the pharmaceu
voluntary compliance guidelines and the relevant compliance guidance promulgat
government or otherwise restrict payments that may be made to healthcare provid
foreign laws that require drug manufacturers to report information related to paym
physicians and other healthcare providers or marketing expenditures; state and loc
the registration of pharmaceutical sales representatives; and state and foreign laws
collection, export, privacy, use and security of biological materials and health info
certain circumstances, many of which differ from each other in significant ways a
the same effect, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties will comply with
healthcare laws and regulations may involve substantial costs. It is possible that go
authorities will conclude that our business practices may not comply with current o
regulations or case law involving applicable fraud and abuse or other healthcare law
regulations. If our operations are found to be in violation of any of these laws or an

governmental regulations that may apply to us, we may be subject to significant civ
administrative penalties, including, without limitation, damages, fines, imprisonme
from participation in government healthcare programs, such as Medicare and Medi
oversight and reporting obligations, and the curtailment or restructuring of our oper
could have a material adverse effect on our business. If any of the physicians or oth
entities with whom we expect to do business, including our collaborators, is found
compliance with applicable laws, it may be subject to criminal, civil or administrati
including exclusions from participation in government healthcare programs, which
materially affect our business.

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

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

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

Our headquarters are located in Burnaby, British Columbia, Canada. We are vulner
disasters such as earthquakes that could disrupt our operations. If a natural disaster,
fire or other event occurred that prevented us from using all or a significant portion
headquarters, that damaged critical infrastructure, such as the manufacturing facilit
or that otherwise disrupted operations, it may be difficult or, in certain cases, impos
continue our business for a substantial period of time. Although we carry insurance
and other natural disasters, we may not carry sufficient business interruption insura
compensate us for all losses that may occur. The disaster recovery and business con
have in place may not be adequate in the event of a serious disaster or similar event
substantial expenses as a result of a natural disaster or earthquake, which could hav
adverse effect on our business. In addition, we may lose samples or other valuable
occurrence of any of the foregoing could have a material adverse effect on our busi

Risks Related to the Securities Markets and Ownership of Our Common Shares

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

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

- announcements by us or our competitors of new products, product candidates or n
existing products, significant contracts, commercial relationships or capital comm
timing of these introductions or announcements;

- actions by any of our collaborators regarding our product candidates they are deve
announcements regarding clinical or regulatory decisions or developments or our
- unanticipated serious safety concerns related to the use of any of our products and
candidates;
- results from or delays of clinical trials of our product candidates;
- failure to obtain or delays in obtaining or maintaining product approvals or clearar
regulatory authorities;
- adverse regulatory or reimbursement announcements;
- announcements by us or our competitors of significant acquisitions, strategic colla
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 s
clinical investigators;
- regulatory or legal developments in Canada, the U.S. or other countries;
- developments or disputes concerning patent applications, issued patents or other p
- the recruitment or departure of key scientific or management personnel;
- our ability to successfully commercialize our future product candidates we develo
if approved;

- the level of expenses related to any of our product candidates or clinical developm
- actual or anticipated changes in estimates as to financial results, development time recommendations by securities analysts;
- actual or anticipated quarterly variations in our financial results or those of our co
- 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 over volume of our common shares;
- failure to comply with covenants or make required payments under loan agreemen
- 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 biote and other factors that may be unrelated to our operating performance or the operat of our competitors, including changes in market valuations of similar companies;
- the other factors described in this “Risk Factors” section.

In addition, the stock market in general, and Nasdaq and the biopharmaceutical ind particular, have from time to time experienced volatility that often has been unrelat operating performance of the underlying companies. These broad market and indus may adversely affect the market price of our common shares, regardless of our ope performance. In several recent situations where the market price of a stock has beer of that stock have instituted securities class action litigation against the company th stock. If any of our shareholders were to bring a lawsuit against us, the defense and the lawsuit could be costly and divert the time and attention of our management an operating results.

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

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

In addition, in the future, we may issue additional common shares, preferred shares or debt securities convertible into common shares in connection with a financing, a litigation settlement, employee arrangements or otherwise. Any such issuance coul substantial dilution to our existing shareholders and could cause the market price o shares to decline.

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

Provisions in our articles and our by-laws, as well as certain provisions under the C Corporations Act, or CBCA, and applicable Canadian securities laws, may discour prevent a merger, acquisition, tender offer or other change in control of us that shar consider favorable, including transactions in which they might otherwise receive a common shares. These provisions could also limit the price that investors might be the future for our common shares, thereby depressing the market price of our comm

addition, because our board of directors is responsible for appointing the members
management team, these provisions may frustrate or prevent any attempts by our sh
replace or remove our current management by making it more difficult for shareho
members of our board of directors. Among other things, these provisions include t

- shareholders cannot amend our articles unless such amendment is approved by sha holding at least two-thirds of the shares entitled to vote on such approval;
- shareholders must give advance notice to nominate directors or to submit proposal consideration at shareholders' meetings; and
- applicable Canadian securities laws generally require, subject to certain exception to remain open for 105 days and that more than 50% of the outstanding securities offeror be tendered before the offeror may take up the securities.

Any provision in our articles, by-laws, under the CBCA or under any applicable Ca
law that has the effect of delaying or deterring a change in control could limit the o
shareholders to receive a premium for their common shares, and could also affect t
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. M
directors and officers reside outside of the U.S., and all or a substantial portion of t
as all or a substantial portion of our assets are located outside the U.S. As a result,
difficult for investors to effect service of process within the U.S. upon us and certai
and officers or to enforce judgments obtained against us or such persons, in U.S. co
action, including actions predicated upon the civil liability provisions of U.S. feder
or any other laws of the U.S. Additionally, rights predicated solely upon civil liabi
U.S. federal securities laws or any other laws of the U.S. may not be enforceable in
or actions to enforce judgments obtained in U.S. courts, brought in Canadian courts
in the Province of British Columbia.

We are governed by the corporate and securities laws of Canada which in some cas
different effect on shareholders than the corporate laws of Delaware, U.S. and U.S.

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

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 assuran
able to maintain an active trading market on Nasdaq or any other exchange in the fu
market for our common shares is not maintained, it may be difficult for our shareho
common shares they have purchased without depressing the market price for the co
at all. Further, an inactive market may also impair our ability to raise capital by sell
common shares and may impair our ability to enter into strategic collaborations or
companies or products by using our common shares as consideration.

We are an emerging growth company and a smaller reporting company, and any de
to comply only with certain reduced reporting and disclosure requirements applicab
companies could make our common shares less attractive to investors.

We are an “emerging growth company,” as defined in the Jumpstart Our Business S
2012, or the JOBS Act and a “smaller reporting company,” as defined under the Se
Act of 1934, as amended, or the Exchange Act. For as long as we continue to be an
company or smaller reporting company, we may choose to take advantage of exem
various reporting requirements applicable to other public companies that are not en
companies or smaller reporting companies, including, but not limited to, reduced di
obligations regarding executive compensation in our periodic reports and proxy sta
exemptions from the requirements of holding a nonbinding advisory vote on execu
and shareholder approval of any golden parachute payments not previously approv
emerging growth company, the JOBS Act allows us to delay adoption of new or re
pronouncements applicable to public companies until such pronouncements are ma
private companies. However, we previously decided to “opt out” of such extended
and as a result, we will comply with new or revised accounting standards on the rel
which adoption of such standards is required for non-emerging growth companies.
the JOBS Act provides that our decision to opt out of the extended transition perio
with new or revised accounting standards is irrevocable. In addition, as a smaller re
we are only required to include two years of audited financial statements in our ann
as an emerging growth company, we are not required to have our independent regis
accounting firm audit our internal control over financial reporting under Section 40
Sarbanes-Oxley Act.

We expect to lose our status as an emerging growth company five years following t
our initial public offering, or on December 31, 2019. We will remain a smaller rep
so long as, as of June 30 of the preceding year, (i) the market value of our common
non-affiliates, or our public float, is less than $250 million; or (ii) we have annual r
$100 million and either we have no public float or our public float is less than $700

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
reduce future disclosure, there may be a less active trading market for our common
market price of our common shares may be more volatile.

Complying with the laws and regulations affecting public companies will increase
demands on management and could harm our operating results and our ability to ac
our financial condition, results of operations or cash flows, which may adversely af
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 com
incur significant legal, accounting and other expenses. In addition, the Sarbanes-Ox
or the Sarbanes-Oxley Act, and the related rules and regulations subsequently impl
SEC, the applicable Canadian securities regulators and Nasdaq impose numerous re
public companies, including requiring changes in corporate governance practices. A
Exchange Act requires, among other things, that we file annual, quarterly and curre
respect to our business and operating results. Our management and other personnel
continue to devote a substantial amount of time to compliance with these laws and
These requirements have increased and will continue to increase our legal, account
compliance costs and have made and will continue to make some activities more ti
and costly. For example, these rules and regulations make it difficult and expensive
maintain director and officer liability insurance and we may be required to accept r
limits and coverage or to incur substantial costs to maintain the same or similar cov
rules and regulations could also make it more difficult for us to attract and retain qu
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 effectiven
internal control over financial reporting annually and the effectiveness of our disclo
procedures quarterly. In particular, Section 404 of the Sarbanes-Oxley Act, or Sect
us to perform system and process evaluation and testing of our internal control ove
reporting to allow management to report on, and our independent registered public
potentially to attest to, the effectiveness of our internal control over financial report
emerging growth company we expect to avail ourselves of the exemption from the
our independent registered public accounting firm attest to the effectiveness of our
over financial reporting under Section 404. However, we may no longer avail ourse
exemption when we cease to be an emerging growth company, which we expect to
December 31, 2019. When our independent registered public accounting firm is req
undertake an assessment of our internal control over financial reporting, the cost of
with Section 404 will correspondingly increase. Our compliance with applicable pr
Section 404 will require that we incur substantial accounting expense and expend s
management time on compliance-related issues as we implement additional corpora
practices and comply with reporting requirements. Moreover, if we are not able to c
requirements of Section 404 applicable to us in a timely manner, or if we or our inc

registered public accounting firm identifies deficiencies in our internal control over reporting that are deemed to be material weaknesses, the market price of our comm decline and we could be subject to sanctions or investigations by the SEC or other authorities, which would require additional financial and management resources.

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

If we fail to maintain an effective system of internal control over financial reportin able to accurately report our financial results or prevent fraud. As a result, shareho confidence in our financial and other public reporting, which would harm our busi market price of our common shares.

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

We are required to disclose changes made in our internal controls and procedures o
basis and our management is required to assess the effectiveness of these controls a
However, for as long as we are an emerging growth company under the JOBS Act,
registered public accounting firm will not be required to attest to the effectiveness o
controls over financial reporting pursuant to Section 404. An independent assessme
effectiveness of our internal controls could detect problems that our management's
not. As of December 31, 2018 and 2017, our independent registered public account
perform an evaluation of our internal control over financial reporting in accordance
provisions of the Sarbanes-Oxley Act. Had our independent registered public accou
performed such an evaluation, control deficiencies may have been identified, and th
deficiencies could have also represented one or more material weaknesses. Undetec
weaknesses in our internal controls could lead to financial statement restatements a
incur the expense of remediation.

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

As of December 31, 2018, stock options to purchase 2,671,906 of our common sha
weighted-average exercise price of $6.96 per common share were outstanding and
Series 1 Preferred Shares were outstanding, which are convertible into our common
one-for-one basis at the option of the holder, subject to certain ownership limitation
requested conversion. During the year ended December 31, 2018, certain funds affi
Partners L.P. exercised their conversion rights to convert 1,852,000 Series 1 Prefer
the same number of common shares. The exercise of any of these stock options or c
remaining Series 1 Preferred Shares would result in dilution to current shareholders
because we will need to raise additional capital to fund our clinical development pr
in the future sell substantial amounts of common shares, preferred shares, or other s
convertible into or exchangeable for common shares. Pursuant to our equity incenti
compensation committee (or a subset or delegate thereof) is authorized to grant equ
incentive awards to our employees, directors and consultants. Future stock option g
issuances of common shares under our share-based compensation plans may have a
on the market price of our common shares.

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

We are at risk of securities class action litigation.

In the past, securities class action litigation has often been brought against a compa
decline in the market price of its securities. This risk is especially relevant for us b
biotechnology companies have experienced significant stock price volatility in rece
face such litigation, it could result in substantial costs and a diversion of manageme
resources, which could harm our business.

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

Our common shares are listed on Nasdaq under the trading symbol “XENE.” Our s
meet the continued listing requirements to be listed on Nasdaq. If Nasdaq delists ou
from trading on its exchange, we could face significant material adverse consequen

- significant impairment of the liquidity for our common shares, which may substan
  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 req
  in our common shares to adhere to more stringent rules and possibly resulting in a
  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 t

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

The trading market for our common shares is influenced by the research and report industry analysts publish about us or our business. If too few securities or industry our company, the market price of our common shares would likely be negatively in securities and industry analysts who cover us downgrade our common shares or pu or unfavorable research about our business, the market price of our common shares decline. If one or more of these analysts cease coverage of our company or fail to p us regularly, demand for our common shares could decrease, which might cause the 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 p and private equity and debt financings and the investment of these proceeds may no favorable return. We may invest the proceeds in ways with which our shareholders

We have broad discretion in the application of the net proceeds to us from previous financings including the net proceeds we have received pursuant to our May 2018 " equity offering program with Stifel; the net proceeds we have received pursuant to "at-the-market" equity offering program with Jefferies and Stifel; the net proceeds 2018 amended and restated loan and security agreement, pursuant to which we hav aggregate of $15.5 million of principal; and the net proceeds from our September 2 offering of common shares. You may not agree with our decisions, and our use of t our existing cash and cash equivalents and marketable securities may not improve operation or enhance the value of our common shares. The results and effectiveness proceeds are uncertain, and we could spend the proceeds in ways that you do not ag do not improve our results of operations or enhance the value of our common share apply these funds effectively could have a material adverse effect on our business, development of our product candidates and cause the market price of our common In addition, until the net proceeds are used, they may be placed in investments that significant income or that may lose value.

We do not anticipate paying any cash dividends on our common shares in the fores

We do not currently intend to pay any cash dividends on our common shares in the future. We currently intend to retain all of our future earnings, if any, to finance th development of our business. In addition, the terms of any future debt agreements from paying dividends. As a result, capital appreciation, if any, of our common sha 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 appr square feet of office and laboratory space. The term of the lease expires in March 2

currently pay an aggregate of approximately $102,388 per month in base rent, prop
area maintenance fees and management fees, and the landlord holds a security depo
approximately $67,637.

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

We believe that our existing facilities are adequate to meet our business requiremer
near-term and that additional space will be available on commercially reasonable te

Item 3. Legal Proceedings

From time to time, we may become involved in legal proceedings or be subject to c
the ordinary course of our business. We are not presently a party to any legal proce
opinion of our management, would reasonably be expected to have a material adve
business, financial condition, operating results or cash flows if determined adversel
Regardless of the outcome, litigation can have an adverse impact on us because of
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
of Equity Securities

Market Information

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

	High	Low
Year Ended December 31, 2019		
First Quarter (through March 1, 2019)	$9.43	$6.17
Year Ended December 31, 2018		
Fourth Quarter	$13.49	$5.41
Third Quarter	$15.92	$8.85
Second Quarter	$11.00	$4.50
First Quarter	$5.05	$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

On March 1, 2019, the last reported sale price of our common shares was $8.94 per

Holders

As of March 1, 2019, there were approximately 147 holders of record of our comm
actual number of shareholders is greater than this number of record holders and inc
shareholders who are beneficial owners but whose common shares are held in stree
brokers and other nominees.

Dividends

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

Canadian withholding tax at a rate of 25% (subject to reduction under the provisio
applicable income tax treaty or convention to which Canada is a signatory) will be
gross amount of a dividend on our common shares paid or credited, or deemed to b

to a holder of our common shares who, for purposes of the Income Tax Act (Canad
not deemed to be) resident in Canada, or a Non-Resident of Canada Holder. The Ca
withholding tax will be deducted directly by us or our paying agent from the amou
otherwise payable and remitted to the Receiver General of Canada. The rate of with
applicable to a dividend paid on our common shares to a Non Resident of Canada
resident of the U.S. for purposes of the Canada U.S. Tax Convention (1980), or th
the beneficial owner of the dividend and qualifies for the full benefits of the Conve
generally be reduced to 15% or, if such a Non-Resident of Canada Holder is a com
(or, for purposes of the Convention, is considered to own) at least 10% of our votin
Not all persons who are residents of the U.S. for purposes of the Convention will q
benefits of the Convention. A Non-Resident of Canada Holder who is a resident of
advised to consult his or her tax advisor in this regard. The rate of withholding tax
also reduced under other bilateral income tax treaties to which Canada is a signator

Securities Authorized for Issuance under Equity Compensation Plans

The information concerning our equity compensation plans is incorporated by refer
our Proxy Statement for the 2019 Annual Meeting of Shareholders to be filed with
120 days after the end of our fiscal year ended December 31, 2018.

Performance Graph

As a smaller reporting company, we are not required to provide the information req
item pursuant to Item 201(e) of Regulation S-K.

Recent Sales of Unregistered Securities

On October 24, 2018 and December 21, 2018, we issued an aggregate of 52,000 an
common shares, respectively to certain funds affiliated with BVF Partners L.P. upo
of 52,000 and 500,000 Series 1 Preferred Shares held by such funds. The conversio
accordance with the terms of our Series 1 Preferred Shares. These issuances were e
registration under the Securities Act of 1933, as amended, pursuant to Section 3(a)(
exchange with an existing security holder where no commission or other remunerat
given for soliciting such exchange.

Issuer Repurchases of Equity Securities

None.

Item 6. Selected Financial Data

As a smaller reporting company, we are not required to provide the information req
item pursuant to Item 301 of Regulation S-K.

Item 7. Management's Discussion and Analysis of Financial Condition and Results
You should read the following discussion and analysis together with Part II, Item 6
Financial Data" and our consolidated financial statements and notes included elsew
Annual Report. The following discussion contains forward-looking statements that
uncertainties. Our actual results could differ from those expressed or implied in any
statements as a result of various factors, including those set forth under the caption
"Risk Factors." Throughout this discussion, unless the context specifies or implies
"Xenon," "we," "us," and "our" refer to Xenon Pharmaceuticals Inc. and its subsid

Overview

We are a clinical stage biopharmaceutical company committed to developing innov
to improve the lives of patients with neurological disorders, including rare central n
CNS, conditions. We are advancing a novel product pipeline of neurology-focused
address areas of high unmet medical need, with a focus on epilepsy. Our clinical de
pipeline includes:

- XEN496 (active ingredient ezogabine) is a Kv7 potassium channel modulator bein
the treatment of KCNQ2 epileptic encephalopathy, or KCNQ2-EE. Ezogabine wa
approved by the U.S. Food and Drug Administration, or FDA, as an anti-epileptic
adjunctive treatment for adults with focal seizures with or without secondary gene
received orphan drug designation, or ODD, from the FDA for XEN496 as a treatm
KCNQ2-EE. A steering committee made up of key opinion leaders in the KCNQ2
epilepsy fields has been established to help guide the clinical development of XEN
to our pre-IND briefing package submission, the FDA indicated that it was accept
XEN496 in infants and children up to 4 years old, and that a single pivotal trial in
patients may be considered adequate in order to demonstrate XEN496's efficacy i
are currently finalizing a pediatric-specific formulation to complete pre-clinical fo
with a final drug product expected in the second quarter of 2019. We expect to file
Investigational New Drug application in the third quarter of 2019, and, based on re
feedback, expect to initiate a Phase 3 clinical trial thereafter. This timeline is based
assumption that the testing of our new XEN496 pediatric formulation in healthy a
will not be a regulatory requirement prior to initiating a Phase 3 clinical trial;
- XEN1101 is a differentiated Kv7 potassium channel modulator being developed f
of epilepsy and potentially other neurological disorders. We announced final data
Phase 1 clinical trial and the related transcranial magnetic stimulation, or TMS, stu
American Epilepsy Society, or AES, Annual Meeting in December 2018. Based o
Phase 1 and Phase 1b TMS data, we have initiated a Phase 2b clinical trial in adul
focal epilepsy. The Phase 2b clinical trial is designed as a randomized, double-blin
placebo-controlled, multicenter study to evaluate the clinical efficacy, safety and t
XEN1101 administered as adjunctive treatment in adult patients with focal epileps
Approximately 300 patients will be randomized in a blinded manner to one of thre
treatment groups or placebo in a 2:1:1:2 fashion (XEN1101 25 mg : 20 mg : 10 m
primary endpoint is the median percent change in monthly focal seizure frequency
compared to treatment period of active versus placebo. An IND application for XE
accepted by the FDA, and site selection and patient enrollment are now underway
Phase 2b clinical trial in the United States, Canada and Europe. Depending upon t
enrollment, top-line results from the XEN1101 Phase 2b clinical trial are anticipat
half of 2020;

- XEN901 is a potent, highly selective Nav1.6 sodium channel inhibitor being deve
treatment of epilepsy. We announced results from a XEN901 Phase 1 clinical trial
pilot TMS study at the AES Annual Meeting in December 2018. The next steps fo
include continued planning for Phase 2 or later clinical development to evaluate X
treatment for adult focal seizures or for rare, pediatric forms of epilepsy, including
Epileptic Encephalopathy, or SCN8A-EE, patients, depending on feedback from p
discussions with regulatory agencies. We expect to receive feedback on the requir
advance XEN901 into pediatric SCN8A-EE patients in the second quarter of 2019
formulation development and juvenile toxicology studies are underway to support
development activities; and
- XEN007 (active ingredient flunarizine) is a CNS-acting calcium channel modulato
Cav2.1 and T-type calcium channels. Other reported mechanisms include dopamin
serotonin inhibition. Flunarizine is available in certain countries outside of the Un
has been reported to have clinical benefit in treating migraine and other neurologic
including hemiplegic migraine, or HM, alternating hemiplegia of childhood, or AH
as adjunctive treatment in certain epilepsies. The FDA has granted a rare pediatric
designation for the treatment of AHC with XEN007. We previously received ODD
for XEN007 for the treatment of both AHC and HM. In addition, we have entered
exclusive licensing agreements in order to access regulatory files and drug produc
both of which may enable advanced clinical development of XEN007. Various de
strategies for XEN007 are under consideration, including the support of at least on
later stage) clinical trial in an orphan neurological indication, with initiation antici

We have funded our operations through the sale of equity securities, funding receiv
licensees and collaborators, debt financing and, to a lesser extent, government fund
2017, we did not recognize significant revenue from our collaboration agreements.
to have sustained profitability for the foreseeable future. We had net losses of $34.5
year ended December 31, 2018 and an accumulated deficit of $207.9 million as of
2018, from expenses incurred in connection with our research programs and from g
administrative costs associated with our operations.

We have not generated any significant royalty revenue from product sales, and do n
anticipate generating revenue from product sales for the foreseeable future, if ever.
our revenue in the near term will be substantially dependent on our collaboration ag
the uncertain nature of clinical development of our current and future product cand
commercialization of current and future products, we cannot predict when or wheth
receive further milestone payments under our current or future collaboration agreem
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 leas
months. We anticipate that our expenses will increase as we:

- continue our research and pre-clinical and clinical development of our product can
from our internal research efforts or through acquiring or in-licensing other produ
technologies;
- seek regulatory and marketing approvals for any of our product candidates that su
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 a
as, to a lesser extent, government funding. We have not generated any significant re
from product sales, and do not otherwise anticipate generating revenue from produc
foreseeable future, if ever.

For the year ended December 31, 2018, we did not recognize any revenue from our
agreements.

As our other internal and partnered products are in various stages of clinical and pr
development, we do not expect to generate any revenue from product sales for at le
several years. We expect that any revenue for the next several years will be derived
payments under our current collaboration agreements and any additional collaborat
that we may enter into in the future. We cannot provide any assurance as to the exte

future milestone payments or royalty payments or that we will receive any future p

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

As of December 31, 2018, we have recognized all deferred revenue from upfront p
under our existing collaboration and licensing agreements.

Operating Expenses

The following table summarizes our operating expenses for the years ended Decem
2017 (in thousands):

	Year Ended December 31,	
	2018	2017
Research and development	$23,634	$25,573
General and administrative	8,382	7,313
Buy-out of future milestones and royalties	6,000	—
Total operating expenses	$38,016	$32,886

Research and Development Expenses

Research and development expenses represent costs incurred to conduct research a
of our proprietary product candidates, including any acquired or in-licensed produc
technology.

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

Project-specific expenses reflect costs directly attributable to our clinical developm
and our pre-clinical candidates once nominated and selected for further developme
pre-clinical and discovery costs supporting a development candidate. All remaining
development expenses are reflected in pre-clinical, discovery and other program ex
given time, we have several active early-stage research and drug discovery program
and infrastructure are typically deployed over multiple projects and are not directly
individual internal early-stage research or drug discovery program. Therefore, we d
financial information for our internal early-stage research and internal drug discove
project-specific basis.

We expense all research and development costs as incurred. We expect that our res
development expenses will increase in the future as we advance our proprietary pro
through clinical development, advance our internal drug discovery programs into p
development and continue our early-stage research. The increase in expense will lik
additional personnel and third-party contracts related to research, formulation, man
pre-clinical studies and clinical trial activities as well as third-party acquisition, lice
collaboration fees and laboratory consumables.

Clinical development timelines, likelihood of regulatory approval, and commercial
associated costs are uncertain, difficult to estimate, and can vary significantly. We
determining which research and development projects to pursue as well as the level
available for each project based on the scientific research and pre-clinical and clinic
product candidate and related regulatory action. We expect our research and develo
to continue to represent our largest category of operating expense for at least the ne
months.

General and Administrative Expenses

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

We expect that general and administrative expenses will increase in the future as w
operating activities to support increased research and development activities.

Buy-out of future milestones and royalties

In September 2018, we entered into a milestone and royalty buy-out agreement wit
Pharmaceuticals Luxembourg S.a.r.l. and Valeant Pharmaceuticals Ireland Limited
Bausch Health, under which all potential clinical development, regulatory and sales
milestones and royalties on commercial sales with respect to XEN1101 that may be
Bausch Health were terminated in exchange for a one-time payment of $6.0 million
expensed in the period.

Other Income (Expense)

Interest Income. Interest income consists of income earned on our cash and investm
anticipate that our interest income will continue to fluctuate depending on our cash
balances and interest rates.

Interest Expense. Interest expense consists of accrual of the final payment fee, amo
discounts, and interest charged on our borrowings with Silicon Valley Bank, or the
accrue interest at a floating per annum rate of 0.5% above the prime rate. During th
December 31, 2018, we also recorded a charge of $0.3 million related to the unaccr
the final payment fee due in connection with entering into our amended and restate
security agreement. For additional information regarding our amended and restated
agreement with the Bank, see "—Contractual Obligations and Commitments—Ter

Foreign Exchange Gain (Loss). Net foreign exchange gains and losses consisted of from the impact of foreign exchange fluctuations on our monetary assets and liabili denominated in currencies other than the U.S. dollar (principally the Canadian doll continue to incur substantial expenses in Canadian dollars and will remain subject t with foreign currency fluctuations.

Gain on Termination of Collaboration Agreement. In March 2018, we entered into agreement terminating by mutual agreement the collaborative development and lice dated December 7, 2012, as amended, with Teva Pharmaceuticals International Gm Canada Limited, or together Teva, that included the cancellation of 1,000,000 of ou owned by Teva. We recorded a one-time gain of $4.4 million on the termination of agreement, net of direct costs incurred in connection with the termination and canc common shares.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of our financial condition and results of based on our consolidated financial statements, which have been prepared in confo generally accepted accounting principles in the U.S., or U.S. GAAP. The preparatio consolidated financial statements requires us to make estimates and assumptions th reported amounts of assets and liabilities and the revenue and expenses incurred du periods. We base estimates on our historical experience, known trends and various we believe are reasonable under the circumstances, the results of which form the ba judgments about the carrying value of assets and liabilities that are not apparent fro Actual results may differ from these estimates under different assumptions or cond

The significant accounting policies that we believe to be most critical in fully unde evaluating our financial results are revenue recognition, research and development stock-based compensation. For additional information, see note 3 of the consolidate statements included in Part II, Item 8 of this report.

Revenue recognition:

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

Our primary sources of historical revenue have been derived from non-refundable u funding for research and development services, milestone payments, and royalties u collaboration agreements.

In contracts where we have more than one performance obligation to provide our c goods or services, each performance obligation is evaluated to determine whether i consideration under the contract is then allocated between the distinct performance on their respective relative stand-alone selling prices. The estimated stand-alone se deliverable reflects our best estimate of what the selling price would be if the deliv regularly sold on a stand-alone basis and is determined by reference to market rates service when sold to others or by using an adjusted market assessment approach if stand-alone basis is not available. We generally recognize revenue from non-refund payments ratably over the estimated term of the performance obligation or period i

underlying benefit is transferred to the customer. We evaluate the measure of progr
reporting period and, if necessary, adjust the measure of performance and related re
recognition.

The consideration allocated to each distinct performance obligation is recognized a
control is transferred to our customer for the related goods or services. Considerati
at-risk substantive performance milestones, including sales-based milestones, is rec
revenue when we determine it is probable that a significant reversal of the cumulati
recognized will not occur. At the end of each subsequent reporting period, we re-ev
probability of achievement of such milestones, and if necessary, adjust our estimate
transaction price. Sales-based royalties received in connection with licenses of inte
are subject to a specific exception in the revenue standards, whereby the considerat
included in the transaction price and recognized in revenue until the customer's sub
usages occur.

Research and development costs:

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

We incur development activity costs, such as pre-clinical costs, manufacturing cost
costs paid to contract research organizations, investigators and other vendors who c
product development activities on our behalf. The amount of expenses recognized i
to service agreements is based on estimates of the work performed using an accrual
accounting. These estimates are based on patient enrollment, services provided and
contractual terms and experience with similar contracts. We monitor these factors a
estimates accordingly.

Stock-based compensation:

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

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

Prior to our initial public offering, our shares did not have a readily available marke
lacked company-specific historical and implied volatility information. Consequentl
the expected volatility of our stock options, we base our estimate on a combination
historical volatility information and a historical volatility analysis of peers that are
respect to industry, stage of development, size, and financial leverage. The expecte
stock options has been determined utilizing our available historical data and we rec
as they occur. We amortize the fair value of stock options using the straight-line me
vesting period of the options.

Results of Operations

Comparison of Years Ended December 31, 2018 and 2017

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

			Ch
Year Ended December 31,			201
2018	2017		Inc

Collaboration revenue	$ —	$ 311	$
Research and development expenses	23,634	25,573	
General and administrative expenses	8,382	7,313	
Buy-out of future milestones and royalties	6,000	—	
Other:			
Interest income	1,216	477	
Interest expense	(1,394)	—	
Foreign exchange gain (loss)	(701)	1,394	
Gain on termination of collaboration agreement	4,398	—	
Net loss	$ (34,497)	$ (30,704)	$

Revenue

We did not recognize any revenue for the year ended December 31, 2018, compare
for the year ended December 31, 2017. The decrease was primarily due to a $0.25 m
payment recognized in July 2017 under the March 2014 genetics collaborative agre
Genentech.

Research and Development Expenses

The following table summarizes research and development expenses for the years e
December 31, 2018 and 2017 together with changes in those items (in thousands):

	Year Ended December 31, 2018	2017	C 2 In
XEN496 expenses	$ 1,469	$ —	$
XEN801 expenses	5	1,353	
XEN901 and Nav1.6 pre-clinical and discovery expenses	11,392	10,157	
XEN1101 expenses	7,883	5,885	
Pre-clinical, discovery and other program expenses	2,885	8,178	
Total research and development expenses	$ 23,634	$ 25,573	$

Research and development expenses were $23.6 million for the year ended Decemb
compared to $25.6 million for the year ended December 31, 2017. The decrease of
primarily attributable to decreased spending on pre-clinical, discovery and other int
expenses, and XEN801, a product candidate which is no longer being developed. T
were partially offset by increased spending on our XEN1101 product candidate, wh
in April 2017, our XEN496 product candidate which was announced in September
XEN901 and Nav1.6 pre-clinical and discovery expenses.

General and Administrative Expenses

The following table summarizes general and administrative expenses for the years
December 31, 2018 and 2017 together with changes in those items (in thousands):

	Year Ended December 31, 2018	2017	Change 2018 vs. Increase/
General and administrative expenses	$ 8,382	$ 7,313	$ 1,069

General and administrative expenses were $8.4 million for the year ended Decembe
compared to $7.3 million for the year ended December 31, 2017. The increase of $
primarily attributable to increased stock-based compensation expense, salaries and
expenses and recruitment fees.

Other Operating Expenses

The following table summarizes other operating expenses for the years ended Dece
and 2017 together with changes in those items (in thousands):

	Year Ended December 31,		Chan 2018
	2018	2017	Increa
Buy-out of future milestones and royalties	$ 6,000	$ —	$ 6

Other operating expenses increased by $6.0 million for the year ended December 3
compared to the year ended December 31, 2017. The increase is due to a one-time
million to Bausch Health for the buy-out of all future milestone payments and roya
Bausch Health with respect to our XEN1101 program.

Other Income

The following table summarizes our other income for the years ended December 3
together with changes in those items (in thousands):

	Year Ended December 31,		Change 2018 vs. 2017
	2018	2017	Increase/(Decrease)
Other income:	$ 3,519	$ 1,871	$ 1,648

63

Other income increased by $1.6 million for the year ended December 31, 2018, as c
year ended December 31, 2017. The increase in other income was primarily driven
gain on the termination of the collaboration agreement with Teva, partially offset b
foreign exchange gains and losses and interest expense incurred on our term loan. W
foreign exchange loss of $0.7 million for the year ended December 31, 2018 as com
million foreign exchange gain for the same period in 2017, largely due to an 8% de
compared to a 7% increase in the value of the Canadian dollar, respectively.

Liquidity and Capital Resources

To date, we have financed our operations primarily through funding received from
license agreements, private placements of our common and preferred shares, public
common shares, debt financing and government funding. As of December 31, 2018
and cash equivalents and marketable securities of $119.3 million. In December 201
into a loan and security agreement with the Bank pursuant to which we borrowed a
principal amount of $12.0 million. In August 2018, we entered into an amended an
and security agreement with the Bank providing for a term loan to us with an aggre
amount of $15.5 million, proceeds from which were used in part to refinance the an
under the December 2017 loan and security agreement. For additional information
amended and restated loan and security agreement with the Bank, see "—Contractu
Commitments—Term Loan" below.

We have incurred significant operating losses since inception. We had a $34.5 mill
the year ended December 31, 2018 and an accumulated deficit of $207.9 million fr
through December 31, 2018. We expect to continue to incur significant expenses in
revenue and expect to incur operating losses over the next several years. Our net lo
fluctuate significantly from quarter to quarter and year to year. We expect to contin
significant expenses and operating losses for the foreseeable future as we continue
pre-clinical and clinical development of our product candidates; expand the scope o
studies for our product candidates; initiate additional pre-clinical, clinical or other s
product candidates, including under our collaboration agreements; change or add m
suppliers and manufacture drug supply and drug products for clinical trials and com
seek regulatory and marketing approvals for any of our product candidates that suc
complete clinical studies; seek to identify, evaluate and validate additional product
acquire or in-license other product candidates and technologies; make milestone or
under our product acquisition and in-license agreements, including, without limitat
the Memorial University of Newfoundland, 1st Order Pharmaceuticals, Inc., and ot
maintain, protect and expand our intellectual property portfolio; attract and retain s
establish a sales, marketing and distribution infrastructure to commercialize any pr
we or one of our collaborators may obtain marketing approval, and maintain comm
create additional infrastructure to support our operations and our product developm
future commercialization efforts; and experience any delays or encounter issues wi
above.

Until such time as we can generate substantial product revenue, if ever, we expect t
cash needs through a combination of collaboration agreements and equity or debt f
example, during the year ended December 31, 2018, we raised $103.2 million, net

paid, but excluding estimated transaction expenses through a combination of “at-th
offerings and an underwritten public offering, selling an aggregate of 9,540,000 co

Except for any obligations of our collaborators to make milestone payments under
with them, we do not have any committed external sources of capital. To the extent
additional capital through the future sale of equity or debt, the ownership interest o
will be diluted, and the terms of these securities may include liquidation or other pr
adversely affect the rights of our existing shareholders. If we raise additional funds
collaboration agreements in the future, we may have to relinquish valuable rights to
technologies, future revenue streams or product candidates or grant licenses on ter
be favorable to us. If we are unable to raise additional funds through equity or debt
needed, we may be required to delay, limit, reduce or terminate our product develo
commercialization efforts or grant rights to develop and market product candidates
otherwise prefer to develop and market ourselves.

Our future capital requirements are difficult to forecast and will depend on many fa

- the number and characteristics of the future product candidates we pursue either fr
research efforts or through acquiring or in-licensing other product candidates or te
- the scope, progress, results and costs of independently researching and developing
product candidates, including conducting pre-clinical research and clinical trials;
- whether our existing collaborations continue to generate substantial milestone pay
ultimately, royalties on future approved products for us;

- the timing of, and the costs involved in, obtaining regulatory approvals for any fut candidates we develop independently;
- the timing and magnitude of potential milestone payments and royalties under our acquisition and in-license agreements;
- the cost of commercializing any future products we develop independently that ar sale;
- the cost of manufacturing our future product candidates and products, if any;
- our ability to maintain existing collaborations and to establish new collaborations, other arrangements and the financial terms of such arrangements;
- the costs of preparing, filing, prosecuting, maintaining, defending and enforcing p litigation costs and the outcome of such litigation; and
- the timing, receipt and amount of sales of, or royalties on our future products, if ar

Based on our research and development plans and our timing expectations related t our programs, we expect that our existing cash and cash equivalents and marketabl the date of this report will enable us to fund our operating expenses and capital exp requirements for at least the next 12 months. We have based this estimate on assum prove to be wrong, and we could use our capital resources sooner than we expect. A process of testing drug candidates in clinical trials is costly, and the timing of progr remains uncertain.

Cash Flows

The following table shows a summary of our cash flows for the years ended Decem 2017 (in thousands):

	Year Ended Dece 31, 2018	2017
Net cash used in operating activities	$(34,724)	$(28,7
Net cash provided by (used in) investing activities	(28,987)	24,2
Net cash provided by financing activities	111,591	7,07

Operating Activities

Net cash used in operating activities totaled $34.7 million in 2018 as compared to $ 2017. The increase in cash used in operating activities was primarily related to a or to Bausch Health of $6.0 million for the buy-out of all future milestone payments a to Bausch Health with respect to our XEN1101 program, interest paid on our term l increase in general and administrative expenses. The increase in cash used in opera was partially offset by a decrease in research and development expenses and an inc income.

Investing Activities

Net cash used in investing activities totaled $29.0 million in 2018 as compared to n by investing activities of $24.3 million in 2017. The change in cash provided by (us

activities was driven by an increase in purchases of marketable securities, net of re

Financing Activities

Net cash provided by financing activities totaled $111.6 million in 2018 as compar
in 2017. The increase in cash provided by financing activities was primarily related
$102.9 million of net proceeds from the issuance of common shares as well as net p
million under the second tranche of our December 2017 loan and security agreeme
and subsequent refinancing in August 2018.

Contractual Obligations and Commitments

The following summarizes our significant contractual obligations as of December 3
thousands):

Contractual Obligations	Total	Less Than 1 Year	1 To 3 Years	3 To 5 Years	M T 5 Y
Operating lease [1]	$3,583	$1,128	$2,199	$256	$
Term loan [2]	$15,500	$—	$11,367	$4,133	
Total contractual obligations	$19,083	$1,128	$13,566	$4,389	$

(1) Represents future minimum lease payments under an operating lease in effect a
December 31, 2018 for our current facility in Burnaby, British Columbia, Cana
(2) Excluding expected interest payments of $0.9 million (less than one year), $1.3
three years), $0.1 million (three to five years) based on the prime rate plus 0.5%
December 31, 2018. Also excluded is the final payment fee of $1.0 million whi
6.5% of the principal amount.

Term Loan

In December 2017, we entered into a Loan and Security Agreement, or Loan Agree
Bank under which we were funded an initial tranche of $7.0 million. In June 2018,
First Loan Modification Agreement, or Modification, to the Loan Agreement, toget
Loan Agreement, pursuant to which the Bank accelerated the availability of a secon
million which was funded in June 2018. Amounts funded under the Modified Loan
interest-only until September 30, 2018 or, subject to the achievement of certain clin
or the Interest-Only Milestone, March 31, 2019. Following the expiration of the int
the first tranche was payable in 30 equal monthly installments or, if the Interest-On
achieved, 24 equal monthly installments of principal plus interest, maturing on Mar
second tranche was payable in 24 equal monthly installments or, if the Interest-Onl
achieved, 18 equal monthly installments of principal plus interest, maturing on Sep
The interest and payment terms of the third and final tranche, if borrowed, remaine
from the Loan Agreement. The Modification did not amend the Loan Agreement's
provisions.

On August 3, 2018, we entered into Amended and Restated Loan Agreement with t
pursuant to which the Bank extended a term loan to us with a principal amount of $
Term Loan, which was used to repay in full outstanding borrowings of $12.0 millio
Modified Loan Agreement and a payment of $0.5 million, which represented the cu
the final payment fee due under the Modified Loan Agreement, as well as for work
other general corporate purposes, including the advancement of our clinical develo

The Term Loan accrues interest at a floating per annum rate of 0.5% above the prin
payable monthly commencing in September 2018. The Term Loan is interest-only

2020, followed by 30 equal monthly installments of principal plus interest, maturin
1, 2022. In addition, we are required to pay a final payment fee of 6.5% of the Ter
date on which the term loan is prepaid, paid or becomes due and payable in full.

We may prepay all, but not less than all, of the Term Loan subject to a prepayment
million, which represents the deferred portion of the final payment fee due under th
Agreement, plus 3.0% if prepaid prior to the first anniversary of the effective date
and Restated Loan Agreement, 2.0% if prepaid on or after the first anniversary, but
second anniversary, or 1.0%, if prepaid on or after the second anniversary but prior
date. As security for its obligations under the Amended and Restated Loan Agreem
the Bank a first priority security interest on substantially all of our assets except its
property and subject to certain other exceptions.

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

In connection with the Amended and Restated Loan Agreement, we issued a warra
purchase 40,000 of our common shares at a price per common share of $9.79. The
immediately exercisable, has a 10-year term and contains a cashless exercise provis

Other Commitments

The contractual obligations table above excludes the following material contractual

In August 2015, we entered into a priority access agreement with Medpace for the
certain clinical development services. Under the terms of the agreement, we comm
Medpace non-exclusively for clinical development services over the five year term
agreement. In consideration for priority access to Medpace resources and preferred
committed to $7.0 million of services over the term of the agreement, $1.7 million
prepaid upon signing of the agreement and an additional $1.3 million was paid in D
we do not meet the commitment to retain Medpace for $7.0 million of services duri
the agreement, we agreed to give Medpace the exclusive right to perform all of our
outsourced clinical development work until such $7.0 million commitment has bee
subject to the availability of appropriate Medpace resources and reasonable service
decide not to retain Medpace for the provision of clinical development services, we
obligations under the priority access agreement by paying Medpace an amount equ
unsatisfied portion of the $7.0 million minimum commitment.

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

In April 2017, we acquired XEN1101 (previously known as 1OP2198) from 1st Or
asset purchase agreement. 1st Order previously acquired 1OP2198 from an affiliate
Health, and assumed certain financial responsibilities under that agreement. Under
agreement, we paid an upfront fee of approximately $0.4 million and milestone pay
totaling $0.7 million, which we expensed as research and development. In Septemb
entered into a milestone and royalty buy-out agreement with Bausch Health under
potential clinical development, regulatory and sales-based milestones and royalties
sales with respect to XEN1101 that may become owed to Bausch Health under the
agreement were terminated in exchange for a one-time payment of $6.0 million wh
in the period. Future potential payments to 1st Order include $0.5 million in clinica
milestones, up to $6.0 million in regulatory milestones, and $1.5 million in other m
may be payable pre-commercially. There are no royalty obligations to 1st Order.

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

In July 2018, we amended our collaborative research and license agreement with G
provide us with greater flexibility in developing additional compounds that target N
to the amendment, we obtained a non-exclusive, irrevocable, perpetual, world-wide
license under the know-how forming part of the Genentech intellectual property de

Nav1.7 collaboration that is necessary or useful to make, use, sell, offer for sale, an
compounds from our Nav1.6 program that are above a certain potency threshold or
products containing those compounds. Our license from Genentech includes comm
rights but we are restricted from developing or commercializing our Nav1.6 compo
certain potency threshold on Nav1.7 in the field of epilepsy and any of our Nav1.6
regardless of their potency on Nav1.7, in the field of pain. In exchange for the right
under this amendment, Genentech is eligible to receive a low single-digit percentag
on net sales of our Nav1.6 compounds, including XEN901, for a period of ten years
commercial sale on a country-by-country basis. Pursuant to the amendment, we gra
royalty-free, non-exclusive, world-wide license under our Nav1.6 intellectual prope
sell, offer for sale and import compounds below a certain potency threshold on Nav
containing those compounds for all uses and indications except epilepsy.

Inflation

We do not believe that inflation has had a material effect on our business, financial
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 entities referred to as variable interest entities, which include special purposes entit structured finance entities.

Related Party Transactions

For a description of our related party transactions, see “Certain Relationships and R Transactions, and Director Independence.”

Outstanding Share Data

As of March 1, 2019, we had 25,751,266 common shares issued and outstanding ar stock options to purchase an additional 2,688,345 common shares. In addition, as o we had 1,016,000 Series 1 Preferred Shares issued and outstanding. The Series 1 Pr are convertible into common shares on a one-for-one basis subject to the holder, tog affiliates, beneficially owning no more than 9.99% of the total number of common outstanding immediately after giving effect to such conversion, or the Beneficial O Limitation. The holder may reset the Beneficial Ownership Limitation to a higher o not to exceed 19.99% of the total number of common shares issued and outstanding after giving effect to such conversion, upon providing written notice to us which w days after delivery of such notice. The holders of the Series 1 Preferred Shares are together with the common shares on an as-converted basis and as a single class, sub of each holder of the Series 1 Preferred Shares to the Beneficial Ownership Limitat Preferred Shares may be “restricted securities” as such term is defined under applic securities laws, as any Series 1 Preferred Shares that are ineligible to be converted shares due to the Beneficial Ownership Limitation, measured as of a given record d for a shareholder meeting or ability to act by written consent, shall be deemed to be securities. For additional information regarding our Series 1 Preferred Shares, see n consolidated financial statements included in Part II, Item 8 of this report.

Recent Accounting Pronouncements

In February 2016, the Financial Accounting Standards Board, or FASB, issued Acc Standards Update, or ASU, 2016-02, Leases (Topic 842): Recognition and Measure Financial Assets and Financial Liabilities. The update requires the recognition of le lease liabilities by lessees for those leases classified as operating leases under previ The new guidance retains a distinction between finance leases and operating leases payments from operating leases classified within operating activities in the statemen These amendments will be effective for public entities for fiscal years and interim p those years, beginning after December 15, 2018. We adopted the standard on Janua can elect to record a cumulative-effect adjustment as of the beginning of the year o apply a modified retrospective transition approach. We have identified one operatin premises which will be subject to the new guidance and will be recognized as an op liability and right-of-use asset upon adoption.

In November 2018, the FASB issued ASU 2018-18, Collaborative Arrangements (T Clarifying the Interaction between Topic 808 and Topic 606. These amendments m

improvements to accounting for collaborative arrangements by clarifying that certa
between collaborative arrangement participants should be accounted for as revenue
when the collaborative arrangement participant is a customer in the context of a un
those situations, all the guidance in Topic 606 should be applied, including recogni
measurement, presentation, and disclosure requirements. In addition, unit-of-accou
Topic 808 was aligned with the guidance in Topic 606 (that is, a distinct good or se
entity is assessing whether the collaborative arrangement or a part of the arrangeme
scope of Topic 606. These amendments will be effective for fiscal years and interim
those fiscal years, beginning after December 15, 2019 and should be applied retrosp
date of initial application of Topic 606. We are currently evaluating the new guidan
the impact it will have on our consolidated financial statements.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

As a smaller reporting company, we are not required to provide the information req
item pursuant to Item 301 of Regulation S-K.

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

Index to Consolidated Financial Statements

Year ended December 31, 2018

Report of Independent Registered Public Accounting Firm

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

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Xenon Pharmac subsidiary (the Company) as of December 31, 2018 and 2017, the related consolida operations and comprehensive loss, shareholders' equity, and cash flows for each o two year period ended December 31, 2018, and the related notes (collectively, the financial statements). In our opinion, the consolidated financial statements present material respects, the financial position of the Company as of December 31, 2018 a results of its operations and its cash flows for each of the years in the two year per December 31, 2018, in conformity with U.S. generally accepted accounting princip

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's ma responsibility is to express an opinion on these consolidated financial statements ba audits. We are a public accounting firm registered with the Public Company Accou Board (United States) (PCAOB) and are required to be independent with respect to accordance with the U.S. federal securities laws and the applicable rules and regula Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those st that we plan and perform the audit to obtain reasonable assurance about whether th financial statements are free of material misstatement, whether due to error or frauc is not required to have, nor were we engaged to perform, an audit of its internal cor financial reporting. As part of our audits, we are required to obtain an understandin control over financial reporting but not for the purpose of expressing an opinion on of the Company's internal control over financial reporting. Accordingly, we expres

Our audits included performing procedures to assess the risks of material misstaten consolidated financial statements, whether due to error or fraud, and performing pr respond to those risks. Such procedures included examining, on a test basis, eviden amounts and disclosures in the consolidated financial statements. Our audits also in evaluating the accounting principles used and significant estimates made by manag evaluating the overall presentation of the consolidated financial statements. We bel 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 6, 2019

XENON PHARMACEUTICALS INC.

Consolidated Balance Sheets

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

	Decem 31, 2018
Assets	
Current assets:	
Cash and cash equivalents	$67,7
Marketable securities	51,5
Accounts receivable	256
Prepaid expenses and other current assets	1,87
	121,4
Prepaid expenses, long-term	—
Property, plant and equipment, net (note 7)	991
Total assets	$122,4
Liabilities and shareholders' equity	
Current liabilities:	
Accounts payable and accrued expenses (note 8)	4,11
Loan payable, current portion (note 9)	—
	4,11
Loan payable, long-term (note 9)	15,0
	$19,1
Shareholders' equity:	
Preferred shares, without par value; unlimited shares authorized; issued and outstanding: 1,016,000 (December 31, 2017 - nil) (note 10)	$7,73
Common shares, without par value; unlimited shares authorized; issued and outstanding: 25,750,721 (December 31, 2017 - 17,998,420) (note 10)	265,9
Additional paid-in capital	38,5
Accumulated deficit	(207
Accumulated other comprehensive loss	(990
	$103,2
Total liabilities and shareholders' equity	$122,4
Collaboration agreements (note 12)	
Commitments and contingencies (note 13)	

The accompanying notes are an integral part of these consolidated financial statem

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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 Dec	
	2018	20
Revenue:		
Collaboration revenue (note 12)	$—	$
	—	
Operating expenses:		
Research and development	23,634	
General and administrative	8,382	
Buy-out of future milestones and royalties (note 13d)	6,000	
	38,016	
Loss from operations	(38,016)	(
Other income (expense):		
Interest income	1,216	
Interest expense	(1,394)	
Foreign exchange gain (loss)	(701)	
Gain on termination of collaboration agreement (note 12a)	4,398	
Net loss and comprehensive loss	(34,497)	(
Net loss attributable to preferred shareholders	(2,881)	
Net loss attributable to common shareholders	(31,616)	(
Net loss per common share (note 6):		
Basic	$(1.63)	$(
Diluted	$(1.63)	$(
Weighted-average common shares outstanding (note 6):		
Basic	19,425,711	
Diluted	19,425,711	

The accompanying notes are an integral part of these consolidated financial statem

XENON pharmaceuticals INC.

Consolidated Statement of Shareholders' Equity

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

	Convertible preferred shares		Common shares		Additional paid-in	Accumula
	Shares	Amount	Shares	Amount	capital	deficit
Balance as of December 31, 2016	—	$—	17,930,590	$173,246	$34,326	$(142,68
Net loss for the year						(30,704
Stock-based compensation expense					2,460	
Issued pursuant to exercise of stock options			67,830	595	(415)	(3
Issuance of warrants					100	
Balance as of December 31, 2017	—	$—	17,998,420	$173,841	$36,471	$(173,388
Net loss for the year						(34,497
Issuance of common shares, net of issuance costs (note 10a)			9,540,000	102,850		
Issued (cancelled)	2,868,000	21,825	(2,868,000)	(21,825)		

pursuant to exchange agreement (note 10d)						
Conversion of preferred shares to common shares (note 10d)	(1,852,000)	(14,093)	1,852,000	14,093		
Cancelled pursuant to termination of collaboration agreement (note 12a)			(1,000,000)	(4,470)		
Stock-based compensation expense					2,652	
Issued pursuant to exercise of stock options and warrants			228,301	1,434	(1,146)	
Issuance of warrants					538	
Balance as of December 31, 2018	1,016,000	$7,732	25,750,721	$265,923	$38,515	$(207,885

(1) Our accumulated other comprehensive loss is entirely related to historical cumu
adjustments from the application of U.S. dollar reporting when the functional cu
Company was the Canadian dollar.

The accompanying notes are an integral part of these consolidated financial statem

XENON PHARMACEUTICALS INC.

Consolidated Statements of Cash Flows

(Expressed in thousands of U.S. dollars)

	Year 31, 2018
Operating activities:	
Net loss	$(34
Items not involving cash:	
Depreciation	586
Amortization of discount on term loan	284
Stock-based compensation	2,62
Unrealized foreign exchange (gain) loss	646
Gain on termination of collaboration agreement (note 12a)	(4,3
Changes in operating assets and liabilities:	
Accounts receivable	175
Prepaid expenses, and other current assets	(92
Prepaid expenses, long term	—
Accounts payable and accrued expenses	783
Net cash used in operating activities	(34
Investing activities:	
Purchases of property, plant and equipment	(50
Purchase of marketable securities	(77
Proceeds from marketable securities	48,3
Net cash provided by (used in) investing activities	(28
Financing activities:	
Proceeds from issuance of refinanced term loan, net of issuance costs (note 9)	8,45
Issuance of common shares, net of issuance costs (note 10a)	102
Issuance of common shares pursuant to exercise of stock options	288
Net cash provided by financing activities	111
Effect of exchange rate changes on cash and cash equivalents	(61
Increase in cash and cash equivalents	47,2
Cash and cash equivalents, beginning of year	20,4
Cash and cash equivalents, end of year	$67,7
Supplemental disclosures:	
Interest paid	$561
Interest received	1,06
Supplemental disclosures of non-cash transactions:	

Fair value of stock options and warrants exercised on a cashless basis	1,1
Issuance of preferred shares in exchange for common shares (note 10d)	21,8
Conversion of preferred shares to common shares (note 10d)	14,0
Termination of Teva agreement through cancellation of common shares (note 12a)	4,47

The accompanying notes are an integral part of these consolidated financial statem

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 Briti
Business Corporations Act and continued federally in 2000 under the Canada Busi
Act, is a clinical stage biopharmaceutical company focused on developing innovati
improve the lives of patients with neurological disorders. Building upon its extensi
human genetics and diseases caused by mutations in ion channels, known as chann
Company is advancing a novel product pipeline of neurology-focused therapies to a
high unmet medical need, with a focus on epilepsy.

The Company has incurred significant operating losses since inception. As of Dece
the Company had an accumulated deficit of $207,885 and a $34,497 net loss for the
December 31, 2018. Management expects to continue to incur significant expenses
revenue and to incur operating losses for the foreseeable future. To date, the Compa
its operations primarily through funding received from collaboration and license ag
placements of common and preferred shares, public offerings of common shares, de
government funding.

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

2. Basis of presentation:
These consolidated financial statements are presented in U.S. dollars and have been
accordance with United States generally accepted accounting principles (“U.S. GA

The Company has one wholly-owned subsidiary as at December 31, 2018, Xenon P
USA Inc., which was incorporated in Delaware on December 2, 2016.

These consolidated financial statements include the accounts of the Company and i
subsidiary. All intercompany transactions and balances have been eliminated on co

3. Significant accounting policies:
(a) Use of estimates:

The preparation of the consolidated financial statements in conformity with U.S. G
management to make estimates and assumptions that affect the reported amounts o
liabilities and disclosure of contingent assets and liabilities at the date of the financ
the reported amounts of revenue and expenses during the reporting period. Signific
estimates include, but are not limited to, the timing of revenue recognition, the dete
stock-based compensation and the amounts recorded as accrued liabilities. Actual r
differ materially from those estimates. Estimates and assumptions are reviewed qua
revisions to accounting estimates are recognized in the period in which the estimate
in any future periods affected.

(b) Cash and cash equivalents:

Cash equivalents are highly liquid investments that are readily convertible into cash
maturity of three months or less when acquired. Cash equivalents are recorded at co
interest. The carrying value of these cash equivalents approximates their fair value.

(c) Marketable securities:

Marketable securities are investments with original maturities exceeding three mon
remaining maturities of less than one year. Marketable securities accrue interest bas
interest rate for the term. The carrying value of marketable securities is recorded at
interest, which approximates their fair value.

(d) Intellectual Property

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

(e) Property, plant and equipment:

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

Property, plant and equipment are amortized over their estimated useful lives using 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 in present, the Company assesses the recoverability of affected assets by determining carrying value of such assets is less than the sum of the undiscounted future cash fl If such assets are found not to be recoverable, the Company measures the amount o impairment by comparing the carrying value of the assets to the fair value of the as value generally determined based on the present value of the expected future cash f with the assets. No impairment of long-lived assets was noted during the years ende 2018 and 2017.

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

Financial instruments that potentially subject the Company to significant concentra risk consist primarily of cash and cash equivalents. Cash and cash equivalents were financial institutions in Canada and the United States. Such deposits may be in exc limits in the event of non-performance by the institutions; however, the Company c non-performance.

(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 meas financial assets and liabilities. This hierarchy prioritizes the inputs to valuation tech measure fair value into three levels: Level 1 (highest priority), Level 2, and Level 3

- Level 1 - Unadjusted quoted prices in active markets for identical instruments.
- Level 2 - Inputs other than quoted prices included within Level 1 that are observal liability, either directly or indirectly. Level 2 inputs include quoted prices for simi

liabilities in active markets, quoted prices for identical or similar assets or liabiliti
are not active, inputs other than quoted prices that are observable for the asset or l
interest rates, yield curves, etc.), and inputs that are derived principally from or co
observable market data by correlation or other means (market corroborated inputs

- Level 3 - Inputs are unobservable and reflect the Company's assumptions as to wh
participants would use in pricing the asset or liability. The Company develops thes
the best information available.

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

The Company's Level 1 assets include cash and cash equivalents and marketable se
quoted prices in active markets. The carrying amount of accounts receivables, acco
accrued expenses approximates fair value due to the nature and short-term of those
Company's term loan bears interest at a rate that approximates prevailing market ra
instruments with similar characteristics and, accordingly, the carrying value of the
approximates fair value.

(i) Revenue recognition:
The Company recognizes the amount of revenue to which it expects to be entitled, promised goods or services to customers under a five-step model: (i) identify contr customer; (ii) identify the performance obligations in the contract; (iii) determine th price; (iv) allocate the transaction price to the performance obligations in the contra recognize revenue when or as a performance obligation is satisfied.

The Company generates revenue primarily through collaboration agreements. Such require the Company to deliver various rights and/or services, including intellectua or licenses and research and development services. Under such collaboration agree Company is generally eligible to receive non-refundable upfront payments, funding development services, milestone payments, and royalties.

In contracts where the Company has more than one performance obligation to prov with goods or services, each performance obligation is evaluated to determine whet based on whether (i) the customer can benefit from the good or service either on its with other resources that are readily available and (ii) the good or service is separat from other promises in the contract. The consideration under the contract is then all the distinct performance obligations based on their respective relative stand-alone s estimated stand-alone selling price of each deliverable reflects the Company's best the selling price would be if the deliverable was regularly sold on a stand-alone bas determined by reference to market rates for the good or service when sold to others adjusted market assessment approach if selling price on a stand-alone basis is not a

The consideration allocated to each distinct performance obligation is recognized a control is transferred to the customer for the related goods or services. Considerati at-risk substantive performance milestones, including sales-based milestones, is rec revenue when it is probable that a significant reversal of the cumulative revenue rec occur. Sales-based royalties received in connection with licenses of intellectual pro to a specific exception in the revenue standards, whereby the consideration is not in transaction price and recognized in revenue until the customer's subsequent sales o

(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 costs, are a component of research and development costs and include fees paid to organizations, investigators and other vendors who conduct certain product develop on behalf of the Company. The amount of expenses recognized in a period related t agreements is based on estimates of the work performed using the accrual basis of a estimates are based on patient enrollment, services provided and goods delivered, c and experience with similar contracts. The Company monitors these factors and adj accordingly. Payments made to third parties under these arrangements in advance o 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 plan described in note 10c.

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

(l) Foreign currency translation:
The functional and reporting currency of the Company and its subsidiary is the U.S
Monetary assets and liabilities denominated in a currency other than the U.S. dollar
are re-measured into U.S. dollars at the exchange rate prevailing as at the balance s
date. Non-monetary assets and liabilities acquired in a currency other than U.S. dol
at historical exchange rates prevailing at each transaction date.

Revenue and expense transactions are translated at the exchange rates prevailing at
date. Exchange gains and losses on translation are included in the consolidated stat
operations and comprehensive income (loss) as foreign exchange gain (loss).

(m) Income taxes:
Deferred income taxes are recognized for the future tax consequences attributable t
between the carrying amounts of assets and liabilities and their respective tax bases
operating loss and credit carryforwards. Deferred income tax assets and liabilities a
enacted rates expected to apply to taxable income in the years in which those tempo
and carryforwards are expected to be recovered or settled. The effect on deferred in
and liabilities of a change in tax rates is recognized in the consolidated statement o
comprehensive income (loss) in the period that includes the enactment date. A valu
is provided when realization of deferred income tax assets does not meet the more-
criterion for recognition.

(n) Deferred tenant inducements:
Deferred tenant inducements, which include leasehold improvements paid for by th
free rent, are included in the consolidated balance sheet as accounts payable and ac
and recognized as a reduction of rent expense on a straight-line basis over the term

(o) Segment and geographic information:
Operating segments are defined as components of an enterprise about which separa
information is available for evaluation by the chief operating decision maker, or de
group, in deciding how to allocate resources and in assessing performance. The Co
operations and manages its business in one operating segment.

4. Changes in significant accounting policies:
The Company adopted the new revenue standard (Accounting Standards Codificati
effective January 1, 2018, using the modified retrospective method under which pr
presented financial statements are not restated and the cumulative effect of adoptin
standard on contracts in process is recognized by an adjustment to retained earning
date. The adoption of the new revenue standard did not change the Company's reco
under its one ongoing significant collaborative research and license agreement with
member of the Roche Group, described in note 12b and no cumulative effect adjust
required. Refer to the Company's Revenue Recognition policy described in note 3i

5. Future changes in accounting policies:
In February 2016, the Financial Accounting Standards Board ("FASB") issued Acc
Update ("ASU") 2016-02, Leases (Topic 842): Recognition and Measurement of F
Financial Liabilities. The update requires the recognition of lease assets and lease l
lessees for those leases classified as operating leases under previous U.S. GAAP. T
retains a distinction between finance leases and operating leases, with cash paymen
leases classified within operating activities in the statement of cash flows. These ar
be effective for public entities for fiscal years and interim periods within those year
December 15, 2018. The Company adopted the standard on January 1, 2019 and ca

cumulative-effect adjustment as of the beginning of the year of adoption or apply a
retrospective transition approach. The Company has identified one operating lease
which will be subject to the new guidance and will be recognized as an operating le
right-of-use asset upon adoption.

In November 2018, the FASB issued ASU 2018-18, Collaborative Arrangements (
Clarifying the Interaction between Topic 808 and Topic 606. These amendments m
improvements to accounting for collaborative arrangements by clarifying that certa
between collaborative arrangement participants should be accounted for as revenue
when the collaborative arrangement participant is a customer in the context of a un
those situations, all the guidance in Topic 606 should be applied, including recogni
measurement, presentation, and disclosure requirements. In addition, unit-of-accou
Topic 808 was aligned with the guidance in Topic 606 (that is, a distinct good or se
entity is assessing whether the collaborative arrangement or a part of the arrangeme
scope of Topic 606. These amendments will be effective for fiscal years and interim
those fiscal years, beginning after December 15, 2019 and should be applied retrosp
date of initial application of Topic 606. The Company is currently evaluating the ne
determine the impact it will have on the Company’s consolidated financial statemen

6. Net income (loss) per common share and preferred share:
Basic net income (loss) per common share is calculated using the two-class method participating securities which includes the convertible preferred shares as a separate preferred shares entitle the holders to participate in dividends and in earnings and lo Company on an equivalent basis as common shares. Accordingly, undistributed ear allocated to common shares and participating preferred shares based on the weighte of each class outstanding during the period.

The treasury stock method is used to compute the dilutive effect of the Company's warrants. Under this method, the incremental number of common shares used in co net income (loss) per common share is the difference between the number of comm assumed issued and purchased using assumed proceeds.

The if-converted method is used to compute the dilutive effect of the Company's co preferred shares. Under the if-converted method, dividends on the preferred shares, added back to earnings attributable to common shareholders, and the preferred shar kind dividends are assumed to have been converted at the share price applicable at period. The if-converted method is applied only if the effect is dilutive.

For the year ended December 31, 2018, all stock options, warrants and convertible were anti-dilutive and were excluded from the diluted weighted average common s for the period. For the year ended December 31, 2017, 2,172,034 stock options and excluded from the calculation of diluted net loss per common share as their inclusio anti-dilutive. No convertible preferred shares were outstanding for the year ended D 2017.

The following is a reconciliation of the numerators and denominators of basic and d per common share and preferred share:

	Year Ended December 31, 2018		2017
	Common	Preferred	Comm
Numerator:	Shares	Shares	Shares
Allocation of loss used attributed to shareholders:			
Basic	$(31,616)	$(2,881)	$(30,7
Adjustment for change in fair value of liability classified stock options	—	—	(187
Diluted	$(31,616)	$(2,881)	$(30,8
Denominator:			
Weighted average number of shares:			
Basic	19,425,711	1,769,900	17,9
Adjustment for dilutive effect of stock options	—	—	16,6
Diluted	19,425,711	1,769,900	18,0
Net loss attributable to shareholders per share - basic	$(1.63)	$(1.63)	$(1.71

Net loss attributable to shareholders per share - diluted	$(1.63)	$(1.63)	$(1.72

7. Property, plant and equipment:

Property, plant and equipment consisted of the following:

	December 31,	
	2018	2017
Research equipment	$7,313	$6,984
Office furniture and equipment	1,046	1,043
Computer equipment	2,461	2,311
Leasehold improvements	6,370	6,370
Less: accumulated depreciation and amortization	(16,199)	(15,6
Net book value	$991	$1,070

8. Accounts payable and accrued expenses:
Accounts payable and accrued expenses consisted of the following:

	December 3	
	2018	201
Trade payables	$665	$1,
Employee compensation, benefits, and related accruals	1,728	1,
Consulting and contracted research	1,404	81
Professional fees	237	25
Other	85	44
Total	$4,119	$3,

9. Term Loan:
In December 2017, the Company entered into a Loan and Security Agreement (the
with Silicon Valley Bank (the "Bank") under which the Company was funded an in
$7,000. In June 2018, the Company entered into a First Loan Modification Amendr
"Modification") to the Loan Agreement (together, the "Modified Loan Agreement"
the Bank accelerated the availability of a second tranche of $5,000 which was fund
the Modification. Amounts funded under the Modified Loan Agreement were interc
September 30, 2018 or, subject to the achievement of certain clinical milestones (th
Milestone"), March 31, 2019. Following the expiration of the interest-only period,
was payable in 30 equal monthly installments or, if the Interest-Only Milestone wa
equal monthly installments of principal plus interest, maturing on March 31, 2021.
tranche was payable in 24 equal monthly installments or, if the Interest-Only Miles
achieved, 18 equal monthly installments of principal plus interest, maturing on Sep
The interest and payment terms of the third and final tranche, if borrowed, remaine
from the Loan Agreement. The Modification did not amend the Loan Agreement's
provisions.

In August 2018, the Company entered into an Amended and Restated Loan and Sec
(the "Amended and Restated Loan Agreement") with the Bank, pursuant to which t
extend a term loan to the Company with a principal amount of $15,500 (the "Term
Loan was used to repay in full outstanding borrowings of $12,000 under the Modif
Agreement and a payment of $485, which represented the current portion of the fin
due under the Modified Loan Agreement, as well as for working capital and other g
purposes, including the advancement of the Company's clinical development progr
Loan accrues interest at a floating per annum rate of 0.5% above the prime rate, wh
monthly commencing in September 2018. The Term Loan is interest-only until Ma
followed by 30 equal monthly installments of principal plus interest, maturing on S
2022. In addition, the Company is required to pay a final payment fee of 6.5% of th
the date on which the term loan is prepaid, paid or becomes due and payable in full

The Company may prepay all, but not less than all, of the Term Loan subject to a p
$295, which represents the deferred portion of the final payment fee due under the
Agreement, plus 3.0% if prepaid prior to the first anniversary of the effective date o
and Restated Loan Agreement, 2.0% if prepaid on or after the first anniversary, but

second anniversary, or 1.0%, if prepaid on or after the second anniversary but prior date. As security for its obligations under the Amended and Restated Loan Agreem granted the Bank a first priority security interest on substantially all of the Compan its intellectual property and subject to certain other exceptions.

In connection with the Modification, the number of common shares exercisable pur warrant issued to the Bank in December 2017 under the Loan Agreement (the "Dec Warrant") increased by 36,008 common shares. The relative fair value of the additi shares exercisable pursuant to the December 2017 Warrant was $247 and was class With this increase, the December 2017 Warrant allowed the Bank to purchase a tot the Company's common shares at a price per common share of $2.43. The Decemb was immediately exercisable, had a 10-year term, and contained a cashless exercise connection with the entry into the Amended and Restated Loan Agreement, the ma common shares exercisable pursuant to the December 2017 Warrant was fixed at 8 per common share of $2.43. In September 2018, the Company issued 72,325 comm cashless exercise of the December 2017 Warrant.

In connection with the Amended and Restated Loan Agreement, the Company issu to the Bank to purchase 40,000 of the Company's common shares at a price per co $9.79. The relative fair value of the common shares exercisable pursuant to this wa and was classified in equity. The warrant is immediately exercisable, has a 10-year contains a cashless exercise provision. This warrant remains outstanding at Decemb

The debt proceeds were allocated based on the relative fair values of the debt instru
warrant instrument. The fair value of the warrant and the closing costs were record
discounts and are being amortized using the effective interest rate method over the
At December 31, 2018, the Company determined the effective interest rate on the A
Restated Loan Agreement with the Bank to be 9.53% (2017 - 9.25%). Amortizatio
discount and accretion of the final payment fee was $284 for the year ended Decem
(2017 - $11). Interest payments are made monthly.

Interest expense was $1,394 and the year ended December 31, 2018 (2017 - $24).

The outstanding loan and unamortized debt discount balances as of December 31, 2
accordance with the repayment terms under Amended and Restated Loan Agreeme

	December 31,	
	2018	2017
Term loan	$15,500	$7,000
Less: unamortized discount on loan	(600)	(203)
Less: current portion	—	(700)
Accrued portion of final payment fee	114	7
Loan payable, long-term	$15,014	$6,104

Scheduled principal payments on outstanding debt as of December 31, 2018, exclu
payment fee of $1,008, are as follows:

2019	$—
2020	5,167
2021	6,200
2022	4,133
Total	$15,500

The Amended and Restated Loan Agreement contains customary representations a
events of default (including an event of default upon the occurrence of a material i
Bank's security interest over the collateral, and a material adverse change of the Co
affirmative and negative covenants, including, among others, covenants that limit c
Company's ability to incur indebtedness, grant liens, merge or consolidate, dispose
investments, make acquisitions, enter into certain transactions with affiliates, engag
of business, pay dividends or make distributions, or repurchase stock, in each case
exceptions. Upon the occurrence and during the continuance of an event of default,
rate will apply that is 5.0% above the otherwise applicable interest rate. The Compa
compliance with these covenants at December 31, 2018.

10. Share capital:

(a) Financing:

In May 2018, the Company entered into an at-the-market equity offering sales agre
Nicolaus & Company, Incorporated ("Stifel") to sell common shares of the Compa
gross proceeds of up to $30,000, from time to time, through an "at-the-market" equ
program under which Stifel would act as sales agent. The Company sold 3,440,000
under the sales agreement for proceeds of approximately $29,200, net of commissi
excluding estimated transaction expenses.

In July 2018, the Company entered into an at-the-market equity offering sales agre
Jefferies LLC ("Jefferies") and Stifel, to sell common shares of the Company havi
proceeds of up to $50,000, from time to time, through an "at-the-market" equity of
under which Jefferies and Stifel would act as sales agent. The Company sold 1,600
shares under the sales agreement for proceeds of approximately $14,820, net of co
but excluding estimated transaction expenses. In connection with the Company's e
2018 sales agreement with Jefferies and Stifel, the May 2018 sales agreement was
terminated by the Company and Stifel.

In September 2018, the Company entered into an underwriting agreement with Jeff
relating to an underwritten public offering of 4,500,000 common shares sold by the
public offering price of $14.00 per common share. The Company received net proc
net of underwriting discounts and commissions, but before offering expenses. In co
Company's entry into the September 2018 underwriting agreement with Jefferies a
2018 sales agreement was mutually terminated by the Company, Jefferies and Stife

(b) Authorized share capital:
The Company's authorized share capital consists of an unlimited number of comm
shares without par value.

(c) Stock-based compensation:
On June 25, 2014, the shareholders of the Company approved the 2014 Equity Ince
"2014 Plan") which permits the grant of stock-based compensation awards to direc
employees and consultants of the Company. The Company's pre-existing stock opt
"Amended and Restated Stock Option Plan") was limited to the granting of stock o
incentive awards whereas the 2014 Plan also allows for the issuance of restricted sh
share units, share appreciation rights and performance shares. The 2014 Plan replac
and Restated Stock Option Plan. No further options will be granted under the Comp
and Restated Stock Option Plan.

The Amended and Restated Stock Option Plan provided for the grant of options for
common shares to directors, officers, employees and consultants prior to the Comp
offering ("IPO"). The options granted under the Amended and Restated Stock Opti
graduated basis over a four-year period or less and each option's maximum term is
Amended and Restated Stock Option Plan will continue to govern the options grant

Under the 2014 Plan, options granted generally vest on a graduated basis over a fou
less. The exercise price of the options is determined by the Board but must at least
fair market value of the common shares on the date of grant. Options may be exerc
maximum term of ten years. As of December 31, 2018, a total of 153,209 stock opt
granted under the 2014 Plan. The number of common shares available for issuance
Plan was increased by 900,000, effective January 1, 2019, as approved by the Boar
with the terms of the 2014 Plan.

Summary of stock option activity is as follows:

	Number of Options	Weighted Average Exercise Price CAD $	U.S. $
Outstanding, December 31, 2016	1,910,823	9.84	7.32
Granted	620,950	8.69	6.69
Exercised[1]	(71,006)	3.72	2.86
Forfeited, cancelled or expired	(120,862)	9.06	6.98
Outstanding, December 31, 2017	2,339,905	9.32	7.41
Granted	706,600	6.73	5.19
Exercised[1]	(251,163)	4.57	3.53
Forfeited, cancelled or expired	(123,436)	13.61	10.50

Outstanding, December 31, 2018	2,671,906	9.49	6.96
Exercisable, December 31, 2018	1,566,435	10.70	7.84

(1) During the year ended December 31, 2018, 49,502 (2017 – 63,425) stock
exercised for the same number of common shares in exchange for cash.
period, the Company issued 106,474 (2017 – 4,405) common shares for
exercise of 201,661 (2017 – 7,581) stock options.

The following table summarizes the stock options outstanding and exercisable at D
2018:

	Options Outstanding				Options Exerc	
Range of Exercise Prices U.S. $	Number of Options Outstanding	Weighted Average Remaining Contractual Life (years)	Weighted Average Exercise Price CAD $	Weighted Average Exercise Price U.S. $	Number of Options Exercisable	W E C
$1.96 - $2.74	529,675	2.34	3.42	2.51	529,675	
$2.75 - $4.70	237,188	8.84	4.80	3.52	59,589	
$4.71 - $5.35	508,050	9.19	6.48	4.75	—	
$5.36 - $7.59	391,469	7.61	9.49	6.96	209,664	
$7.60 - $8.35	269,354	6.13	10.69	7.84	232,869	
$8.36 - $8.98	365,052	8.17	11.47	8.41	184,322	
$8.99 - $18.70	371,118	6.39	22.43	16.45	350,316	
	2,671,906	6.73	9.49	6.96	1,566,435	

At December 31, 2018, there were 1,566,435 options exercisable with a weighted a
contractual life of 5.25 years.

A summary of the Company's non-vested stock option activity and related informa
ended December 31, 2018 is as follows:

	Number of Options	Weighted Average Grant D CAD $	U
Non-vested, January 1, 2018	900,604	7.12	
Granted	706,600	4.84	
Vested	(437,771)	8.47	
Forfeited or cancelled	(63,962)	6.70	
Non-vested, December 31, 2018	1,105,471	5.61	

The aggregate fair value of options vested during the year ended December 31, 201
(2017 – $2,047).

The fair value of stock options at the date of grant is estimated using the Black-Sch
option-pricing model which requires multiple subjective inputs. The risk-free intere
options is based on the U.S. Treasury yield curve in effect at the date of grant for a
the expected term of the option. Prior to the Company's IPO in November 2014, th

shares did not have a readily available market; therefore, the Company lacked com
historical and implied volatility information. Consequently, the expected volatility
was estimated based on a combination of the Company's available historical volati
and historical volatility analysis of peers that were similar to the Company with res
stage of life cycle, size, and financial leverage. Expected life assumptions are base
Company's historical data. The dividend yield is based on the fact that the Compan
cash dividends and has no present intention to pay cash dividends. Forfeitures are r
occur.

The weighted-average option pricing assumptions are as follows:

	Years ended December 31	
	2018	2017
Average risk-free interest rate	2.79%	2.35%
Expected volatility	75 %	80 %
Average expected term (in years)	7.38	7.37
Expected dividend yield	0.00%	0.00%
Weighted average fair value of options granted	$3.74	$5.02

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

	Years ended December 31,	
	2018	2017
Research and development	$988	$985
General and administrative	1,772	1,251
	$2,760	$2,236

As of December 31, 2018, the unrecognized stock-based compensation cost related
stock options was $3,919, which is expected to be recognized over a weighted-aver
2.41 years.

(d) Exchange agreement with certain funds affiliated with BVF Partners L.P. (colle
In March 2018, the Company and BVF entered into an exchange agreement pursua
Company issued to BVF 2,868,000 Series 1 Preferred Shares in exchange for 2,868
shares which were subsequently cancelled by the Company.

The Company filed articles of amendment creating an unlimited number of Series
Shares. The Series 1 Preferred Shares are convertible into common shares on a one
subject to the holder, together with its affiliates, beneficially owning no more than
number of common shares issued and outstanding immediately after giving effect t
(the “Beneficial Ownership Limitation”). The holder may reset the Beneficial Own
a higher or lower number, not to exceed 19.99% of the total number of common sh
outstanding immediately after giving effect to such conversion, upon providing wri
Company which will be effective 61 days after delivery of such notice. Each Series
Share is also convertible into one common share at any time at the Company’s opti
payment of additional consideration, provided that prior to any such conversion, th
with its affiliates, beneficially owns less than 5.00% of the total number of commo
and outstanding and such conversion will not result in the holder, together with its
beneficially holding more than 5.00% of the total number of common shares issued
immediately after giving effect to such conversion. In the event of a change of cont
Series 1 Preferred Shares shall be issued one common share for each outstanding S
Share held immediately prior to the change of control (without regard to the Benefi
Limitation), and following such conversion, will be entitled to receive the same kin
securities, cash or property that a holder of common shares is entitled to receive in
such change of control.

The Series 1 Preferred Shares rank equally to the common shares in the event of liq
dissolution or winding up or other distribution of the assets of the Company among
and the holders of the Series 1 Preferred Shares are entitled to vote together with th
on an as-converted basis and as a single class, subject in the case of each holder of
Preferred Shares to the Beneficial Ownership Limitation. Any Series 1 Preferred Sh
ineligible to be converted into common shares due to the Beneficial Ownership Lim
measured as of a given record date that applies for a shareholder meeting or ability

consent, shall be deemed to be non-voting securities of the Company. Holders of S
Shares are entitled to receive dividends (without regard to the Beneficial Ownershi
the same basis as the holders of common shares. The Company may not redeem the
Preferred Shares.

The Company recorded the issuance of Series 1 Preferred Shares and correspondin
common shares at $7.61 per share, the estimated weighted average cost at which B
common shares. The Series 1 Preferred Shares are recorded wholly as equity under
no bifurcation of conversion feature from the host contract, given that the Series 1
cannot be cash settled and have no redemption features.

During the year ended December 31, 2018, BVF converted 1,852,000 Series 1 Pref
exchange for an equal number of common shares of the Company.

11. Concentrations of market risk:

(a) Foreign currency risk:

At December 31, 2018, the Company had U.S. dollar denominated cash and cash e
marketable securities of $110,771 (2017 - $28,028) and Canadian denominated cas
equivalents and marketable securities of CAD$11,644 (2017 - CAD$19,619).

The Company faces foreign currency exchange rate risk in part, as a result of enteri
transactions denominated in currencies other than U.S. dollars, particularly those de
Canadian dollars. The Company also holds non-U.S. dollar denominated cash and c
marketable securities, accounts receivable and accounts payable, which are denomi
Canadian dollars.

Changes in foreign currency exchange rates can create significant foreign exchange
to the Company. The Company's current foreign currency risk is with the Canadian
majority of non-U.S. dollar denominated expenses are denominated in Canadian do
portion of cash and cash equivalents and marketable securities are held in Canadian
Company does not currently hedge its exposure and thus assumes the risk of future
on the amounts of Canadian dollars held.

(b) Interest Rate Risk:
At December 31, 2018, the Company had cash and cash equivalents and marketabl
$119,306. The Company's interest rate risk is primarily attributable to its cash and
and marketable securities. The Company believes that it does not have any materia
changes in the fair value of these assets as a result of changes in interest rates due t
nature of cash and cash equivalents and marketable securities. The Company does n
investments for trading or speculative purposes and has not used any derivative fin
to manage interest rate exposure.

The Company had a total outstanding loan balance of $15,500 as of December 31,
$nil was due within 12 months. The interest rate on borrowings under the Amended
Loan Agreement with the Bank accrues at a floating per annum rate of 0.5% above

12. Collaboration agreements:
The Company has entered into a number of collaboration agreements under which
received non-refundable upfront payments. Each arrangement is assessed in accord
606 under the five-step model as described in note 3i. The Company generally reco
from non-refundable upfront payments ratably over the estimated term of the perfo
or period in which the underlying benefit is transferred to the customer. If non-refu
fees have values to the customer on a standalone basis, separate from the undeliver
obligations, they are recognized upon delivery. The Company evaluates the measur
each reporting period and, if necessary, adjusts the measure of performance and rel
recognition.

Research and development milestones in the Company's collaboration agreements
following types of events:

- completion of pre-clinical research and development work leading to selection of
  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 Jap
investigational new drug applications and new drug applications; and
- marketing approval in a major market, such as the U.S., Europe or Japan.

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

The Company evaluates each arrangement that includes research and development milestone payments to determine whether the milestones are considered probable o and estimates the amount to be included in the transaction price using the most like method. If it is probable that a significant revenue reversal would not occur, the as milestone value is included in the transaction price. Milestone payments that are no control of the Company are not considered probable of being achieved and the tran then allocated to each performance obligation on a relative stand-alone selling price the Company recognizes revenue as or when the performance obligations under the satisfied. At the end of each subsequent reporting period, the Company re-evaluate of achievement of such milestones, and if necessary, adjusts its estimate of the ove price.

(a) Teva Pharmaceutical Industries Ltd. (“Teva Pharmaceutical”) collaborative dev
license agreement:

In December 2012, the Company entered into a collaborative development and lice
with Teva Pharmaceutical, through its subsidiary, Ivax International GmbH, pursua
Company granted Teva Pharmaceutical an exclusive worldwide license to develop
commercialize certain products, including TV-45070 (formerly XEN402). In the ye
December 31, 2018, no revenue has been recognized with respect to this agreement
March 2018, the Company and Teva Pharmaceuticals International GmbH and Tev
(together, “Teva”), entered into a termination agreement terminating by mutual agr
collaborative development and license agreement. In connection with the terminati
and the Company cancelled 1,000,000 common shares that were owned by Teva. P
terms of the termination agreement, Teva has also returned, licensed or assigned to
certain intellectual property, including certain patent rights and transferred regulato
to TV-45070 to the Company. The termination agreement requires the Company to
single-digit percentage royalty to Teva based on net sales of approved products, if a
from any continued development and commercialization of TV-45070 by the Comp
sublicensee during the period that assigned or licensed patents cover such products
sales have occurred. The Company recorded a gain on the termination of the collab
agreement of $4,398, net of direct costs incurred in connection with the termination
of 1,000,000 common shares, based on the estimated fair value represented by the
the common shares prior to the closing of the transaction.

(b) Genentech collaborative research and license agreement:

In December 2011, the Company entered into a collaborative research and license a
Genentech and its affiliate, F. Hoffman-La Roche Ltd. to discover and develop sele
inhibitors of Nav1.7 for the treatment of pain. Pursuant to this agreement, the Comp
Genentech a worldwide exclusive license to develop and commercialize compound
Nav1.7 and products incorporating such compounds for all uses. The Company also
Genentech a worldwide non-exclusive license to diagnostic products for the purpos
or commercializing such compounds.

Under the terms of the agreement, Genentech paid the Company an upfront fee of $
Genentech also provided funding to the Company for certain of the Company’s full
performing the research collaboration plan, which concluded in December 2016.

The Company received and recorded a $5,000 milestone payment in 2013 for the se
compound for development and an $8,000 payment in 2014 upon the approval by F
the clinical trial application. No additional milestone payments or royalties have be
date.

The Company is eligible to receive pre-commercial and commercial milestone pay
respect to the licensed products totaling up to an additional $613,000, comprised of
pre-clinical and clinical milestone payments, up to $387,500 in regulatory milestone
up to $180,000 in sales-based milestone payments for multiple products and indica
the Company is eligible to receive royalties based on net sales of the licensed produ
from a mid single-digit percentage to ten percent for small-molecule inhibitors for
such products are covered by the licensed patents and a low single-digit percentage
the date that is ten years after first commercial sale on a country-by-country basis,
single-digit percentage for large-molecule inhibitors of Nav1.7 for a period of ten y

commercial sale on a country-by-country basis. The pre-commercial and commerci
payments and royalties may be subject to reductions based on the period in which t
is selected for development and commercialization was initially conceived.

At execution of the collaborative research and license agreement with Genentech, t
price included only the $10,000 upfront consideration received. None of the at-risk
performance milestones, including research and development and sales-based miles
included in the transaction price, as all milestone amounts are outside the control o
and contingent upon Genentech's efforts and success in future clinical trials. Consi
associated with at-risk substantive performance milestones is recognized when it is
significant reversal of the cumulative revenue recognized will not occur. Any consi
to sales-based royalties will be recognized when the related sales occur as they wer
relate predominantly to the license granted to Genentech and therefore have also be
the transaction price. The Company will re-evaluate the transaction price in each re
and as uncertain events are resolved or other changes in circumstances occur.

The collaborative research and license agreement with Genentech was amended mu
May 2015, November 2015, March 2016, May 2017, July 2018 and September 201
extend the term of the research program or to provide the Company with greater fle
developing compounds that target Nav1.6. Pursuant to the current amendment, th
obtained a non-exclusive, irrevocable, perpetual, world-wide, sublicensable license
know-how forming part of the Genentech intellectual property developed under the
collaboration that is necessary or useful to make, use, sell, offer for sale, and impor
from the Company's Nav1.6 program that are above a certain potency threshold on
products containing those compounds. The Company's license from Genentech inc
commercialization rights but we are restricted from developing or commercializing
Nav1.6 compounds below a certain potency threshold on Nav1.7 in the field of epil
the Company's Nav1.6 compounds, regardless of their potency on Nav1.7, in the fi
exchange for the rights granted to the Company under this amendment, Genentech
receive a low single-digit percentage, tiered royalty on net sales of the Company's
compounds, including XEN901, for a period of ten years from first commercial sal
country-by-country basis. Pursuant to the amendment, Genentech was granted a roy
non-exclusive, world-wide license under the Company's Nav1.6 intellectual proper
sell, offer for sale and import compounds below a certain potency threshold on Nav
containing those compounds for all uses and indications except epilepsy.

In March 2014, the Company entered into a new agreement with Genentech for pai
focused on identifying genetic targets associated with rare phenotypes where indivi
inability to perceive pain or where individuals have non-precipitated spontaneous s
Pursuant to the terms of this agreement, any intellectual property arising out of the
jointly owned by the Company and Genentech. The Company also granted Genente
time-limited, exclusive right of first negotiation on a target-by-target basis to form
discovery collaborations. Under the terms of this agreement, Genentech paid an up
$1,500 and two $250 milestone payments related to the identification of novel pain
September 2015 and July 2017. Genentech's time-limited, exclusive right of first n
was exercisable throughout the research term, expired at the same time as the agree
2018. Despite such termination, the Company remains eligible for up to an addition
milestone payments.

Pursuant to the terms of the Company's agreement with the Memorial University o
the Company must pay to the Memorial University of Newfoundland certain milest
single-digit percentage of net sales for pain products the Company sells directly an
percentage of royalties received for sales of pain products by Genentech.

13. Commitments and contingencies:

(a) Lease commitments:

The Company entered into an amended lease agreement for research laboratories a
Burnaby, British Columbia, Canada for a 120-month term from April 1, 2012 to M
which included an element of free rent and tenant inducement that is amortized ove
lease.

Lease expense for the year ended December 31, 2018 was $1,194 (2017 – $1,079)
annual lease payments under existing operating lease commitments are as follows:

Year ending December 31:	
2019	1,128
2020	1,130
2021	1,069
2022	256
Total	$3,583

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

In August 2015, the Company entered into a priority access agreement with Medpa
provision of certain clinical development services. Under the terms of the agreemer
has committed to using Medpace non-exclusively for clinical development services
year term of the agreement. In consideration for priority access to Medpace resourc
service rates, the Company has committed to $7,000 of services over the term of th
$3,000 of which was paid in the year ended December 31, 2015.

(c) License, manufacture and supply agreement:
In March 2017, the Company entered into a license, manufacture and supply agreer
pharmaceutical contract manufacturing organization for the access and use of certa
documents as well as for the manufacture and supply of clinical and commercial dr
support the development of XEN007. Under the terms of the agreement, the Compa
upfront fee of $500 CAD and will be required to pay a low single-digit percentage
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 (previously known as 1OP2198) from 1st Or
asset purchase agreement. 1st Order previously acquired 1OP2198 from Valeant Ph
Luxembourg S.a.r.l., an indirect subsidiary of Bausch Health Companies Inc. (toge
Pharmaceuticals Ireland Limited, “Bausch Health”) and the Company has assumed
responsibilities under that agreement. Under the terms of the agreement, the Compa
upfront fee of $350 and milestone payments in 2017 totaling $700, which were exp
and development.

In September 2018, the Company entered into a milestone and royalty buy-out agre
Bausch Health under which all potential clinical development, regulatory and sales
and royalties on commercial sales with respect to XEN1101 that may become owed
Health under the asset purchase agreement were terminated in exchange for a one-t
$6,000 which was expensed in the period.

Future potential payments to 1st Order include $500 in clinical development milest
$6,000 in regulatory milestones, and $1,500 in other milestones, which may be pay
pre-commercially. There are no royalty obligations to 1st Order.

(e) License agreement:
In July 2017, the Company entered into a license agreement with a pharmaceutical
access and use of certain regulatory documents to support the development of XEN
terms of the agreement, the Company paid an upfront fee of $1,000, which was exp
and development. Future potential payments include $2,000 in clinical developmen
to $7,000 in regulatory milestones, plus a low-to-mid single-digit percentage royalt
any products developed and commercialized under the agreement.

(f) Guarantees and indemnifications:
The Company has entered into license and research agreements with third parties th
indemnification provisions that are customary in the industry. These indemnificatio
generally require the Company to compensate the other party for certain damages a
as a result of third party claims or damages arising from these transactions.

The maximum amount of potential future indemnification is unlimited; however, th
currently holds commercial and product liability insurance. This insurance limits th
exposure and may enable it to recover a portion of any future amounts paid. Histori
Company has not made any indemnification payments under such agreements and
believes that the fair value of these indemnification obligations is minimal. Accord
Company has not recognized any liabilities relating to these obligations for any per

14. Income taxes:

Income tax (recovery) expense varies from the amounts that would be computed by
expected Canadian and provincial statutory income tax rate of 27% (2017 – 27%)
income taxes as shown in the following table:

	2018	2017
Computed recoveries at Canadian federal and provincial tax rates	$(9,273)	$(8,000
Change in valuation allowance	10,472	9,210
Investment tax credits earned	(1,567)	(1,393
Tax attributes expired/utilized	911	683
Non-deductible expenditures	(473)	594
Effect of tax rate increases	—	(1,444
Other	(70)	350
Income tax (recovery) expense	$—	$—

Deferred income tax assets and liabilities result from the temporary differences bet
of assets and liabilities recognized for financial statement and income tax purposes
components of the Company's net deferred income tax assets are as follows:

	2018	201
Deferred income tax assets		
Scientific research and experimental development pool	$26,572	$25
Investment tax credits	23,808	22
Non-capital losses	22,035	13
Depreciable assets	5,710	5,
Deferred financing fees	1,303	57
Other	98	11
Less - valuation allowance	(79,526)	(6
Net deferred income tax assets	$—	$—

The realization of deferred income tax assets is dependent upon the generation of s
income during future periods in which the temporary differences are expected to re
valuation allowance is reviewed on a quarterly basis and if the assessment of the "n
not" criteria changes, the valuation allowance is adjusted accordingly. A full valuat
continues to be applied against deferred income tax assets as the Company has asse
realization of such assets does not meet the "more likely than not" criteria.

At December 31, 2018, the Company has unclaimed tax deductions for scientific re
experimental development expenditures of $98,412 (2017 – $92,799) with no expir

At December 31, 2018, the Company has $22,253 (2017 – $21,066) of investment
available to offset federal taxes payable and $7,640 (2017 – $7,560) of provincial t
to offset provincial taxes payable in the future.

At December 31, 2018, the Company has non-capital losses, net of uncertain tax po
forward for tax purposes, which are available to reduce taxable income of future ye
approximately $81,611 (2017 – $50,536).

The investment tax credits and loss carry forwards expire over various years to 203

As of December 31, 2018, the total amount of the Company's unrecognized tax ben
tax positions were $6,350 (2017 – $6,350). If recognized in future periods, the unre
benefits would affect the Company's effective tax rate. The Company recognizes p
interest and penalties related to unrecognized tax benefits within the income tax pro
and penalties have not been accrued at December 31, 2018 as none would be owing
unrecognized tax benefits due to the availability of non-capital losses to shelter any
income arising thereon.

The Company does not currently expect any significant increases or decreases to th
tax benefits within 12 months of the reporting date.

The Company files income tax returns in Canada and the United States, the jurisdic
the Company believes that it is subject to tax. In jurisdictions in which the Compan
believe it is subject to tax and therefore does not file income tax returns, the Compa
no certainty that tax authorities in those jurisdictions will not subject one or more ta
the inception of the Company) to examination. Further, while the statute of limitati
jurisdiction where an income tax return has been filed generally limits the examina
result of loss carry-forwards, the limitation period for examination generally does n
several years after the loss carry-forwards are utilized. Other than routine audits by
for tax credits and tax refunds that the Company claims, the Company is not aware
material income tax examination currently in progress by any taxing jurisdiction. T
from 2002 to 2017 remain subject to Canadian income tax examinations.

15. Related Parties:

(a) Exchange agreement with BVF:

In March 2018, the Company and BVF entered into an exchange agreement pursua
Company issued 2,868,000 Series 1 Preferred Shares in exchange for 2,868,000
which were subsequently cancelled by the Company. Prior to the closing of the tra
contemplated in the exchange agreement, BVF held a number of common shares re
approximately 19.9% of the Company's then outstanding common shares. For addi
regarding the Series 1 Preferred Shares, refer to note 10d.

(b) Termination of collaboration agreement with Teva:
In March 2018, the Company and Teva, entered into a termination agreement termi
agreement the collaborative development and license agreement dated December 7
amended. In connection with the termination, the Company cancelled 1,000,000 co
were owned by Teva. Prior to the share cancellation, Teva owned more than 5% of
outstanding common shares. For additional information regarding the termination a
share cancellation, refer to note 12a.

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

Item 9A. Controls and Procedures
Evaluation of disclosure controls and procedures. Our management, with the partic
Chief Executive Officer and our Chief Financial Officer, evaluated the effectivenes
disclosure controls and procedures as of December 31, 2018. The term "disclosure
procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act,
and other procedures of a company that are designed to ensure that information req
disclosed by a company in the reports that it files or submits under the Exchange A
processed, summarized and reported, within the time periods specified in the SEC'
Disclosure controls and procedures include, without limitation, controls and proced
ensure that information required to be disclosed by a company in the reports that it
under the Exchange Act is accumulated and communicated to the company's mana
its principal executive and principal financial officers, as appropriate to allow timel
regarding required disclosure.

Management recognizes that any controls and procedures, no matter how well desi
operated, can provide only reasonable assurance of achieving their objectives and r
necessarily applies its judgment in evaluating the cost-benefit relationship of possib
procedures. Based on the evaluation of our disclosure controls and procedures as o
2018, our Chief Executive Officer and our Chief Financial Officer concluded that,
our disclosure controls and procedures were, in design and operation, effective at th
assurance level.

Management's Annual Report on Internal Control over Financial Reporting. Our m
the participation of our Chief Executive Officer and our Chief Financial Officer, is
establishing and maintaining adequate internal control over our financial reporting,
defined in Rule 13a-15(f) and Rule 15d-15(f) of the Securities Exchange Act of 19
control over financial reporting is a process to provide reasonable assurance regard
of financial reporting and the preparation of financial statements for external purpo
with generally accepted accounting principles. Our internal control over financial r
those policies and procedures that:

(i) pertain to the maintenance of records that, in reasonable detail, accurately and f
transactions and dispositions of our assets;
(ii)

provide reasonable assurance that transactions are recorded as necessary to per
financial statements in accordance with generally accepted accounting principl
receipts and expenditures are being made only in accordance with authorizatio
management and directors; and

(iii) provide reasonable assurance regarding prevention or timely detection of unau
acquisition, use or disposition of our assets that could have a material effect o
statements.

The effectiveness of any system of internal control over financial reporting, includi
subject to inherent limitations, including the exercise of judgment in designing, imp
operating, and evaluating the controls and procedures, and the inability to eliminate
completely. Accordingly, any system of internal control over financial reporting, in
matter how well designed and operated, can only provide reasonable, not absolute,
projections of any evaluation of effectiveness to future periods are subject to the ris
may become inadequate because of changes in conditions or that the degree of com
policies or procedures may deteriorate. Management has assessed the effectiveness
control over financial reporting as at December 31, 2018. In making its assessment
used the criteria set forth by the Committee of Sponsoring Organizations of the Tre
Commission (COSO) in Internal Control – Integrated Framework (2013) to evaluat
of our internal control over financial reporting. Based on this assessment using thos
management has concluded that our internal control over financial reporting was ef
December 31, 2018.

Changes in internal control over financial reporting. There was no change in our in
over financial reporting identified in connection with the evaluation required by Ru
15d-15(d) of the Exchange Act that occurred during the three months ended Decem
has materially affected, or is reasonably likely to materially affect, our internal con
reporting.

Item 9B. Other Information

We have a written code of conduct that applies to all of our directors, officers and e
copy of the most up-to-date version of our code of conduct is available within the "
on our company website located at http://www.xenon-pharma.com and on SEDAR
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
Statement for the 2019 Annual Meeting of Shareholders to be filed with the SEC w
after the end of the fiscal year ended December 31, 2018.

Item 11. Executive Compensation
The information required by Item 11 of Form 10-K is incorporated by reference to
Statement for the 2019 Annual Meeting of Shareholders to be filed with the SEC w
after the end of the fiscal year ended December 31, 2018.

Item 12. Security Ownership of Certain Beneficial Owners and Management and R
Shareholder Matters
The information required by Item 12 of Form 10-K is incorporated by reference to
Statement for the 2019 Annual Meeting of Shareholders to be filed with the SEC w
after the end of the fiscal year ended December 31, 2018.

Item 13. Certain Relationships and Related Transactions, and Director Independenc
The information required by Item 13 of Form 10-K is incorporated by reference to
Statement for the 2019 Annual Meeting of Shareholders to be filed with the SEC w
after the end of the fiscal year ended December 31, 2018.

Item 14. Principal Accounting Fees and Services
The information required by Item 14 of Form 10-K is incorporated by reference to
Statement for the 2019 Annual Meeting of Shareholders to be filed with the SEC w
after the end of the fiscal year ended December 31, 2018.

PART IV

Item 15. Exhibits, Financial Statement Schedules

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

(a)(2) Financial Statement Schedules — All schedules have been omitted because t
applicable or required, or the information required to be set forth therein is include
consolidated Financial Statements or notes thereto included in Item 8 of this Annua
Form 10-K.

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

(b) Exhibits — The exhibits listed on the Exhibit Index (following the Signatures s
are filed herewith or are incorporated by reference to exhibits previously filed with

Item 16. Form 10-K Summary

Not applicable.

EXHIBIT INDEX

Exhibit Number	Description of Document	Incorporated by Refere Form	File No.	E
3.1	Articles of the Company.	10-Q	001-36687	3.
3.1A	Articles of Amendment to the Articles of the Company, creating the Series 1 Preferred Shares.	8-K	001-36687	3.
3.2	Amended and Restated By-laws of the Company.	10-Q	001-36687	3.
4.1	Form of Common Share Certificate.	S-1/A	333-198666	4.
4.2	Specimen Series 1 Preferred Share Certificate.	8-K	001-36687	4.
4.3	Warrant to Purchase Shares, dated August 3, 2018, by and between Xenon Pharmaceuticals Inc. and Silicon Valley Bank.	8-K	001-36687	4.

10.1†	Exclusive Collaborative Research and Option Agreement, dated June 10, 2009, by and between the Company and Merck Sharp & Dohme Research Ltd, as amended.	S-1/A	333-198666	1
10.2†	Collaborative Research and License Agreement, dated December 22, 2011, by and among the Company, Genentech, Inc. and F. Hoffmann-La Roche Ltd, as amended.	S-1/A	333-198666	1
10.3#	Stock Option Plan, as amended, and form of option agreement thereunder.	S-1/A	333-198666	1
10.4#	2014 Equity Incentive Plan.	S-1	333-198666	1
10.5#	Form of Share Option Agreement, as amended, under the 2014 Equity Incentive Plan.	10-K	001-36687	1
10.6#	Offer Letter, dated October 3, 2014, by and between the Company and Simon Pimstone.	S-1/A	333-198666	1
10.7#	Offer Letter, dated October 3, 2014, by and between the Company and Ian Mortimer.	S-1/A	333-198666	1
10.8#	Offer Letter, dated October 3, 2014, by and between the Company and Robin Sherrington.	S-1/A	333-198666	1

Exhibit Number	Description of Document	Incorporated by Refere Form	File No.	Ex
10.9	Lease, dated as of 2001, by and between the Company and Discovery Parks Incorporated, as amended through July 1, 2014.	S-1	333-198666	10
10.10#	Form of Director and Executive Officer Indemnification Agreement.	S-1/A	333-198666	10
10.11†	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.	10-Q	001-36687	10
10.12	Lease Modification Agreement, effective July 1, 2015, by and between the Company and Redstone Enterprises Ltd.	10-Q	001-36687	10
10.13	Lease Modification Agreement, effective December 1, 2015, by and between the Company and Redstone Enterprises Ltd.	10-K	001-36687	10
10.14†	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.	10-K	001-36687	10
10.15†	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.	10-Q	001-36687	10
10.16#	Offer letter, effective January 1, 2017, by and between Xenon Pharmaceuticals USA Inc. and James Empfield.	10-K	001-36687	10
10.17†	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.	10-Q	001-36687	10
10.18†	Asset Purchase Agreement, dated April 25, 2017, by and between the Company and 1st Order Pharmaceuticals, Inc.	10-Q	001-36687	10

10.19	Loan and Security Agreement, dated December 18, 2017, by and among Xenon Pharmaceuticals Inc., Xenon Pharmaceuticals USA Inc. and Silicon Valley Bank.	8-K	001-36687	10
10.20†	Termination Agreement by and among Xenon Pharmaceuticals Inc., Teva Pharmaceuticals International GmbH and Teva Canada Limited dated March 7, 2018.	8-K	001-36687	10
10.21	Exchange Agreement, dated March 23, 2018, by and among the Company and the shareholders listed in Schedule B thereto.	8-K	001-36687	10
10.22	At-the-Market Equity Offering Sales Agreement, dated as of May 8, 2018, between Xenon Pharmaceuticals Inc. and Stifel, Nicolaus & Company, Incorporated.	8-K	001-36687	1.1
10.23	First Loan Modification to Loan and Security Agreement, dated June 12, 2018, by and among Xenon Pharmaceuticals Inc., Xenon Pharmaceuticals USA Inc. and Silicon Valley Bank.	8-K	001-36687	10
10.24†	Letter Amendment #7, dated July 25, 2018, to the Collaborative Research and License Agreement, dated December 22, 2011, by and among the Company, Genentech, Inc. and F. Hoffmann-La Roche Ltd, as amended.	10-Q	001-36687	10

Exhibit Number	Description of Document	Incorporated by Refe Form	File No.	Ex
10.25	At-the-Market Equity Offering Sales Agreement, dated as of July 11, 2018, by and among Xenon Pharmaceuticals Inc., Jefferies LLC and Stifel, Nicolaus & Company, Incorporated.	8-K	001-36687	1.1
10.26	Amended and Restated Loan and Security Agreement, dated August 3, 2018, by and among Xenon Pharmaceuticals Inc., Xenon Pharmaceuticals USA Inc. and Silicon Valley Bank.	8-K	001-36687	10
10.27	Milestone and Royalty Buy-Out Agreement, dated September 7, 2018, by and among Xenon Pharmaceuticals Inc., Valeant Pharmaceuticals Ireland Limited and Valeant Pharmaceuticals Luxembourg S.a.r.l.	8-K	001-36687	10
10.28†	Amended and Restated Amendment #7, dated September 27, 2018, to the Collaborative Research and License Agreement, dated December 22, 2011, by and among the Company, Genentech, Inc. and F. Hoffmann-La Roche Ltd, as amended.	10-Q	001-36687	10
21.1	List of Subsidiaries of the Company.	10-K	001-36687	21
23.1	Consent of KPMG LLP, Independent Registered Public Accounting Firm.			
24.1	Powers of Attorney (contained on signature page).			
31.1	Rule 13a-14(a) / 15d-14(a) Certification of Principal Executive Officer			
31.2	Rule 13a-14(a) / 15d-14(a) Certification of Principal Financial Officer			
32.1*	Section 1350 Certification of Principal Executive Officer			
32.2*	Section 1350 Certification of Principal Financial Officer			
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 ex
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
10-K are not deemed filed with the Securities and Exchange Commission and are
incorporated by reference into any filing of Xenon Pharmaceuticals Inc. under the
1933, as amended, or the Securities Exchange Act of 1934, as amended, whether
after the date of this Form 10-K, irrespective of any general incorporation languag
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
Registrant has duly caused this report to be signed on its behalf by the undersigned
authorized.

Dated: March 6, 2019 XENON PHARMACEUTICALS INC.

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

POWER OF ATTORNEY

Each person whose signature appears below hereby constitutes and appoints Simon
Ian Mortimer, and each of them severally, as his or her true and lawful attorneys-in
with full power to act without the other and with full power of substitution and resu
him or her and in his or her name, place and stead, in any and all capacities (includ
capacity as a director and/or officer of Xenon Pharmaceuticals Inc.) to sign any and
and supplements to this report, and any and all other instruments necessary or incid
connection herewith, and to file the same, with all exhibits thereto, and all other do
connection therewith, with the Commission.

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

Signature	Title
/s/ Simon Pimstone	
Simon Pimstone	Chief Executive Officer (Principal Executive Officer)
/s/ Ian Mortimer	
Ian Mortimer	President and Chief Financial Officer (Principal Financial and Accounting Officer)

/s/ Michael Tarnow

Michael Tarnow — Chair of the Board of Directors

/s/ Mohammad Azab

Mohammad Azab — Director

/s/ Steven Gannon

Steven Gannon — Director

/s/ Michael Hayden

Michael Hayden — Director

/s/ Frank Holler

Frank Holler — Director

/s/ Gary Patou

Gary Patou — Director
Director

/s/ Richard Scheller

Richard Scheller

/s/ Dawn Svoronos

Dawn Svoronos Director

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