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

FORM 10-Q

(Mark One)

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

For the quarterly period ended March 31, 2021

OR

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

For the transition period from _____ to _____

Commission File Number: 001-36687

XENON PHARMACEUTICALS INC.

(Exact name of Registrant as Specified in its Charter)

Canada	**98-0661854**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
200-3650 Gilmore Way	
Burnaby, British Columbia, Canada	**V5G 4W8**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (604) 484-3300

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Shares, without par value	XENE	The Nasdaq Stock Market LLC (The Nasdaq Global Market)

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

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted 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 such files). Yes ☒ No ☐

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

Large accelerated filer	☐	Accelerated filer	☐
Non-accelerated filer	☒	Smaller reporting company	☒
Emerging growth company	☐		

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

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

As of May 7, 2021, the registrant had 40,967,221 common shares, without par value, outstanding.

XENON PHARMACEUTICALS INC.
QUARTERLY REPORT ON FORM 10-Q
FOR THE QUARTER ENDED MARCH 31, 2021

TABLE OF CONTENTS

In this Quarterly Report on Form 10-Q, "we," "our," "us," "Xenon," and "the Company" refer to Xenon Pharmaceuticals Inc. and its subsidiary. "Xenon" and the Xenon logo are the property of Xenon Pharmaceuticals Inc. and are registered in the United States and used or registered in various other jurisdictions. This report contains references to our trademarks and to trademarks belonging to other entities. Solely for convenience, trademarks and trade names referred to in this report may appear without the ® or ™ symbols, but such references are not intended to indicate, in any way, that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto. We do not intend our use or display of other companies' trade names or trademarks to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

Risk Factor Summary

Our business is subject to numerous risks and uncertainties, including those highlighted in the section of this report captioned "Risk Factors." The following is a summary of the principal risks we face:

- We have incurred significant losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future;
- We will likely need to raise additional funding, which may not be available on acceptable terms, if at all. Failure to obtain this necessary capital when needed may force us to delay, limit or terminate our product development efforts or other operations;
- Clinical drug development involves a lengthy and expensive process with uncertain timelines and uncertain outcomes. If clinical trials are prolonged, delayed, not completed, unsuccessful or inconclusive, we could experience material harm to our business and the market price of our common shares. In addition, we, or our collaborators, may be unable to commercialize our product candidates on a timely basis or at all;
- Clinical trials may fail to demonstrate adequately the safety and efficacy of our or our collaborators' product candidates at any stage of clinical development. Terminating the development of any of our or our collaborators' product candidates could materially harm our business and the market price of our common shares;
- We or our collaborators may find it difficult to enroll patients in our clinical studies, including for ultra-orphan, orphan or niche indications, which could delay or prevent clinical studies of our product candidates;
- The regulatory approval processes of the FDA, EMA, Health Canada and regulators in other jurisdictions are lengthy, time-consuming and inherently unpredictable. If we, or our collaborators, are unable to obtain regulatory approval for our product candidates in a timely manner, or at all, our business will be substantially harmed;
- If, in the future, we are unable to establish our own sales, marketing and distribution capabilities or enter into agreements for these purposes, we may not be successful in independently commercializing any future products;
- Our prospects for successful development and commercialization of our partnered products and product candidates are dependent upon the research, development and marketing efforts of our collaborators;
- We depend on our collaborative relationship with Neurocrine Biosciences to further develop and commercialize NBI-921352, and if our relationship is not successful or is terminated, we may not be able to effectively develop and/or commercialize NBI-921352, which could have a material adverse effect on our business;
- We intend to rely on third-party manufacturers to produce our clinical product candidates and commercial supplies. Any failure by a third-party manufacturer to produce acceptable supplies for us may delay or impair our ability to initiate or complete our clinical trials, gain regulatory approvals or commercialize approved products;
- We rely on third parties to conduct our pre-clinical studies and clinical trials. If these third parties do not successfully carry out their contractual duties including to comply with applicable laws and regulations or meet expected deadlines, our business could be substantially harmed;
- We could be unsuccessful in obtaining or maintaining adequate patent protection for one or more of our products or product candidates;
- We may not be able to protect our intellectual property rights throughout the world;
- Our business and operations could suffer in the event of an information security incident such as a cybersecurity breach, system failure, or other compromise of our systems or those of a contractor or vendor;
- Health pandemics or epidemics, including the COVID-19 pandemic and other public health crises may materially and adversely affect our business, financial condition and results of operations;
- The market price of our common shares may be volatile, and purchasers of our common shares could incur substantial losses;
- Future sales and issuances of our common shares, preferred shares, or rights to purchase common shares, including warrants or pursuant to our equity incentive plans, could cause you to incur dilution and could cause the market price of our common shares to fall; and
- We are at risk of securities class action litigation.

PART I. FINANCIAL INFORMATION

Item 1. Financial Statements

XENON PHARMACEUTICALS INC.
Consolidated Balance Sheets
(Unaudited)
(Expressed in thousands of U.S. dollars except share amounts)

	March 31, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 87,985	$ 45,009
Marketable securities	186,718	131,988
Accounts receivable	5,060	1,822
Prepaid expenses and other current assets	3,497	2,964
	283,260	181,783
Operating lease right-of-use asset, net (note 6)	3,206	3,326
Property, plant and equipment, net	3,691	3,554
Deferred tax assets (note 11)	514	523
Total assets	$ 290,671	$ 189,186
Liabilities and shareholders' equity		
Current liabilities:		
Accounts payable and accrued expenses (note 7)	$ 7,580	$ 10,874
Deferred revenue (note 10)	3,642	3,642
Operating lease liability (note 6)	270	265
	11,492	14,781
Operating lease liability, long-term (note 6)	2,902	3,050
	14,394	17,831
Shareholders' equity:		
Preferred shares, without par value; unlimited shares authorized; issued and outstanding: 1,016,000 (December 31, 2020 - 1,016,000) (note 9)	$ 7,732	$ 7,732
Common shares, without par value; unlimited shares authorized; issued and outstanding: 40,962,715 (December 31, 2020 - 35,012,125) (note 9)	498,334	397,748
Additional paid-in capital	65,457	45,357
Accumulated deficit	(294,256)	(278,492)
Accumulated other comprehensive loss	(990)	(990)
	$ 276,277	$ 171,355
Total liabilities and shareholders' equity	$ 290,671	$ 189,186
Commitments and contingencies (note 12)		

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

XENON PHARMACEUTICALS INC.
Consolidated Statements of Operations and Comprehensive Loss
(Unaudited)
(Expressed in thousands of U.S. dollars except share and per share amounts)

	Three Months Ended March 31,	
	2021	2020
Revenue (note 10)	$ 4,358	$ 7,078
Operating expenses:		
Research and development	16,308	11,791
General and administrative	4,109	3,320
	20,417	15,111
Loss from operations	(16,059)	(8,033)
Other income (expense):		
Interest income	72	1,116
Interest expense	—	(330)
Foreign exchange gain (loss)	155	(238)
Loss before income taxes	(15,832)	(7,485)
Income tax recovery (note 11)	68	1
Net loss and comprehensive loss	(15,764)	(7,484)
Net loss attributable to preferred shareholders	(423)	(222)
Net loss attributable to common shareholders	$ (15,341)	$ (7,262)
Net loss per common share (note 4):		
Basic and diluted	$ (0.42)	$ (0.22)
Weighted-average common shares outstanding (note 4):		
Basic and diluted	36,824,619	33,189,733

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

XENON PHARMACEUTICALS INC.
Consolidated Statements of Shareholders' Equity
(Unaudited)
(Expressed in thousands of U.S. dollars except share amounts)

	Convertible preferred shares		Common shares		Additional paid-in capital	Accumulated deficit	Accumulated other comprehensive loss (1)	Total shareholders' equity
	Shares	*Amount*	*Shares*	*Amount*				
Balance as of December 31, 2019	1,016,000	$ 7,732	28,139,228	$ 294,244	$ 40,646	$ (249,655)	$ (990)	$ 91,977
Net loss for the period						(7,484)		(7,484)
Issuance of common shares, net of issuance costs (note 9a)			6,759,187	102,456				102,456
Stock-based compensation expense					1,015			1,015
Issued pursuant to exercise of stock options			57,857	607	(593)			14
Balance as of March 31, 2020	1,016,000	$ 7,732	34,956,272	$ 397,307	$ 41,068	$ (257,139)	$ (990)	$ 187,978
Balance as of December 31, 2020	1,016,000	$ 7,732	35,012,125	$ 397,748	$ 45,357	$ (278,492)	$ (990)	$ 171,355
Net loss for the period						(15,764)		(15,764)
Issuance of common shares and pre-funded warrants, net of issuance costs (note 9a and note 9c)			5,868,135	99,846	18,769			118,615
Stock-based compensation expense					1,965			1,965
Issued pursuant to exercise of stock options			82,455	740	(634)			106
Balance as of March 31, 2021	1,016,000	$ 7,732	40,962,715	$ 498,334	$ 65,457	$ (294,256)	$ (990)	$ 276,277

(1) The accumulated other comprehensive loss is entirely related to historical cumulative translation adjustments from the application of U.S. dollar reporting when the functional currency of the Company was the Canadian dollar.

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

XENON PHARMACEUTICALS INC.
Consolidated Statements of Cash Flows
(Unaudited)
(Expressed in thousands of U.S. dollars)

	Three Months Ended March 31,	
	2021	2020
Operating activities:		
Net loss	$ (15,764)	$ (7,484)
Items not involving cash:		
Depreciation	196	104
Amortization of discount on term loan	—	137
Deferred income tax expense	9	52
Stock-based compensation	1,965	1,015
Unrealized foreign exchange (gain) loss	(204)	522
Unrealized (gain) loss on marketable securities	74	(281)
Changes in operating assets and liabilities:		
Accounts receivable	(3,238)	(824)
Prepaid expenses and other current assets	(533)	113
Accounts payable and accrued expenses	(3,213)	(577)
Deferred revenue	—	(5,844)
Net cash used in operating activities	(20,708)	(13,067)
Investing activities:		
Purchases of property, plant and equipment	(404)	(647)
Purchases of marketable securities	(100,655)	(107,482)
Proceeds from marketable securities	45,955	55,204
Net cash used in investing activities	(55,104)	(52,925)
Financing activities:		
Proceeds from issuance of common shares and pre-funded warrants, net of issuance costs (note 9a)	118,615	102,456
Issuance of common shares pursuant to exercise of stock options	106	14
Net cash provided by financing activities	118,721	102,470
Effect of exchange rate changes on cash and cash equivalents	67	(725)
Increase in cash and cash equivalents	42,976	35,753
Cash and cash equivalents, beginning of period	45,009	24,755
Cash and cash equivalents, end of period	$ 87,985	$ 60,508
Supplemental disclosures:		
Interest paid	$ —	$ 206
Interest received	651	1,172
Cash paid for operating lease	202	159
Supplemental disclosures of non-cash transactions:		
Fair value of stock options exercised on a cashless basis	448	583

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

1. Nature of the business:

Xenon Pharmaceuticals Inc. (the "Company"), incorporated in 1996 under the predecessor to the Business Corporations Act (British Columbia) and continued federally in 2000 under the Canada Business Corporations Act, is a clinical stage biopharmaceutical company focused on developing innovative therapeutics to improve the lives of patients with neurological disorders, with a focus on epilepsy.

The Company has incurred significant operating losses since inception. As of March 31, 2021, the Company had an accumulated deficit of $294,256 and a $15,764 net loss for the three months ended March 31, 2021. Management expects to continue to incur significant expenses in excess of revenue and to incur operating losses for the foreseeable future. To date, the Company has financed its operations primarily through funding received from collaboration and license agreements, private placements of common and preferred shares, public offerings of common shares and pre-funded warrants and debt financings.

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

2. Basis of presentation:

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

The Company has one wholly-owned subsidiary as of March 31, 2021, Xenon Pharmaceuticals USA Inc., which was incorporated in Delaware on December 2, 2016.

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

The accompanying unaudited interim consolidated financial statements have been prepared in accordance with United States generally accepted accounting principles ("U.S. GAAP") and pursuant to the rules and regulations of the United States Securities and Exchange Commission ("SEC") for interim financial information. Accordingly, these consolidated financial statements do not include all of the information and footnotes required for complete consolidated financial statements and should be read in conjunction with the audited consolidated financial statements and notes for the year ended December 31, 2020 and included in the Company's 2020 Annual Report on Form 10-K filed with the SEC and with the securities commissions in British Columbia, Alberta and Ontario on March 1, 2021.

These unaudited interim consolidated financial statements reflect all adjustments, consisting of normal recurring adjustments, which, in the opinion of management, are necessary for a fair presentation of results for the interim periods presented. The results of operations for the three months ended March 31, 2021 and 2020 are not necessarily indicative of results that can be expected for a full year. These unaudited interim consolidated financial statements follow the same significant accounting policies as those described in the notes to the audited consolidated financial statements of the Company included in the Company's 2020 Annual Report on Form 10-K for the year ended December 31, 2020, with the exception of the policies described in note 3 below.

3. Changes in significant accounting policies:

In December 2019, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") 2019-12, Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes. These amendments simplify accounting for income taxes, change the accounting for certain income tax transactions and make certain improvements to the codification. The Company has adopted this standard as of January 1, 2021 on a prospective basis. The adoption of the standard had no impact on the Company's consolidated balance sheets, consolidated statements of operations and comprehensive loss and consolidated statements of cash flows.

4. Net income (loss) per common share:

Basic net income (loss) per common share is calculated using the two-class method required for participating securities which includes 1,016,000 Series 1 Preferred Shares as a separate class for the three months ended March 31, 2021 (2020 – 1,016,000). The convertible preferred shares entitle the holders to participate in dividends and in earnings and losses of the Company on an equivalent basis as common shares. Accordingly, undistributed earnings (losses) are allocated to common shares and participating preferred shares based on the weighted-average shares of each class outstanding during the period.

The weighted average number of common shares used in the basic and diluted net income (loss) per common share calculations for the three months ended March 31, 2021 include the pre-funded warrants issued in connection with the Company's March 2021 underwritten public offering (note 9c) as the pre-funded warrants are exercisable at any time for nominal cash consideration.

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

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

For the three months ended March 31, 2021 and 2020, all stock options, warrants and convertible preferred shares were anti-dilutive and were excluded from the diluted weighted average common shares outstanding for the period.

5. Fair value of financial instruments:

Certain financial instruments and other items are measured at fair value.

To determine the fair value, the Company uses the fair value hierarchy for inputs used to measure fair value of financial assets and liabilities. This hierarchy prioritizes the inputs to valuation techniques used to measure fair value into three levels: Level 1 (highest priority), Level 2, and Level 3 (lowest priority).

- *Level 1* - Unadjusted quoted prices in active markets for identical instruments.
- *Level 2* - Inputs other than quoted prices included within Level 1 that are observable for the asset or liability, either directly or indirectly. Level 2 inputs include quoted prices for similar assets or liabilities in active markets, quoted prices for identical or similar assets or liabilities in markets that are not active, inputs other than quoted prices that are observable for the asset or liability (i.e., interest rates, yield curves, etc.), and inputs that are derived principally from or corroborated by observable market data by correlation or other means (market corroborated inputs).
- *Level 3* - Inputs are unobservable and reflect the Company's assumptions as to what market participants would use in pricing the asset or liability. The Company develops these inputs based on the best information available.

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

The Company's Level 1 assets include cash and cash equivalents and marketable securities with quoted prices in active markets. The carrying amount of accounts receivables, accounts payable and accrued expenses approximates fair value due to the nature and short-term of those instruments.

6. Leases:

The Company has one operating lease for research laboratories and office space in Burnaby, British Columbia. In October 2020, the Company entered into a lease amendment for a 21–month committed term from October 1, 2020 to June 30, 2022. A renewal option for a portion of the facility for a 5-year term that is reasonably certain of exercise has been included in the determination of the right-of-use asset and lease liability.

The cost components of the operating lease were as follows for the three months ended March 31, 2021 and 2020:

	Three Months Ended March 31,	
	2021	2020
Lease Cost		
Operating lease expense	$ 139	$ 109
Variable lease expense(1)	184	136
Lease Term and Discount Rate		
Remaining lease term (years)	6.25	2
Discount rate	2.45%	3.75%

(1) Variable lease costs are payments that vary because of changes in facts or circumstances and include common area maintenance and property taxes related to the premises. Variable lease costs are excluded from the calculation of minimum lease payments.

Future minimum lease payments as of March 31, 2021 were as follows:

Year ending December 31:	
2021	$ 618
2022	703
2023	576
2024	576
2025 and thereafter	1,441
Total future minimum lease payments	$ 3,914
Less: imputed interest	(268)
Less: future lease incentives reasonably certain of use	(474)
Present value of lease liabilities	$ 3,172

7. Accounts payable and accrued expenses:

Accounts payable and accrued expenses consisted of the following:

	March 31, 2021	December 31, 2020
Trade payables	$ 2,132	$ 3,041
Employee compensation, benefits, and related accruals	1,323	2,859
Consulting and contracted research	3,754	4,738
Professional fees	289	167
Other	82	69
Total	$ 7,580	$ 10,874

8. Term loan:

In August 2018, the Company entered into an Amended and Restated Loan and Security Agreement (the “Amended and Restated Loan Agreement”) with Silicon Valley Bank (the “Bank”), pursuant to which the Bank agreed to extend a term loan to the Company with a principal amount of $15,500. The Term Loan accrued interest at a floating per annum rate of 0.5% above the prime rate. The Term Loan was interest-only until March 31, 2020, followed by 30 equal monthly installments of principal plus interest, originally maturing on September 1, 2022. In addition, the Company was required to pay a final payment fee of 6.5% of the Term Loan on the date on which the term loan was prepaid, paid or became due and payable in full.

In May 2020, the Company repaid the total outstanding term loan balance ahead of the maturity date. The repayment consisted of (i) the outstanding principal balance, (ii) a final payment fee of $1,008, which was partially accrued up to the date of repayment, and (iii) a prepayment fee of $225. At the time of repayment, all liabilities and obligations under the Amended and Restated Loan Agreement terminated automatically. The Company recorded a loss on repayment of the term loan of $988, which represents the difference between the carrying value of the term loan on the repayment date and the amount paid to extinguish the term loan. The repayment did not affect the Bank’s rights in connection with the warrant to the Bank to purchase 40,000 of our common shares at a price per common share of $9.79 which will remain outstanding until exercised or expired in August 2028.

9. Share capital:

(a) Financing:

In November 2019, the Company entered into an at-the-market equity offering sales agreement with Jefferies LLC ("Jefferies") and Stifel, Nicolaus & Company, Incorporated ("Stifel") to sell common shares of the Company having aggregate gross proceeds of up to $50,000 from time to time, through an "at-the-market" equity offering program under which Jefferies and Stifel would act as sales agents. As of December 31, 2019, the Company had sold 805,643 common shares under the sales agreement for proceeds of approximately $10,729, net of commissions paid and transaction expenses. In January 2020, the Company sold an additional 2,446,687 common shares for proceeds of approximately $37,796, net of commissions paid and transaction expenses.

In January 2020, the Company entered into an underwriting agreement with Jefferies, Stifel and Guggenheim Securities, LLC, relating to an underwritten public offering of 3,750,000 common shares sold by the Company at a public offering price of $16.00 per common share, and granted the underwriters an option for a period of 30 days to purchase up to an additional 562,500 common shares. The public offering was completed in January 2020, and the Company received net proceeds of $56,265, net of underwriting discounts, commissions and offering expenses. The underwriters exercised their option in full in February 2020 and the Company received additional proceeds of $8,395, net of underwriting discounts, commissions and offering expenses.

In August 2020, the Company entered into an at-the-market equity offering sales agreement with Jefferies and Stifel to sell common shares of the Company having aggregate gross proceeds of up to $100,000, from time to time, through an "at-the-market" equity offering program under which Jefferies and Stifel would act as sales agents. As of March 31, 2021, 733,000 common shares have been sold under the sales agreement for proceeds of approximately $10,693, net of commissions paid and transaction expenses.

In March 2021, the Company entered into an underwriting agreement with Jefferies and Stifel, relating to an underwritten public offering of 5,135,135 common shares, including 810,810 common shares sold upon the full exercise of the underwriters' over-allotment option, at a public offering price of $18.50 per common share and pre-funded warrants to purchase 1,081,081 common shares (the "Pre-Funded Warrants") at $18.4999 per Pre-Funded Warrant (note 9c). The public offering was completed in March 2021, and the Company received proceeds of $107,922, net of underwriting discounts, commissions and offering expenses.

(b) Exchange agreement with certain funds affiliated with BVF Partners L.P. (collectively, "BVF"):

In March 2018, the Company and BVF entered into an exchange agreement pursuant to which the Company issued to BVF 2,868,000 Series 1 Preferred Shares in exchange for 2,868,000 common shares which were subsequently cancelled by the Company.

The Company filed articles of amendment creating an unlimited number of Series 1 Preferred Shares. The Series 1 Preferred Shares are convertible into common shares on a one-for-one basis subject to the holder, together with its affiliates, beneficially owning no more than 9.99% of the total number of common shares issued and outstanding immediately after giving effect to such conversion (the "Beneficial Ownership Limitation"). The holder may reset the Beneficial Ownership Limitation to a higher or lower number, not to exceed 19.99% of the total number of common shares issued and outstanding immediately after giving effect to such conversion, upon providing written notice to the Company which will be effective 61 days after delivery of such notice. Each Series 1 Preferred Share is also convertible into one common share at any time at the Company's option without payment of additional consideration, provided that prior to any such conversion, the holder, together with its affiliates, beneficially owns less than 5.00% of the total number of common shares issued and outstanding and such conversion will not result in the holder, together with its affiliates, beneficially holding more than 5.00% of the total number of common shares issued and outstanding immediately after giving effect to such conversion. In the event of a change of control, holders of Series 1 Preferred Shares shall be issued one common share for each outstanding Series 1 Preferred Share held immediately prior to the change of control (without regard to the Beneficial Ownership Limitation), and following such conversion, will be entitled to receive the same kind and amount of securities, cash or property that a holder of common shares is entitled to receive in connection with such change of control.

The Series 1 Preferred Shares rank equally to the common shares in the event of liquidation, dissolution or winding up or other distribution of the assets of the Company among its shareholders and the holders of the Series 1 Preferred Shares are entitled to vote together with the common shares on an as-converted basis and as a single class, subject in the case of each holder of the Series 1 Preferred Shares to the Beneficial Ownership Limitation. Any Series 1 Preferred Shares that are ineligible to be converted into common shares due to the Beneficial Ownership Limitation, measured as of a given record date that applies for a shareholder meeting or ability to act by written consent, shall be deemed to be non-voting securities of the Company. Holders of Series 1 Preferred Shares are entitled to receive dividends (without regard to the Beneficial Ownership Limitation) on the same basis as the holders of common shares. The Company may not redeem the Series 1 Preferred Shares.

The Company recorded the issuance of Series 1 Preferred Shares and corresponding cancellation of common shares at $7.61 per share, the estimated weighted average cost at which BVF acquired the common shares. The Series 1 Preferred Shares are recorded wholly as equity under ASC 480, with no bifurcation of conversion feature from the host contract, given that the Series 1 Preferred Shares cannot be cash settled and have no redemption features.

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

BVF was a related party of the Company prior to the closing of the exchange agreement, and continues to be a related party as of March 31, 2021.

(c) Pre-Funded Warrants:

In connection with an underwritten public offering completed in March 2021, the Company issued 1,081,081 Pre-Funded Warrants at a price of $18.4999 per Pre-Funded Warrant which grants the holder the right to purchase up to 1,081,081 common shares at an exercise price of $0.0001 per share. The Pre-Funded Warrants are exercisable at the holder's discretion from the date of issuance until the date the Pre-Funded Warrant is exercised in full. The Company may not affect the exercise of any Pre-Funded Warrant, and a holder will not be entitled to exercise any portion of any Pre-Funded Warrant that, upon giving effect to such exercise, would cause: (i) the aggregate number of common shares beneficially owned by such holder, together with its affiliates, to exceed 4.99% of the total number of common shares outstanding immediately after giving effect to the exercise; or (ii) the combined voting power of the Company's securities beneficially owned by such holder, together with its affiliates, to exceed 4.99% of the combined voting power of all of the Company's securities immediately outstanding after giving effect to the exercise, which percentage may be changed at the holder's election to a higher or lower percentage not in excess of 19.99% upon at least 61 days' notice to the Company.

Since the Pre-Funded Warrants meet the condition for equity classification, proceeds from issuance of the Pre-Funded Warrants of $18,769, net of underwriting discounts, commissions and offering expenses, are recorded in additional paid-in capital. Upon exercise of the Pre-Funded Warrants, the historical costs recorded in additional paid-in capital along with the exercise price collected from holder will be recorded in common shares. As of March 31, 2021, no Pre-Funded Warrants have been exercised. Pre-funded warrants to purchase 1,081,081 common shares are not included in the number of issued and outstanding common shares as of March 31, 2021.

(d) Stock-based compensation:

The following table presents stock option activity for the period:

	Three Months Ended March 31,	
	2021	**2020**
Outstanding, beginning of period	4,758,997	3,534,236
Granted	1,111,950	1,118,350
Exercised(1)	(122,403)	(98,326)
Forfeited, cancelled or expired	(5,936)	(26,268)
Outstanding, end of period	5,742,608	4,527,992
Exercisable, end of period	2,769,438	1,992,705

(1) During the three months ended March 31, 2021, 46,296 (2020 – 1,972) stock options were exercised for the same number of common shares in exchange for cash. In the same period, the Company issued 36,159 (2020 – 55,885) common shares for the cashless exercise of 76,107 (2020 – 96,354) stock options.

The fair value of each stock option granted is estimated using the Black-Scholes option-pricing model with the following weighted-average assumptions:

	Three Months Ended March 31,	
	2021	2020
Average risk-free interest rate	1.15%	0.80%
Expected volatility	68%	68%
Average expected term (in years)	6.53	6.73
Expected dividend yield	0%	0%
Weighted average fair value of stock options granted	$ 12.86	$ 7.41

10. Revenue:

Revenue was as follows for the three months ended March 31, 2021 and 2020:

	Three Months Ended March 31,	
	2021	2020
Neurocrine Biosciences:		
Recognition of the transaction price	$ —	$ 5,844
Research and development services	1,358	1,234
Flexion:		
Milestone payments	3,000	—
Total collaboration revenue	$ 4,358	$ 7,078

(a) Neurocrine Biosciences license and collaboration agreement:

In December 2019, the Company entered into a License and Collaboration Agreement with Neurocrine Biosciences Inc. (“Neurocrine Biosciences”). Pursuant to this agreement, the Company granted an exclusive license to XEN901, now known as NBI-921352, and an exclusive license to pre-clinical compounds for development, XEN393, XPC’535 and XPC’391 (collectively, the “DTCs”). The agreement also includes a two-year research collaboration to discover, identify and develop additional novel Nav1.6 and Nav1.2/1.6 inhibitors (“Research Compounds”), with an option to extend for an additional year. The Company and Neurocrine Biosciences are collaborating on the conduct of two collaboration programs: (a) a joint research collaboration to discover, identify and preclinically develop Research Compounds (the “Research Program”) and (b) a collaborative development program for XEN901 and two DTCs selected by the joint steering committee (the “Initial Development Program”).

At execution of the agreement, Neurocrine Biosciences paid the Company an upfront cash payment of $30,000 and a $20,000 equity investment in the Company. The equity investment was measured at fair value of $16,667 on the date of issuance and the resulting premium $3,333, together with the upfront cash payment totaling $33,333, was the transaction price of the arrangement for allocation to the performance obligations. The agreement includes the following performance obligations: (i) an exclusive license to XEN901 with associated technology and know-how transfer, (ii) an exclusive license to the DTCs with associated know-how transfer, (iii) a license to Research Compounds and research services under the Research Program, (iv) development services under the Initial Development Program for XEN901, and (v) development services under the Initial Development Program for the DTCs. The total transaction price of $33,333 was allocated to performance obligation (v) based on its estimated standalone selling price determined based on internal development plans and budget, with the balance allocated to performance obligations (i) and (ii) by the residual approach. The Company allocated the transaction price as follows: $28,807 to performance obligations (i) and (ii), completed as of December 2020, and $5,118, which includes $592 of variable consideration, to performance obligation (v), which is expected to be completed by Q1 2022.

The arrangement consideration related to the services under performance obligations (iii) and (iv) to be performed on behalf of Neurocrine Biosciences were excluded from the initial transaction price allocation because the consideration and performance are contingent upon Neurocrine Biosciences requesting performance of the services and these services are priced at an estimated fair value. None of the at-risk substantive performance milestones, including development, regulatory and sales-based milestones, were included in the transaction price, as all milestone amounts are outside the control of the Company and contingent upon Neurocrine Biosciences’s efforts and success in future clinical trials. The Company will re-evaluate the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur.

During the three months periods ended March 31, 2021 and 2020, the Company recognized $1,358 and $7,078 of revenue, respectively, which comprised of $nil and $5,761, respectively, associated with (i) the exclusive license to XEN901 and (ii) the exclusive license to the DTCs; $1,358 and $1,234, respectively, for the research and development services under (iii) the Research Program and (iv) the Initial Development Program for XEN901; and $nil and $83, respectively, for (v) development services under the Initial Development Program for the DTCs. As of March 31, 2021, there is $1,358 of accounts receivable and $3,642 of deferred revenue related to the Neurocrine Collaboration Agreement, which is classified as current on the balance sheet based on the period the services are expected to be delivered.

The Company has an option to co-fund 50% of the development costs of XEN901 or another product candidate in the U.S., exercisable upon achievement of certain milestones, in exchange for increased U.S. royalties. The Company has not exercised this option as of March 31, 2021.

(b) Flexion definitive agreement:

In September 2019, the Company entered into an agreement with Flexion Therapeutics Inc. ("Flexion") pursuant to which Flexion acquired all rights with respect to XEN402, and a related compound (collectively "XEN402"), including certain regulatory documentation, intellectual property rights, reports, data and all quantities of XEN402, now known as FX301, owned or controlled by the Company.

During the three months ended March 31, 2021, the U.S. Food and Drug Administration cleared the first investigational new drug application for FX301 and Flexion initiated a Phase 1b clinical trial, resulting in milestone payments of $1,000 and $2,000 due to the Company, respectively. Pursuant to terms of the agreement, the Company will also be eligible for a development milestone payment of $5,000 upon initiation of a Phase 2 proof-of-concept clinical trial. Following successful proof-of-concept, the Company may be entitled to future clinical development and global regulatory approval milestone payments of up to $40,750, commercial milestone payments of up to $75,000, as well as future royalties ranging from mid-single to low-double digit percentages. These additional amounts will be recognized as determinable.

11. Income taxes:

Income tax recovery for the three months ended March 31, 2021 and 2020 arose from the operations of Xenon Pharmaceuticals USA Inc., the Company's wholly-owned subsidiary in the United States. Deferred income tax assets recorded on the consolidated balance sheets as of March 31, 2021 and December 31, 2020 resulted from the temporary differences between the amounts of assets and liabilities recognized for financial statement and income tax purposes related to the operations of Xenon Pharmaceuticals USA Inc. The realization of deferred income tax assets is dependent upon the generation of sufficient taxable income during future periods in which the temporary differences are expected to reverse.

12. Commitments and contingencies:

(a) Priority access agreement with Medpace Inc. ("Medpace"):

In August 2015, the Company entered into a priority access agreement with Medpace for the provision of certain clinical development services, under which the Company has committed to using Medpace non-exclusively for clinical development services over the five-year term of the agreement which ended in August 2020. The Company has committed to $7,000 of services over the term of the agreement of which $3,461 of services have been received and $3,539 remains committed as of March 31, 2021. As the Company did not meet the commitment to retain Medpace for $7,000 of services prior to August 2020, the Company is required to provide Medpace the exclusive right to perform all subsequent outsourced clinical development work until such $7,000 commitment has been satisfied, subject to the availability of appropriate Medpace resources and reasonable service rates. If the Company decides not to retain Medpace for the provision of clinical development services, the Company may satisfy its obligations under the priority access agreement by paying Medpace an amount equal to half of the unsatisfied portion. The Company intends to continue to utilize Medpace for clinical development work where suitable in order to fulfill the remaining commitment; therefore, no liability has been recognized as of March 31, 2021 with respect to the unsatisfied portion under the priority access agreement.

(b) License, manufacture and supply agreement:

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

(c) Asset purchase agreement with 1st Order Pharmaceuticals, Inc. ("1st Order"):

In April 2017, the Company acquired XEN1101 (previously known as 1OP2198) from 1st Order pursuant to an asset purchase agreement. In August 2020, the Company and 1st Order amended the asset purchase agreement to amend certain definitions in the agreement and to modify the payment schedule for certain milestones. Future potential payments to 1st Order related to the XEN1101 program include up to $1,200 in clinical development milestones, up to $6,000 in regulatory milestones, and $500 in other milestones. To date, the Company has paid $300 based on progress against these milestones. There are no royalty obligations to 1st Order.

(d) License agreement

In July 2017, the Company entered into a license agreement with a pharmaceutical company for the access and use of certain regulatory documents to support the development of XEN007. Future potential payments include $2,000 in clinical development milestones, up to $7,000 in regulatory milestones, plus a low-to-mid single-digit percentage royalty on net sales of any products developed and commercialized under the agreement. No amounts have been accrued to date based on the progress against these milestones.

(e) Guarantees and indemnifications:

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

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

ITEM 2. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

This section should be read in conjunction with our unaudited interim consolidated financial statements and related notes included in Part I, Item 1 of this report and our audited consolidated financial statements and related notes thereto and management's discussion and analysis of financial condition and results of operations for the year ended December 31, 2020 included in our Annual Report on Form 10-K filed with the U.S. Securities and Exchange Commission on March 1, 2021 and with the securities commissions in British Columbia, Alberta and Ontario on March 1, 2021.

Forward-Looking Statements

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

- our ability to identify additional products or product candidates either from our internal research efforts or though acquiring or in-licensing other product candidates or technologies;
- the initiation, timing, cost, progress and success of our research and development programs, pre-clinical studies, and clinical trials;

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

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

In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this Quarterly Report on Form 10-Q, and although we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted a thorough inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and you are cautioned not to unduly rely upon these statements.

Overview

We are a clinical stage biopharmaceutical company committed to developing innovative therapeutics to improve the lives of patients with neurological disorders. We are advancing a novel product pipeline of neurology-focused therapies to address areas of high unmet medical need, with a focus on epilepsy.

Proprietary Programs

- XEN1101 is a differentiated Kv7 potassium channel modulator being developed for the treatment of epilepsy and potentially other neurological disorders. Designed as a randomized, double-blind, placebo-controlled, multicenter study, the "X-TOLE" study is an ongoing Phase 2b clinical trial to evaluate the clinical efficacy, safety, and tolerability of XEN1101 administered as adjunctive treatment in approximately 300 adult patients with focal epilepsy. The primary endpoint is the median percent change in monthly focal seizure frequency from baseline compared to treatment period of active versus placebo. Patient screening has now been completed with the final patients currently in the baseline period. Patient randomization is expected to be complete in June, with topline data anticipated by the end of the third quarter of 2021.

- We also continue to evaluate opportunities to develop XEN1101 in neurological indications outside of epilepsy that could be well-suited to its unique mechanism of action. On March 8, 2021, we announced a collaboration with the Icahn School of Medicine at Mount Sinai to facilitate an investigator-sponsored Phase 2 proof-of-concept, randomized, parallel-arm, placebo-controlled clinical trial of XEN1101 for the treatment of major depressive disorder, or MDD, and anhedonia, which is expected to be initiated in the coming months. In parallel, we are planning a company-sponsored clinical study in MDD supported by promising pre-clinical data with XEN1101 and clinical data generated from both an open-label study and a randomized, placebo-controlled clinical trial that explored the targeting of KCNQ channels as a treatment for MDD using ezogabine.

- XEN496, a Kv7 potassium channel modulator, is a proprietary pediatric formulation of the active ingredient ezogabine being developed for the treatment of KCNQ2 developmental and epileptic encephalopathy, or KCNQ2-DEE. We have received Fast Track designation and Orphan Drug Designation for XEN496 for the treatment of seizures associated with KCNQ2-DEE from the U.S. Food and Drug Administration, or FDA, as well as orphan medicinal product designation from the European Commission. A Phase 3 randomized, double-blind, placebo-controlled, parallel group, multicenter clinical trial, called the "EPIK" study, is underway to evaluate the efficacy, safety, and tolerability of XEN496 administered as adjunctive treatment in approximately 40 pediatric patients aged one month to less than 6 years with KCNQ2-DEE.

- XEN007 (active ingredient flunarizine) is a CNS-acting Cav2.1 and T-type calcium channel modulator that is being studied in treatment-resistant childhood absence epilepsy, or CAE, and potentially other neurological disorders. An investigator-led Phase 2 proof-of-concept study is ongoing to examine the potential clinical efficacy, safety, and tolerability of XEN007 as an adjunctive treatment in pediatric patients diagnosed with treatment-resistant CAE. A presentation of promising interim data collected from a small number of patients was presented at the virtual annual meeting of the American Epilepsy Society in December 2020. We continue to work with the lead investigator to include additional sites and expects that topline results from a larger data set will be available in the second half of 2021, which will inform our decision anticipated this year regarding the future development of XEN007 in CAE.

Partnered Programs

- We have an ongoing collaboration with Neurocrine Biosciences, Inc., or Neurocrine Biosciences, to develop treatments for epilepsy. Neurocrine Biosciences has an exclusive license to XEN901, now known as NBI-921352, a clinical stage selective Nav1.6 sodium channel inhibitor with potential in SCN8A developmental and epileptic encephalopathy, or SCN8A-DEE, and other forms of epilepsy. The FDA has provided feedback on an Investigational New Drug, or IND, application submitted by Neurocrine Biosciences in support of a Phase 2 clinical trial in SCN8A-DEE patients. Based on this feedback, Neurocrine Biosciences anticipates initiating a Phase 2 clinical trial in adolescent patients (aged 12 years and older) with SCN8A-DEE in the third quarter of 2021, and the trial protocol will be amended to include younger pediatric patients (aged 2-11 years) with SCN8A-DEE as soon as the FDA has reviewed and approved additional non-clinical information. In parallel, Neurocrine Biosciences is advancing clinical plans to develop NBI-921352 for the treatment of adult focal epilepsy and expects to initiate a Phase 2 clinical trial in 2021. Upon IND or equivalent regulatory acceptance for NBI-921352 in adult focal epilepsy, we are eligible to receive a $10.0 million milestone payment; upon FDA acceptance of a protocol amendment for NBI-921352 in pediatric patients (aged 2-11 years) with SCN8A-DEE, we are eligible to receive a $25.0 million milestone payment, or a $15.0 million milestone payment if the IND acceptance for adult focal epilepsy occurs first. Both milestone payments are in the form of 45% cash and a 55% equity investment in our common shares at a 15% premium to our 30-day trailing volume weighted average price at that time.

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

We have funded our operations primarily through the sale of equity securities, funding received from our licensees and collaborators, and debt financing. For the three months ended March 31, 2021 and 2020, we recognized revenue of $4.4 million and $7.1 million, respectively, in connection with our agreements with Neurocrine Biosciences and Flexion. We had a net loss of $15.8 million for the three months ended March 31, 2021 and an accumulated deficit of $294.3 million as of March 31, 2021, from expenses incurred in connection with our research and development programs and from general and administrative costs associated with our operations.

We do not generate any royalty revenue from product sales, and do not otherwise anticipate generating revenue from product sales for the foreseeable future, if ever. We expect that our revenue in the near term will be substantially dependent on our collaboration agreements. Given the uncertain nature of clinical development of our current and future product candidates and the commercialization of current and future products, we cannot predict when or whether we will receive further milestone payments under our current or future collaboration agreements or whether we will be able to report either revenue or net income in future years.

We expect to continue to incur significant expenses and operating losses for the foreseeable future. We anticipate that our expenses will increase as we:

- continue our research and pre-clinical and clinical development of our product candidates either from our internal research efforts or through acquiring or in-licensing other product candidates or technologies;
- seek regulatory and marketing approvals for any of our product candidates that successfully complete clinical trials;
- make milestone and other payments under our in-license or other agreements;
- maintain, protect and expand our intellectual property portfolio;
- attract, hire and retain skilled personnel; and
- create additional infrastructure to support our operations.

Financial Operations Overview

Revenue

To date, our revenue has been primarily derived from collaboration and licensing agreements. We do not generate any royalty revenue from product sales, and do not otherwise anticipate generating revenue from product sales for the foreseeable future, if ever.

The following table is a summary of revenue recognized from our current collaboration and licensing agreements for the three months ended March 31, 2021 and 2020 (in thousands):

	Three Months Ended March 31,	
	2021	2020
Neurocrine Biosciences:		
Recognition of the transaction price	$ —	$ 5,844
Research and development services	1,358	1,234
Flexion:		
Milestone payments	3,000	—
Total collaboration revenue	$ 4,358	$ 7,078

Pursuant to the terms of our license and collaboration agreement with Neurocrine Biosciences, we received an upfront cash payment of $30.0 million and a $20.0 million equity investment in our common shares. The equity investment was measured at fair value on the date of issuance and the resulting premium, together with the upfront cash payment and variable consideration which is probable that a significant reversal of the cumulative revenue recognized will not occur, is the transaction price of the arrangement for allocation to the performance obligations. The allocation was based on the relative estimated standalone selling prices of each obligation under the agreement including: (i) an exclusive license to XEN901 (now known as NBI-921352) with associated technology and know-how transfer, (ii) an exclusive license to pre-clinical compounds for development, XEN393, XPC'535 and XPC'391, collectively referred to as the development track candidates, or the DTCs, with associated know-how transfer, and (iii) development services under the initial development program for the DTCs. In the three months ended March 31, 2021, we did not recognize into revenue any portion of the transaction price allocated to performance obligations (i), (ii) and (iii), compared to $5.8 million recognized for the three months ended March 31, 2020. Performance obligations (i) and (ii) were completed as of December 31, 2020. Performance obligation (iii) is expected to be completed by Q1 2022. Research and development services are recognized into revenue at fair market value as the services are rendered.

In the three months ended March 31, 2021, we recognized revenue of $3.0 million in connection with our agreement with Flexion for the global rights to develop and commercialize FX301 which included a $1.0 million milestone for the clearance of an IND by the FDA and a $2.0 million milestone for the initiation of a Phase 1b clinical trial. No revenue was recognized for the three months ended March 31, 2020 in connection with our agreement with Flexion.

As our other internal and partnered products are in various stages of clinical and pre-clinical development, we do not expect to generate any revenue from product sales for at least the next several years. We expect that any revenue for the next several years will be derived from milestone payments and research and development funding under our current collaboration agreements and any additional collaboration agreements that we may enter into in the future. We cannot provide any assurance as to the extent or timing of future milestone payments or royalty payments or that we will receive any future payments at all.

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

As of March 31, 2021, there is $3.6 million remaining in deferred revenue from the upfront payments received under our license and collaboration agreement with Neurocrine Biosciences.

Operating Expenses

The following table summarizes our operating expenses for the three months ended March 31, 2021 and 2020 (in thousands):

	Three Months Ended March 31,	
	2021	2020
Research and development	$ 16,308	$ 11,791
General and administrative	4,109	3,320
Total operating expenses	$ 20,417	$ 15,111

Research and Development Expenses

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

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

Project-specific expenses reflect costs directly attributable to our clinical development candidates for which we have incurred significant expenses. All remaining research and development expenses are reflected in pre-clinical, discovery and other internal program expenses. At any given time, we have several active early-stage research and drug discovery programs. Our personnel and infrastructure are typically deployed over multiple projects and are not directly linked to any individual internal early-stage research or drug discovery program. Therefore, we do not maintain financial information for our internal early-stage research and internal drug discovery programs on a project-specific basis.

We expense all research and development costs as incurred. We expect that our research and development expenses will increase in the future as we advance our proprietary product candidates through clinical development, advance our internal drug discovery programs into pre-clinical development and continue our early-stage research. The increase in expense will likely include added personnel and third-party contracts related to research, formulation, process development and manufacturing, pre-clinical studies and clinical trial activities as well as third-party acquisition, license and collaboration fees and laboratory consumables.

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

General and Administrative Expenses

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

We expect that general and administrative expenses will increase in the future as we expand our operating activities to support increased research and development activities and the potential commercialization of our product candidates.

Other Income (Expense)

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

Interest Expense. Interest expense consists of accrual of the final payment fee, amortization of debt discounts, and interest charged on our borrowings with Silicon Valley Bank. In May 2020, we repaid the total outstanding term loan balance ahead of the maturity date.

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

Critical Accounting Policies and Significant Judgments and Estimates

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

Critical accounting policies and significant judgments and estimates are those that we consider the most important to the portrayal of our financial condition and results of operations because they require our most difficult, subjective or complex judgments, often as a result of the need to make estimates about the effect of matters that are inherently uncertain. Our critical accounting policies and significant estimates include those related to:

- revenue recognition;
- research and development costs; and
- stock-based compensation

There have been no material changes in our critical accounting policies and significant judgments and estimates during the three months ended March 31, 2021, as compared to those disclosed in "Management's Discussion and Analysis of Financial Conditions and Results of Operations - Critical Accounting Policies and Significant Judgments and Estimates" included in our 2020 Annual Report on Form 10-K filed with the U.S. Securities and Exchange Commission, or SEC, and with the securities commissions in British Columbia, Alberta and Ontario, or the Canadian Securities Commissions, on March 1, 2021. We believe that the accounting policies discussed in the Annual Report are critical to understanding our historical and future performance, as these policies relate to the more significant areas involving management's judgments and estimates.

Results of Operations

Comparison of three months ended March 31, 2021 and 2020

The following table summarizes the results of our operations for the three months ended March 31, 2021 and 2020 together with changes in those items (in thousands):

	Three Months Ended March 31,		Change 2021 vs. 2020 Increase/(Decrease)
	2021	2020	
Revenue	$ 4,358	$ 7,078	$ (2,720)
Research and development expenses	16,308	11,791	4,517
General and administrative expenses	4,109	3,320	789
Other:			
Interest income	72	1,116	(1,044)
Interest expense	—	(330)	330
Foreign exchange gain (loss)	155	(238)	393
Loss before income taxes	$ (15,832)	$ (7,485)	$ (8,347)

Revenue

Revenue decreased by $2.7 million in the three months ended March 31, 2021 as compared to the three months ended March 31, 2020. Revenue for the three months ended March 31, 2021 related to $1.4 million for research and development services under our license and collaboration agreement with Neurocrine Biosciences, compared to recognition of $5.8 million of deferred revenue and $1.2 million for research and development services for the three months ended March 31, 2020. Revenue for the three months ended March 31, 2021 also included $3.0 million in milestone revenue recognized in connection with our agreement with Flexion, whereas no revenue was recognized in connection with this agreement for the three months ended March 31, 2020.

Research and Development Expenses

The following table summarizes research and development expenses for the three months ended March 31, 2021 and 2020 together with changes in those items (in thousands):

	Three Months Ended March 31,		Change 2021 vs. 2020 Increase/(Decrease)
	2021	2020	
XEN1101	$ 6,469	$ 5,241	$ 1,228
XEN496	5,677	2,667	3,010
XEN901 (now known as NBI-921352)	356	714	(358)
Pre-clinical, discovery and other programs	3,806	3,169	637
Total research and development	$ 16,308	$ 11,791	$ 4,517

Research and development expenses increased by $4.5 million in the three months ended March 31, 2021 as compared to the three months ended March 31, 2020. The increase was primarily attributable to increased spending on our clinical development product candidates XEN1101 and XEN496, and, to a lesser extent, increased spending on our pre-clinical, discovery and other internal programs. This was partially offset by decreased spending on XEN901 (now known as NBI-921352) as clinical developments costs associated with the development of product candidates under the Neurocrine Biosciences collaboration including NBI-921352 are borne by Neurocrine Biosciences. Certain costs related to NBI-921352 development activities have been incurred by us in the period; Neurocrine Biosciences reimburses us for development services we incur at fair market value with the exception of certain near-term manufacturing costs which continue to be borne by us under the terms of the collaboration agreement.

General and Administrative Expenses

The following table summarizes general and administrative expenses for the three months ended March 31, 2021 and 2020 together with changes in those items (in thousands):

	Three Months Ended March 31,		Change 2021 vs. 2020
	2021	2020	Increase/(Decrease)
General and administrative	$ 4,109	$ 3,320	$ 789

General and administrative expenses increased by $0.8 million in the three months ended March 31, 2021 as compared to the three months ended March 31, 2020. The increase was primarily attributable to increased stock-based compensation expense due to an increase in the number of options granted at a higher fair value and higher salaries and benefits due to increased headcount to support our expanding research and development activities, partially offset by a decrease in human resources costs due to timing of recruitment fees.

Other Income

The following table summarizes our other income for the three months ended March 31, 2021 and 2020 together with changes in those items (in thousands):

	Three Months Ended March 31,		Change 2021 vs. 2020
	2021	2020	Increase/(Decrease)
Other income	$ 227	$ 548	$ (321)

Other income decreased by $0.3 million in the three months ended March 31, 2021 as compared to the three months ended March 31, 2020. The decrease was primarily attributable to lower interest income due to a decrease in market yields on investments. This was partially offset by an increase in foreign exchange gains and a decrease in interest expense due to the repayment of our term loan in May 2020.

Liquidity and Capital Resources

To date, we have financed our operations primarily through funding received from collaboration and license agreements, private placements of our common and preferred shares, public offerings of our common shares and pre-funded warrants, and debt financing. As of March 31, 2021, we had cash and cash equivalents and marketable securities of $274.7 million.

We have incurred significant operating losses since inception. We had a $15.8 million net loss for the three months ended March 31, 2021 and an accumulated deficit of $294.3 million from inception through March 31, 2021. We expect to continue to incur significant expenses in excess of our revenue and expect to incur operating losses over the next several years. Our net losses may fluctuate significantly from quarter to quarter and year to year. We expect to continue to incur significant expenses and operating losses for the foreseeable future as we continue our research and pre-clinical and clinical development of our product candidates; expand the scope of our current studies for our product candidates; initiate additional pre-clinical, clinical or other studies for our product candidates, including under our collaboration agreements; change or add manufacturers or suppliers and manufacture drug supply and drug products for clinical trials and commercialization; seek regulatory and marketing approvals for any of our product candidates that successfully complete clinical studies; seek to identify, evaluate and validate additional product candidates; acquire or in-license other product candidates and technologies; make milestone or other payments under our product acquisition and in-license agreements, including, without limitation, payments to the Memorial University of Newfoundland, 1st Order Pharmaceuticals, Inc., and other third parties; maintain, protect and expand our intellectual property portfolio; attract and retain skilled personnel; establish a sales, marketing and distribution infrastructure to commercialize any products for which we or one of our collaborators may obtain marketing approval, and maintain commercial rights; create additional infrastructure to support our operations and our product development and planned future commercialization efforts; and experience any delays or encounter issues with any of the above.

Until such time as we can generate substantial product revenue, if ever, we expect to finance our cash needs through a combination of collaboration agreements and equity or debt financings. For example, in March 2021 we entered into an underwriting agreement with Jefferies LLC, or Jefferies, and Stifel, Nicolaus & Company, Incorporated, or Stifel, relating to an underwritten public offering of 5,153,135 common shares, including 810,810 shares sold upon the full exercise of the underwriters' option to purchase additional shares, and pre-funded warrants to purchase 1,081,081 common shares. The common shares were offered at a public offering price of $18.50 per common share and the pre-funded warrants were offered at a price of $18.4999 per pre-funded warrant, for proceeds of $107.9 million, net of underwriting discounts, commissions and offering expenses. In August 2020, we entered into an at-the-market equity offering sales agreement with Jefferies and Stifel, to sell our common shares having aggregate sales proceeds of up to $100.0 million, from time to time, through an "at-the-market" equity offering program under which Jefferies and Stifel are acting as sales agents. As of March 31, 2021, we had sold an aggregate of 733,000 common shares for proceeds of $10.7 million, net of commissions paid and transaction expenses. In addition, in January 2020, we entered into an underwriting agreement with Jefferies, Stifel, and Guggenheim Securities, LLC, relating to an underwritten public offering of 3,750,000 common shares at a public offering price of $16.00 per common share, and granted the underwriters an option for a period of 30 days to purchase up to an additional 562,500 common shares. The public offering was completed in January 2020 and the underwriters' option was exercised in full in February 2020. We issued an aggregate of 4,312,500 common shares and raised total proceeds of $64.7 million, net of underwriting discounts, commissions and offering expenses. Further, in November 2019, we entered into an at-the-market equity offering sales agreement with Jefferies and Stifel, to sell our common shares having aggregate sales proceeds of up to $50.0 million, from time to time, through an "at-the-market" equity offering program under which Jefferies and Stifel acted as sales agent. As of January 2020, we had sold an aggregate of 3,252,330 common shares for proceeds of $48.5 million, net of commissions paid and transaction expenses.

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

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

- the number and characteristics of the future product candidates we pursue either from our internal research efforts or through acquiring or in-licensing other product candidates or technologies;
- the scope, progress, results and costs of independently researching and developing any of our future product candidates, including conducting pre-clinical research and clinical trials;
- whether our existing collaborations continue to generate substantial milestone payments and, ultimately, royalties on future approved products for us;
- the timing of, and the costs involved in, obtaining regulatory approvals for any future product candidates we develop independently;
- the timing and magnitude of potential milestone payments and royalties under our product acquisition and in-license agreements;

- the cost of commercializing any future products we develop independently that are approved for sale;
- the cost of manufacturing our future product candidates and products, if any;
- our ability to maintain existing collaborations and to establish new collaborations, licensing or other arrangements and the financial terms of such arrangements;
- the costs of preparing, filing, prosecuting, maintaining, defending and enforcing patents, including litigation costs and the outcome of such litigation; and
- the timing, receipt and amount of sales of, or royalties on our future products, if any.

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

Cash Flows

The following table shows a summary of our cash flows for the three months ended March 31, 2021 and 2020 (in thousands):

	Three Months Ended March 31,	
	2021	2020
Net cash used in operating activities	$ (20,708)	$ (13,067)
Net cash used in investing activities	(55,104)	(52,925)
Net cash provided by financing activities	118,721	102,470

Operating Activities

For the three months ended March 31, 2021, net cash used in operating activities totaled $20.7 million, compared to $13.1 million for the same period in 2020. The increase in cash used in operating activities was primarily related to higher expenditures for the clinical development of our proprietary product candidates, lower interest income for the three months ended March 31, 2021 as compared to the same period in 2020, and changes in operating assets and liabilities primarily attributable to the timing of payments for accrued clinical trial costs and accrued expenses in the normal course of business.

Investing Activities

For the three months ended March 31, 2021, net cash used in investing activities totaled $55.1 million, compared to $52.9 million for the same period in 2020. The change in cash used in investing activities was driven primarily by an increase in purchases of marketable securities, net of redemptions.

Financing Activities

For the three months ended March 31, 2021, net cash provided by financing activities totaled $118.7 million, compared to $102.5 million for the same period in 2020. The increase in cash provided by financing activities was primarily related to net proceeds of $118.6 million from the issuance of common shares and pre-funded warrants during the three months ended March 31, 2021 as compared to $102.5 million from the issuance of common shares for the same period in 2020.

Contractual Obligations and Commitments

Our future significant contractual obligations as of December 31, 2020 were reported in our Annual Report on Form 10-K, filed with the SEC and the Canadian Securities Commissions on March 1, 2021.

As of March 31, 2021, there have been no material changes from the contractual commitments previously disclosed in the Annual Report on Form 10-K.

Inflation

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

Off-Balance Sheet Arrangements

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

Outstanding Share Data

As of May 7, 2021, we had 40,967,221 common shares issued and outstanding, outstanding pre-funded warrants to purchase an additional 1,081,081 common shares, outstanding stock options to purchase an additional 5,685,736 common shares and an outstanding warrant to purchase an additional 40,000 common shares. In addition, we had 1,016,000 Series 1 Preferred Shares issued and outstanding. The Series 1 Preferred Shares are convertible into common shares on a one-for-one basis subject to the holder, together with its affiliates, beneficially owning no more than 9.99% of the total number of common shares issued and outstanding immediately after giving effect to such conversion, or the Beneficial Ownership Limitation. The holder may reset the Beneficial Ownership Limitation to a higher or lower number, not to exceed 19.99% of the total number of common shares issued and outstanding immediately after giving effect to such conversion, upon providing written notice to us which will be effective 61 days after delivery of such notice. The holders of the Series 1 Preferred Shares are entitled to vote together with the common shares on an as-converted basis and as a single class, subject in the case of each holder of the Series 1 Preferred Shares to the Beneficial Ownership Limitation. The Series 1 Preferred Shares may be “restricted securities” as such term is defined under applicable Canadian securities laws, as any Series 1 Preferred Shares that are ineligible to be converted into common shares due to the Beneficial Ownership Limitation, measured as of a given record date that applies for a shareholder meeting or ability to act by written consent, shall be deemed to be non-voting securities. For additional information regarding our Series 1 Preferred Shares, see note 10b to our consolidated financial statements included in Part I, Item 1 of this report.

Item 3. Quantitative and Qualitative Disclosures About Market Risk

As a smaller reporting company, we are not required to provide the information requested by this item pursuant to Item 305(e) of Regulation S-K.

Item 4. Controls and Procedures

(a) Evaluation of disclosure controls and procedures. Our management, with the participation of our Chief Executive Officer and our Chief Financial Officer, have evaluated our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended) as of the end of the period covered by this quarterly report. Based on that evaluation, our Chief Executive Officer and our Chief Financial Officer have concluded that, as of the end of the period covered by this quarterly report, our disclosure controls and procedures were effective, in design and operation, at the reasonable assurance level.

(b) Changes in internal control over financial reporting. There were no changes in our internal control over financial reporting during the period ended March 31, 2021 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Inherent limitation on the effectiveness of internal control.

The effectiveness of any system of internal control over financial reporting, including ours, is subject to inherent limitations, including the exercise of judgment in designing, implementing, operating, and evaluating the controls and procedures, and the inability to eliminate misconduct completely. Accordingly, any system of internal control over financial reporting, including ours, no matter how well designed and operated, can only provide reasonable, not absolute assurances. In addition, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate. We intend to continue to monitor and upgrade our internal controls as necessary or appropriate for our business, but cannot assure you that such improvements will be sufficient to provide us with effective internal control over financial reporting.

PART II. OTHER INFORMATION

Item 1. Legal Proceedings

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

Item 1A. Risk Factors

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

Risks Related to Our Financial Condition and Capital Requirements

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

We do not expect to have sustained profitability for the foreseeable future. We had a net loss of $15.8 million for the three months ended March 31, 2021 and an accumulated deficit of $294.3 million as of March 31, 2021, which were driven by expenses incurred in connection with our research and development programs and from general and administrative costs associated with our operations.

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

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

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

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

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

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

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

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

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

Since our inception, we have dedicated most of our resources to the discovery and development of our pre-clinical and clinical product candidates, and we expect to continue to expend substantial resources doing so for the foreseeable future. These expenditures will include costs associated with research and development, potential milestone payments and royalties to third parties, manufacturing of product candidates and products approved for sale, conducting pre-clinical experiments and clinical trials and obtaining and maintaining regulatory approvals, as well as commercializing any products later approved for sale. During the three months ended March 31, 2021, we incurred $16.3 million of costs associated with research and development, exclusive of costs incurred by our collaborators in developing our product candidates.

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

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

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

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

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

We may allocate our limited resources to pursue a particular product candidate or indication and fail to capitalize on other product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

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

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

The terms of any financing arrangements we enter into may adversely affect the holdings or the rights of our shareholders and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our common shares to decline. The sale of additional equity or convertible securities also would dilute all of our shareholders. For example, in November 2019, we entered into the November 2019 sales agreement with Jefferies LLC, or Jefferies, and Stifel, Nicolaus & Company, Incorporated, or Stifel, to sell up to $50.0 million of our common shares, from time to time, through an "at-the-market" equity offering program under which Jefferies and Stifel acted as sales agents. As of January 2020, we had sold an aggregate of 3,252,330 common shares for proceeds of $48.5 million, net of commissions paid and transaction expenses. In January 2020, we completed an underwritten public offering of 3,750,000 of our common shares at a public offering price of $16.00 per share for proceeds of $56.3 million, net of underwriting discounts, commissions and offering expenses. In February 2020, the underwriters of the January 2020 public offering exercised their option to purchase an additional 562,500 of our common shares at a public offering price of $16.00 per share, raising additional proceeds of $8.4 million, net of underwriting discounts, commissions and offering expenses. Further, in August 2020, we entered into the August 2020 sales agreement with Jefferies and Stifel to sell up to $100.0 million of our common shares, from time to time, through an "at-the-market" equity offering program under which Jefferies and Stifel are acting as sales agents. As of March 31, 2021, we had sold an aggregate of 733,000 common shares for proceeds of $10.7 million, net of commissions paid and transaction expenses. In March 2021, we completed an underwritten public offering of 5,135,135 of our common shares, including 810,810 shares sold upon the full exercise of the underwriters' option to purchase additional shares, and pre-funded warrants to purchase 1,081,081 common shares. The common shares were offered at a public offering price of $18.50 per common share and the pre-funded warrants were offered at a price of $18.4999 per pre-funded warrant, for proceeds of $107.9 million, net of underwriting discounts, commissions and offering expenses. We were also party to an amended and restated loan and security agreement with Silicon Valley Bank pursuant to which we had borrowed an aggregate principal amount of $15.5 million. The restated loan and security agreement was secured by substantially all of our assets except intellectual property and required compliance with various affirmative and negative covenants. In May 2020, we repaid the total outstanding term loan balance ahead of the maturity date and all encumbrances were removed by Silicon Valley Bank. Any future incurrence of indebtedness would result in increased fixed payment obligations and, potentially, the imposition of restrictive covenants. Such covenants could include limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. We could also be required to seek funds through arrangements with collaborators or otherwise at an earlier stage than otherwise would be desirable resulting in the loss of rights to some of our product candidates or other unfavorable terms, any of which may have a material adverse effect on our business, operating results and prospects. In addition, any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates.

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

As of March 31, 2021, approximately 4% of our cash and cash equivalents and marketable securities were denominated in Canadian dollars. We incur significant expenses in Canadian dollars in connection with our operations in Canada. We do not currently engage in foreign currency hedging arrangements for our Canadian dollar expenditures, and, consequently, foreign currency fluctuations may adversely affect our earnings; however, in the future, we may engage in exchange rate hedging activities in an effort to mitigate the impact of exchange rate fluctuations. Any hedging technique we implement may fail to be effective. If our hedging activities are not effective, changes in currency exchange rates may have a more significant impact on the market price of our common shares.

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

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

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

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

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

Risks Related to Our Business and Industry

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

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. We face potential competition in drug discovery and product development from many different approaches and sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions, governmental agencies, as well as public and private research institutions. Any product candidates that we or our collaborators successfully develop and commercialize will compete with existing products and any new products that may become available in the future.

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

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

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

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

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

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

As a company, we have no previous experience in completing a Phase 3 clinical trial or in completing clinical trials in pediatric indications, and related regulatory requirements or the commercialization of products. We have not yet demonstrated our ability to independently and repeatedly conduct clinical development after Phase 2, conduct a pivotal clinical trial, obtain regulatory approval, manufacture drug product on a commercial scale or arrange for a third party to do so on our behalf, and commercialize therapeutic products. We will need to develop such abilities if we are to execute on our business strategy to develop and independently commercialize product candidates. To execute on our business plan for the development of independent programs, we will need to successfully:

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

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

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

We have built a product development pipeline by identifying product candidates either from our internal research efforts or through acquiring or in-licensing other product candidates or technologies. To date, our internal discovery efforts have yielded multiple development candidates, including XEN901, which we licensed to Neurocrine Biosciences and is now known as NBI-921352, and XEN402, which has been acquired by Flexion to use in its product candidate FX301. Both our internal discovery efforts and our assessment of potential acquisition or in-licensing opportunities require substantial technical, financial and human resources, regardless of whether we identify any viable product candidates.

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

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

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

We could experience difficulties attracting and retaining qualified employees as competition for qualified personnel in the biotechnology and pharmaceutical field is intense. We are highly dependent upon our senior management, particularly Dr. Simon Pimstone, our current Chief Executive Officer, who will begin serving as the Executive Chair of the board of directors effective as of the date of our 2021 annual meeting of shareholders, or AGM, and Mr. Ian Mortimer, our current President and Chief Financial Officer who will take on the role of Chief Executive Officer while retaining his current responsibilities as our President and principal operating officer as of the date of our 2021 AGM, as well as other employees. The loss of services of either of these individuals or one or more of our other members of senior management could materially delay or even prevent the successful development of our product candidates.

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

Our employees, collaborators and other personnel may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading.

We are exposed to the risk of fraud or other misconduct by our employees, collaborators, vendors, principal investigators, consultants and commercial partners. Misconduct by these parties could include intentional failures to comply with the regulations of the FDA, EMA, Health Canada and other regulators, provide accurate information to the FDA, EMA, Health Canada and other regulators, comply with data privacy and security and healthcare fraud and abuse laws and regulations in the U.S. and abroad, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. Additionally, laws regarding data privacy and security, including the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, the General Data Protection Regulation (EU) 2016/679, or GDPR, and the Personal Information Protection and Electronic Documents Act, or PIPEDA, as well as comparable laws in other jurisdictions, may impose obligations with respect to safeguarding the privacy, use, security and transmission of individually identifiable health information such as genetic material or information we have obtained through our direct-to-patient web-based recruitment approach for identifying patients with rare or extreme phenotypes or patients identified for clinical trials.

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

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

Our business strategy involves continued development and, where development is successful, commercialization of select product candidates. In order to execute on this strategy, we will need to build out a regulatory, sales, manufacturing, supply chain and marketing infrastructure and expand our development capabilities or contract with third parties to provide these capabilities and infrastructure for us. To achieve this, we will need to identify, hire and integrate personnel who have not worked together as a group previously. As our operations expand, we expect that we will need to manage additional relationships with various strategic collaborators, suppliers and other third parties.

Future growth will impose significant added responsibilities on members of management including the need to identify, recruit, maintain, motivate and integrate additional employees. Also, our management may need to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities.

We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our business, give rise to operational errors, loss of business opportunities, loss of employees and reduced productivity amongst remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of existing and additional product candidates. If we are unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate and grow revenue could be reduced, and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize product candidates and compete effectively will depend, in part, on our ability to effectively manage any future growth.

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

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

To date, we have not experienced any material impact to our business, financial position or operations resulting from information security incidents or cyberattacks such as phishing, social engineering, ransomware or malware attacks; however, because of the frequently changing attack techniques, along with the increased volume and sophistication of such attacks, our business, financial position or operations could be adversely impacted in the future. This impact could result in reputational, competitive, operational or other business harm as well as financial costs and regulatory action. Moreover, the prevalent use of mobile devices that access confidential information and ability to work remotely increases the risk of data security breaches, which could lead to the loss of confidential information, trade secrets or other intellectual property. These risks may be heightened during the current COVID-19 pandemic due to the increase in our and our vendors' and contractors' personnel working remotely. As cyber threats continue to evolve, we may be required to expend significant additional resources to continue to modify or enhance our protective measures or to investigate and remediate any information security vulnerabilities. While we have implemented security measures and, to date, have not detected a cybersecurity breach of our systems nor experienced a material system failure, our computer systems and the external systems and services used by our third-party contract manufacturers, or CMOs, third-party contract research organizations, or CROs, or other contractors, vendors, consultants, directors and partners remain potentially vulnerable to these events.

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

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

- different regulatory requirements for initiating clinical trials and maintaining approval of drugs in foreign countries;
- reduced protection for intellectual property rights in certain countries;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, political instability or open conflict in particular foreign economies and markets;
- differing and multiple payor reimbursement regimes, government payors or patient self-pay systems;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations of doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in North America;
- controlled substance legislation differs between countries and legislation in certain countries may restrict or limit our ability to manufacture and/or transport our product candidates;
- likelihood of potential or actual violations of domestic and international anti-corruption laws, such as the U.S. Foreign Corrupt Practices Act and the U.K. Bribery Act, or of U.S. and international import, export and re-export control and sanctions laws and regulations, which likelihood may increase with an increase of operations in foreign jurisdictions;
- tighter restrictions on privacy and the collection, use and retention of data, including clinical data and genetic material, may apply in jurisdictions outside of North America;

- business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters including earthquakes, typhoons, floods and fires; and
- supply and other disruptions resulting from the impact of public health epidemics, including the COVID-19 pandemic, on our strategic partners, third-party manufacturers, suppliers and other third parties upon which we rely.

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

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

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

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

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

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

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

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

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

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

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

In addition, if we are or become a PFIC (or our PFIC status is uncertain), it may deter certain U.S. investors from purchasing our common shares, which could have an adverse impact on the market price of our common shares.

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

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

Acquisitions, joint ventures or other strategic transactions could disrupt our business, cause dilution to our shareholders and otherwise harm our business.

We actively evaluate various strategic transactions on an ongoing basis, including the acquisition of other businesses, products or technologies as well as pursuing strategic alliances, joint ventures, licensing transactions or investments in complementary businesses. Any of these transactions could be material to our financial condition and operating results and expose us to many risks, including:

- disruption in our relationships with collaborators or suppliers as a result of such a transaction;
- unanticipated liabilities related to acquired companies;
- difficulties integrating acquired personnel, technologies and operations into our existing business;
- retention of key employees;
- diversion of management time and focus from operating our business to pursuing strategic transactions and managing any such strategic alliances, joint ventures or acquisition integration challenges;
- dilution to our shareholders if we issue equity in connection with such transactions;
- increases in our expenses and reductions in our cash available for operations and other uses; and
- possible write-offs or impairment charges relating to acquired businesses.

Foreign acquisitions involve unique risks in addition to those mentioned above, including those related to integration of operations across different cultures and languages, currency risks and the particular economic, political and regulatory risks associated with specific countries.

Also, the anticipated benefit of any strategic alliance, joint venture or acquisition may not materialize. Future acquisitions or dispositions could result in potentially dilutive issuances of our equity securities, the incurrence of debt, contingent liabilities or amortization expenses or write-offs of goodwill, any of which could harm our financial condition. We cannot predict the number, timing or size of future joint ventures or acquisitions, or the effect that any such transactions might have on our operating results.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

- the FDA, EMA, Health Canada or other regulatory authorities may disagree with the design or implementation of our or our collaborators' clinical trials;
- we or our collaborators may be unable to demonstrate to the satisfaction of the FDA, EMA, Health Canada or other regulatory authorities that a product candidate is safe and effective for its proposed indication;
- the results of clinical trials may not meet the level of statistical significance required by the FDA, EMA, Health Canada or other regulatory authorities for approval;

- we, or our collaborators, may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- the FDA, EMA, Health Canada or other regulatory authorities may disagree with our or our collaborators' interpretation of data from pre-clinical studies or clinical trials;
- the data collected from clinical trials of our product candidates may not be sufficient to support the submission of a New Drug Application, or NDA, or other submission or to obtain regulatory approval in the U.S. or elsewhere;
- the FDA, EMA, Health Canada or other regulatory authorities may fail to approve the manufacturing processes, controls or facilities of third-party manufacturers with which we or our collaborators contract for clinical and commercial supplies;
- the pre-approval inspections of manufacturing, clinical sites or clinical service providers, conducted by regulatory authorities may identify errors or omissions that may results in the product candidate not being approved; and
- the approval policies or regulations of the FDA, EMA, Health Canada or other regulatory authorities may significantly change in a manner rendering our or our collaborators' clinical data insufficient for approval.

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

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

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

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

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

- side effects or adverse events in study participants presenting an unacceptable safety risk;
- inability to reach agreement with prospective CROs and clinical trial sites, or the breach of such agreements;
- failure of third-party contractors, such as CROs, or investigators to comply with regulatory requirements, including GCPs;
- delay or failure in obtaining the necessary approvals from regulators or institutional review boards, or IRBs, in order to commence a clinical trial at a prospective trial site, or their suspension or termination of a clinical trial once commenced;
- a requirement to undertake and complete additional pre-clinical studies to generate data required to initiate clinical development or to support the continued clinical development of a product candidate or submission of an NDA;
- inability to enroll sufficient patients to complete a protocol, particularly in orphan diseases;
- difficulty in having patients complete a trial, adhere to the trial protocol, or return for post-treatment follow-up;
- clinical sites deviating from trial protocol or dropping out of a trial;
- problems with 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 substance or drug product sufficient to complete our pre-clinical studies and clinical trials;
- unforeseen disruptions, caused by man-made or natural disasters or public health pandemics or epidemics or other business interruptions, including, for example, the COVID-19 pandemic; and
- governmental or regulatory delays and changes in regulatory requirements, policy and guidelines.

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

The results of any Phase 3 or other pivotal clinical trial, including without limitation our EPIK trial, may not be adequate to support marketing approval. These clinical trials are lengthy and, with respect to non-orphan indications, usually involve many hundreds to thousands of patients. With respect to orphan indications like KCNQ2-DEE, SCN8A-DEE or childhood absence epilepsy, or CAE, clinical trials can also be lengthy due to the challenge of identifying and recruiting patients. In addition, if the FDA, EMA, Health Canada or another regulator disagrees with our or our collaborators' choice of the key testing criterion, or primary endpoint, the results for the primary endpoint are not robust or significant relative to the control group of patients not receiving the experimental therapy, or our statistical analysis is inconclusive, such regulator may refuse to approve our product candidate in the region in which it has jurisdiction. The FDA, EMA, Health Canada or other regulators also may require additional clinical trials as a condition for approving any of these product candidates.

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

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

We may also be required to develop and implement additional clinical trial policies and procedures designed to help protect subjects from the COVID-19 virus which have and are expected to continue to increase the cost of our clinical trials. Since March 2020, the FDA, EMA and Health Canada have issued guidance documents describing a number of considerations for sponsors conducting clinical trials during the pandemic.

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

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

Clinical trials may fail to demonstrate adequately the safety and efficacy of our or our collaborators' product candidates, at any stage of clinical development. Terminating the development of any of our or our collaborators' product candidates could materially harm our business and the market price of our common shares.

Our and our collaborators' clinical product candidates, which include XEN1101, XEN496, XEN007, NBI-921352 (previously known as XEN901 and being developed by our collaborator Neurocrine Biosciences), and FX301 (being developed by Flexion Therapeutics, Inc., or Flexion), along with product candidates we expect to enter clinical development which include our pre-clinical compounds, are in varying stages of development and will require substantial clinical development, testing and regulatory approval prior to commercialization.

Before obtaining regulatory approvals for the commercial sale of our products, we or our collaborators must demonstrate through lengthy, complex and expensive pre-clinical testing and clinical trials that the product candidate is both safe and effective for use in each target indication. Failure can occur at any time during the clinical trial process. Clinical trials often fail to demonstrate safety and efficacy of the product candidate studied for the target indication. Most product candidates that commence clinical trials are never approved as products. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials. In addition to the safety and efficacy trials of any product candidate, clinical trial failures may result from a multitude of factors including flaws in trial design, dose selection, statistical analysis plan, placebo effect, patient enrollment criteria, patient compliance and trial execution. Data obtained from trials and studies are susceptible to varying interpretations, and regulators may not interpret our data as favorably as we do, which may delay, limit or prevent regulatory approval. Failure of a clinical trial due to any of these reasons could materially harm our business and the market price of our common shares.

In the case of some of our and our collaborators' product candidates, we and our collaborators are seeking to develop treatments for certain diseases for which there is relatively limited clinical experience, and clinical trials may use novel endpoints and measurement methodologies or subjective patient feedback, which adds a layer of complexity to these clinical trials and may delay regulatory approval. Negative or inconclusive results from our or our collaborators' clinical trials could lead to a decision or requirement to conduct additional pre-clinical testing or clinical trials or result in a decision to terminate the continued development of a product candidate. For example, we currently anticipate releasing topline data from our X-TOLE Phase 2b clinical trial of XEN1101 in adult patients with focal epilepsy by the end of the third quarter of 2021. If these topline data fail to meet the trial endpoints or are otherwise inconclusive, we may cease development of XEN1101 as a treatment for adult patients with focal epilepsy or potentially abandon development of XEN1101 entirely. Even if the data from our X-TOLE Phase 2b clinical trial are positive, there can be no assurance that we will be able to successfully advance development of this product candidate into later stage clinical trials or obtain regulatory approval of XEN1101. Any of the foregoing outcomes would materially and adversely impact our business, product candidate pipeline and future prospects.

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

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

We or our collaborators may not be able to identify, recruit and enroll a sufficient number of patients, or those with required or desired characteristics to achieve diversity in a study, to complete clinical studies in a timely manner, or at all. Patient enrollment for clinical trials for ultra-orphan, orphan and niche indications and for more prevalent conditions is affected by factors including:

- severity of the disease under investigation;
- design of the study protocol;
- size of the patient population and geographic dispersion;
- identification of patients;
- eligibility criteria for the study in question;
- perceived risks and benefits of the product candidate under study;
- proximity and availability of clinical study sites for prospective patients;

- availability of competing therapies and clinical studies;
- efforts to facilitate timely enrollment in clinical studies; and
- patient referral practices of physicians.

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

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

Although we have pending provisional and non-provisional patent applications related to XEN496 and XEN007, these product candidates are not currently covered by any issued patents and we may have to rely solely on orphan drug designation to gain market exclusivity for these product candidates. Currently, this designation provides market exclusivity in the U.S. and the EU for seven years and ten years, respectively, if a product is the first such product approved for such orphan indication. This market exclusivity does not, however, pertain to indications other than those for which the drug was specifically designated in the approval, nor does it prevent other types of drugs from receiving orphan designations or approvals in these same indications. Further, even after an orphan drug is approved, the FDA can subsequently approve a drug with similar chemical structure for the same condition if the FDA concludes that the new drug is clinically superior to the orphan product or a market shortage occurs.

In the EU, orphan exclusivity may be reduced to six years if the drug no longer satisfies the original designation criteria or can be lost altogether if the marketing authorization holder consents to a second orphan drug application or cannot supply enough drug, or when a second applicant demonstrates its drug is "clinically superior" to the original orphan drug. XEN007, a drug we are evaluating for potential development in CAE, HM, or AHC, has received orphan drug designation from the FDA for HM and AHC. We have also received orphan drug designation from the FDA and orphan medicinal product designation was granted by the European Commission to XEN496 as a treatment of KCNQ2-DEE. If we seek orphan drug designations for other indications or in other jurisdictions, we may fail to receive such orphan drug designations and, even if we succeed, such orphan drug designations may fail to result in or maintain orphan drug exclusivity upon approval, which would harm our competitive position. Further, not all jurisdictions, such as Canada, have orphan drug designations. Neither orphan drug designation, nor rare pediatric disease, or RPD, designation gives the drug any advantage in the regulatory review or approval process other than potential fee reductions, and in the case of RPD, priority review vouchers.

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

Our product candidate XEN007 has received RPD designation from the FDA for the treatment of AHC and NBI-921352, being developed by our collaborator Neurocrine Biosciences, has received RPD designation for the treatment of SCN8A-DEE. The FDA defines a "rare pediatric disease" as a disease that affects fewer than 200,000 individuals in the U.S. primarily under the age of 18 years old. Under the FDA's RPD priority review voucher program, upon the approval of a new drug application, NDA, or a biologics license application, BLA, for the treatment of an RPD, the sponsor of such application would be eligible for a priority review voucher that can be used to obtain priority review for a subsequent NDA or BLA. There is no assurance we or Neurocrine Biosciences will receive a RPD priority review voucher or that use of the priority review voucher will result in a faster review or approval for a subsequent marketing application. It is possible that even if we or Neurocrine Biosciences obtain approval for XEN007 in AHC or NBI-921352 in SCN8A-DEE, respectively, and qualify for such a priority review voucher, the program may no longer be in effect at the time of approval of either of these product candidates. Also, although priority review vouchers may be freely sold or transferred to third parties, there is no guarantee that we will be able to realize any value if we were to sell a priority review voucher to a third party. In addition, as part of the Coronavirus Response and Relief Supplemental Consolidated Appropriations Act of 2021, Congress extended FDA authorization to operate the RPD Priority Review Voucher Program through fiscal year 2024. RPD Designation does not lead to faster development or regulatory review of the product, or increase the likelihood that it will receive marketing approval.

Results of pre-clinical studies and/or earlier clinical trials may not be predictive of the results of later-stage clinical trials and the results of our clinical trials may not satisfy the requirements of the FDA, EMA, Health Canada or foreign regulatory authorities.

The results of pre-clinical studies, either generated by us, such as for XEN901 (which we licensed to Neurocrine Biosciences and is now known as NBI-921352) or XEN402 (which was acquired by Flexion for use in its product candidate FX301), by our CROs or by other third parties from which we have in-licensed or acquired a product candidate, such as for XEN1101, may not be predictive of results in clinical testing. Moreover, pre-clinical results can often be difficult to compare across different studies for a variety of reasons, including differences in experimental protocols and techniques, personnel, equipment and other factors, which may make the pre-clinical results less reliable and predictive of clinical trial results. In addition, published clinical data or case reports from third parties or early clinical trial data of our product candidates may not be predictive of the results of later-stage clinical trials. Interpretation of results from early, usually smaller, studies that suggest a clinically meaningful response in some patients, requires caution. Results from later stages of clinical trials enrolling more patients may fail to show the desired safety and efficacy results or otherwise fail to be consistent with the results of earlier trials of the same product candidate. Later clinical trial results may not replicate earlier clinical trials for a variety of reasons, including differences in trial design, different trial endpoints (or lack of trial endpoints in exploratory studies), patient population, number of patients, patient selection criteria, trial duration, drug dosage and formulation and lack of statistical power in the earlier studies. These uncertainties are enhanced where the diseases under study lack established clinical endpoints, validated measures of efficacy, as is often the case with orphan diseases for which no drugs have been developed previously and where the product candidates target novel mechanisms. For example, to our knowledge, NBI-921352 is the first selective Nav1.6 sodium channel inhibitor being developed for the treatment of epilepsy and therefore standard pre-clinical models may not be predictive of clinical efficacy due to its novel molecular mechanism.

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

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

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

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

If our discovery activities fail to identify novel targets for drug discovery, or such targets prove to be unsuitable for treating human disease, or if we are unable to develop product candidates with specificity and selectivity for such targets, we will fail to develop viable products. If we fail to develop and commercialize viable products, we will not achieve commercial success.

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

As product candidates are developed through pre-clinical to late stage clinical trials towards approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods and formulations, are altered along the way in an effort to optimize products, processes and results, to extend patent protection and/or to target different populations. For example, XEN496 is a pediatric-specific formulation of ezogabine and we have also developed a pediatric formulation for NBI-921352 that was included in the license to Neurocrine Biosciences. Any of these changes could cause our product candidates to perform differently and not provide the same drug exposure profile in children and/or cause side effects different to those observed with formulations previously tested in adults. Unexpected changes in the performance of a new formulation may affect the results of planned clinical trials or other future clinical trials conducted with the altered materials. This could delay completion of clinical trials, require the conduct of additional bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs and/or delay or jeopardize approval of our product candidates and/or jeopardize our or our collaborators' ability to commence product sales and generate revenue.

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

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

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

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

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

Risks Related to Commercialization

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

We do not have a sales or marketing infrastructure and, as a company, have no sales, marketing or distribution experience. Our strategy involves building our own commercial infrastructure to selectively commercialize future products in certain commercial markets which will be expensive and time consuming. For certain products and/or commercial markets, we may seek commercial partners and may seek to retain the right to participate in the future development and commercialization of such products if we believe such involvement would advance our business.

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

- the maintenance of existing or the establishment of new supply arrangements with third-party logistics providers and secondary packagers;
- the maintenance of existing or the establishment of new scaled production arrangements with third-party manufacturers to obtain finished products that are appropriately packaged for sale;
- a continued acceptable safety profile following any marketing approval;

- our inability to recruit and retain adequate numbers of qualified sales and marketing personnel or develop alternative sales channels;
- the inability of our products to secure acceptance from physicians, healthcare providers, patients, third-party payors and the medical community including identifying an adequate number of physicians and patients, especially for ultra-orphan, orphan or niche indications;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines;
- unforeseen costs and expenses associated with creating and maintaining an independent sales and marketing organization; and
- our ability to compete with other therapies.

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

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

Any regulatory approvals that we receive for the product candidates we commercialize, alone or with a collaborator, will be subject to limitations on the approved indicated uses for which the product may be marketed or subject to certain conditions of approval and may contain requirements for potentially costly post-approval trials, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the marketed product and compliance with the approved package insert. In addition, our product candidates may receive schedule classifications under the Controlled Substances Act of 1970 (or scheduling classifications under similar legislation outside of the U.S.) which will result in additional complexity in manufacturing, supply chain, licensing, import/export and distribution.

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

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

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

In addition, prescription drugs may be promoted only for the approved indications in accordance with the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label use may be subject to significant liability. However, physicians may, in their independent medical judgment, prescribe legally available products for off-label uses. The FDA does not regulate the behavior of physicians in their choice of treatments but the FDA and other foreign regulators do restrict manufacturer's communications on the subject of off-label use of their products.

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

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

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

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

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

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

Some of our and our collaborators' target patient populations in orphan and niche indications, such as KCNQ2-DEE, SCN8A-DEE and CAE. In order for therapies that are designed to treat smaller patient populations to be commercially viable, the pricing, coverage and reimbursement for such therapies needs to be higher, on a relative basis, to account for the lack of volume. Accordingly, we will need to implement pricing, coverage and reimbursement strategies for any approved product that accounts for the smaller potential market size. If we are unable to establish or sustain coverage and adequate reimbursement for our current and any future products from third party payers or the government, the adoption of those products and sales revenue will be adversely affected, which, in turn, could adversely affect the ability to market or sell those products.

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

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

For example, in 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, collectively, the PPACA, was enacted and includes measures that have significantly changed the way healthcare is financed by both governmental and private insurers. Since its enactment, there have been legislative and judicial efforts to repeal, replace, or change some or all of the PPACA. For example, various portions of the PPACA have been the subject of legal and constitutional challenges, including legal proceedings in the Fifth Circuit Court of Appeals. The Supreme Court of the United States held oral arguments on the Fifth Circuit Court case in November 2020 and is expected to issue a decision later in 2021. Litigation and legislation over the PPACA are likely to continue, with unpredictable and uncertain results. It is unclear how this Supreme Court decision, future litigation, and healthcare measures promulgated by the Biden administration will impact the implementation of the PPACA, our business, financial condition and results of operations. Complying with any new legislation or reversing changes implemented under the PPACA could be time-intensive and expensive, resulting in a material adverse effect on our business.

In addition, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for pharmaceutical products. For example, HHS and CMS issued final rules in November and December of 2020 that are expected to impact, among others, price reductions from pharmaceutical manufacturers to plan sponsors under Part D, fee arrangements between pharmacy benefit managers and manufacturers, prescription drug importation, manufacturer price reporting requirements under the Medicaid Drug Rebate Program, including regulations that affect manufacturer-sponsored patient assistance programs subject to pharmacy benefit manager accumulator programs and Best Price reporting related to certain value-based purchasing arrangements. Multiple lawsuits have been brought against the HHS challenging various aspects of these new rules. In January 2021, the Biden administration issued a "regulatory freeze" memorandum that directs department and agency heads to review new or pending rules of the prior administration. It is unclear whether these new regulations will be withdrawn or when they will become fully effective under the current administration. Under the American Rescue Plan Act of 2021, effective January 1, 2024, the statutory cap on Medicaid Drug Rebate Program rebates that manufacturers pay to state Medicaid programs will be eliminated. Elimination of this cap may require pharmaceutical manufacturers to pay more in rebates than it receives on the sale of products, which could have a material impact on our business. The impact of these regulations and any future healthcare measures and agency rules implemented by the Biden administration on us and the pharmaceutical industry as a whole is currently unknown. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. These and other health reform measures that are implemented may have a material adverse effect on our operations.

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

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

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

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the U.S. or in other jurisdictions. If we or our collaborators are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or our collaborators are not able to maintain regulatory compliance, our product candidates may lose any marketing approval that may have been obtained and we may not achieve or sustain profitability, which would adversely affect our business.

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

In most foreign countries, particularly those in the EU and Canada, prescription drug pricing and/or reimbursement is subject to governmental control. In those countries that impose price controls, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we or our collaborators may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. As of April 2021, Canada is in the midst of implementing new drug pricing regulations and additional pricing guidance that will affect the price at which patented medicines can be sold.

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

Risks Related to Our Dependence on Third Parties

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

We have no control over the resources, time and effort that our collaborators may devote to our programs and limited access to information regarding or resulting from such programs. We are dependent on our collaborators, including Neurocrine Biosciences, Flexion and Genentech, to fund and conduct the research and any clinical development of product candidates under our agreements with each of them, and for the successful regulatory approval, marketing and commercialization of one or more of such products or product candidates. Such success will be subject to significant uncertainty.

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

- a collaborator may shift its priorities and resources away from our programs due to a change in business strategies, or a merger, acquisition, sale or downsizing of its company or business unit;
- a collaborator may cease development in therapeutic areas which are the subject of our strategic alliances;
- a collaborator may change the success criteria for a particular program or product candidate thereby delaying or ceasing development of such program or candidate;
- a significant delay in initiation of certain development activities by a collaborator will also delay payment of milestones tied to such activities, thereby impacting our ability to fund our own activities;

- a collaborator could develop a product that competes, either directly or indirectly, with our current or future products, if any;
- a collaborator with commercialization obligations may not commit sufficient financial or human resources to the marketing, distribution or sale of a product;
- a collaborator with manufacturing responsibilities may encounter regulatory, resource or quality issues and be unable to meet demand requirements;
- a collaborator may exercise its rights under the agreement to terminate our collaboration;
- a dispute may arise between us and a collaborator concerning the research or development of a product candidate, commercialization of a product or payment of royalties or milestone payments, any of which could result in a delay in milestones, royalty payments or termination of a program and possibly resulting in costly litigation or arbitration which may divert management attention and resources;
- a collaborator may not adequately protect the intellectual property rights associated with a product or product candidate;
- a collaborator may use our proprietary information or intellectual property in such a way as to invite litigation from a third party; and
- disruptions caused by man-made or natural disasters or public health pandemics or epidemics or other business interruptions, including, for example, the COVID-19 pandemic.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

We do not currently own or operate any manufacturing facilities nor do we have significant in-house manufacturing experience or personnel. We rely on our collaborators, either directly or through CMOs, to manufacture product candidates licensed to them or work with multiple CMOs to produce sufficient quantities of materials required for the manufacture of our product candidates for pre-clinical testing and clinical trials and intend to do so for the commercial manufacture of our products. If we or our collaborators are unable to arrange for such third-party manufacturing sources, or fail to do so on commercially reasonable terms, we or our collaborators may not be able to successfully produce sufficient supply of a product candidate or we or our collaborators may be delayed in doing so. Such failure or substantial delay could materially harm our business.

Reliance on third-party manufacturers entails risks to which we would not be subject if we manufactured product candidates ourselves, including reliance on the third party for regulatory compliance and quality control and assurance, volume production, the possibility of breach of the manufacturing agreement by the third party because of factors beyond our control (including a failure to synthesize and manufacture our product candidates in accordance with our product specifications) and the possibility of termination or nonrenewal of the agreement by the third party at a time that is costly or damaging to us. In addition, the FDA, EMA, Health Canada and other regulatory authorities require that our product candidates be manufactured according to cGMP and similar foreign standards. Pharmaceutical manufacturers and their subcontractors are required to register their facilities and/or products manufactured at the time of submission of the marketing application and then annually thereafter with the FDA, EMA, Health Canada and other regulatory agencies. They are also subject to pre-approval inspections and periodic unannounced inspections by the FDA, EMA, Health Canada and other regulatory agencies. Any subsequent discovery of problems with a product, or a manufacturing or laboratory facility used by us or our collaborators, may result in restrictions on the product or on the manufacturing or laboratory facility, including product recall, suspension of manufacturing, product seizure or a voluntary withdrawal of the drug from the market. Any failure by our or our collaborators' third-party manufacturers to comply with cGMP or any failure to deliver sufficient quantities of product candidates in a timely manner, could lead to a delay in, or failure to obtain, regulatory approval of any of our product candidates.

We rely on third parties to conduct our pre-clinical studies and clinical trials. If these third parties do not successfully carry out their contractual duties including to comply with applicable laws and regulations or meet expected deadlines, our business could be substantially harmed.

We rely on entities outside of our control, which may include academic institutions, CROs, hospitals, clinics and other third-party collaborators, to monitor, support, conduct and/or oversee pre-clinical and clinical studies of our current and future product candidates. As a result, we have less control over the timing and cost of these studies and the ability to recruit trial subjects than if we conducted these trials with our own personnel. For example, XEN007 is currently being evaluated under a physician-led, multi-center, Phase 2 proof-of-concept study as an adjunctive treatment in pediatric patients diagnosed with treatment-resistant CAE. In addition, we expect to initiate in the coming months, a Phase 2 proof-of-concept clinical trial examining XEN1101 in major depressive disorder and anhedonia in partnership with academic collaborators at the Icahn School of Medicine at Mount Sinai.

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

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

We, our CROs and CMOs are required to comply with current good laboratory practices, or cGLP, cGCP and cGMP regulations and guidelines enforced by the FDA, Health Canada, the competent authorities of the member states of the European Economic Area and comparable foreign regulatory authorities for products in clinical development. Regulatory authorities enforce these regulations through periodic inspections of clinical trial sponsors, principal investigators, clinical trial sites, manufacturing facilities, nonclinical testing facilities and other contractors. If we or any of our CROs or CMOs fail to comply with these applicable regulations, the clinical data generated in our nonclinical studies and clinical trials may be deemed unreliable and our submission of marketing applications may be delayed or the FDA, EMA, Health Canada or another regulatory authority may require us to perform additional clinical trials before approving our marketing applications. Upon inspection, the FDA, EMA, Health Canada or another regulatory authority could determine that any of our clinical trials fail or have failed to comply with applicable cGCP regulations. In addition, our clinical trials must be conducted with product produced under the cGMP regulations enforced by the FDA, EMA, Health Canada and other regulatory authorities, and our clinical trials may require a large number of test subjects. Our failure to comply with cGLP, cGCP and cGMP regulations may require us to repeat clinical trials or manufacture additional batches of drug which would delay the regulatory approval process and increase our costs. Moreover, our business may be implicated if any of our CROs or CMOs violates federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws.

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

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

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

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

Risks Related to Intellectual Property

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

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

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

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

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

The following examples are illustrative:

- others may be able to make compounds that are similar to our product candidates but that are not covered by the claims of the patents that we or our collaborators own or have exclusively licensed;
- others may independently develop similar or alternative technologies without infringing our intellectual property rights;
- issued patents that we own or have exclusively licensed may not provide us with any competitive advantages, or may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- we may obtain patents for certain compounds many years before we obtain marketing approval for products containing such compounds, and because patents have a limited life, which may begin to run out prior to the commercial sale of the related product, the commercial value of our patents may be limited;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may fail to develop additional proprietary technologies that are patentable;
- the laws of certain foreign countries may not protect our intellectual property rights to the same extent as the laws of the U.S., or we may fail to apply for or obtain adequate intellectual property protection in all the jurisdictions in which we operate; and
- the patents of others may have an adverse effect on our business, for example by preventing us from marketing one or more of our product candidates for one or more indications.

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

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

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

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

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

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

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

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

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

There have been and may be times in the future when certain patents that relate to our product candidates or any approved products are controlled by our licensees, sublicensees, licensors or other collaborators. Although we may, under such arrangements, have rights to consult with our collaborators on actions taken as well as back-up rights of prosecution and enforcement, we have in the past and may in the future relinquish rights to prosecute and maintain patents and patent applications within our portfolio as well as the ability to assert such patents against infringers. For example, currently the rights relating to the patent portfolio for XEN901 (now known as NBI-921352), other selective Nav1.6 inhibitors and dual Nav1.2/1.6 inhibitors are exclusively licensed to Neurocrine Biosciences, some of the rights relating to the patent portfolio for novel Nav1.7 inhibitors are held by Genentech and the rights to the patent portfolio for XEN402 (which was acquired by Flexion for use in its product candidate FX301) were sold to Flexion.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Under our existing license and other agreements, including those associated with the XEN007 program, we are subject to various obligations, including diligence obligations such as development and commercialization obligations, as well as potential milestone payments and other obligations. If we fail to comply with any of these obligations or otherwise breach our license agreements, our licensing partners may have the right to terminate the applicable license in whole or in part, or convert an exclusive license to a non-exclusive license. Generally, the loss of any one of our current licenses, or license exclusivity, or any other license we may acquire in the future, could materially harm our business, prospects, financial condition and results of operations.

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

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

Recent court decisions could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.

The patent positions of pharmaceutical and biopharmaceutical companies can be highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved. No consistent policy regarding the breadth of claims allowed in patents in these fields has emerged to date in the U.S. There have been recent changes regarding how patent laws are interpreted, and both the U.S. Patent and Trademark Office, or USPTO, and Congress have recently made significant changes to the patent system. There have been U.S. Supreme Court decisions that now show a trend of the Supreme Court which is distinctly negative on some patents. The trend of these decisions along with resulting changes in patentability requirements being implemented by the USPTO could make it increasingly difficult for us to obtain and maintain patents on our products. We cannot accurately predict future changes in the interpretation of patent laws or changes to patent laws which might be enacted into law. Those changes may materially affect our patents, our ability to obtain patents, the costs to prosecute our patent applications and enforce our patents and/or the patents and applications of our collaborators. The patent situation in these fields outside the U.S. also has uncertainties. Changes in either the patent laws or in interpretations of patent laws in the U.S. and other countries may diminish the value of our intellectual property or narrow the scope of our patent protection. Accordingly, we cannot predict the breadth of claims that may be allowed or enforced in the patents we own or to which we have a license or third-party patents.

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

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

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

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

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

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

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

Risks Related to Ownership of Our Common Shares

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

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

- announcements by us or our competitors of new products, product candidates or new uses for existing products, significant contracts, commercial relationships or capital commitments and the timing of these introductions or announcements;
- actions by any of our collaborators regarding our product candidates they are developing, including announcements regarding clinical or regulatory decisions or developments of our collaboration;
- unanticipated serious safety concerns related to the use of any of our products and product candidates;
- negative or inconclusive results from clinical trials of our product candidates, leading to a decision or requirement to conduct additional pre-clinical testing or clinical trials or resulting in a decision to terminate the continued development of a product candidate;
- delays of clinical trials of our product candidates;
- failure to obtain or delays in obtaining or maintaining product approvals or clearances from regulatory authorities;
- adverse regulatory or reimbursement announcements;
- announcements by us or our competitors of significant acquisitions, strategic collaborations, licenses, joint ventures or capital commitments;
- the results of our efforts to discover or develop additional product candidates;
- our dependence on third parties, including our collaborators, CROs, clinical trial sponsors and clinical investigators;
- regulatory or legal developments in Canada, the U.S. or other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key scientific or management personnel;
- our ability to successfully commercialize our future product candidates we develop independently, if approved;

- the level of expenses related to any of our product candidates or clinical development programs;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- actual or anticipated quarterly variations in our financial results or those of our competitors;
- any change to the composition of our board of directors or key personnel;
- sales of common shares by us or our shareholders in the future, as well as the overall trading volume of our common shares;
- failure to comply with covenants or make required payments under loan agreements;
- changes in the structure of healthcare payment systems;
- commencement of, or our involvement in, litigation;
- the impact of the COVID-19 pandemic on our business and the macroeconomic environment;
- general economic, industry and market conditions in the pharmaceutical and biotechnology sectors and other factors that may be unrelated to our operating performance or the operating performance of our competitors, including changes in market valuations of similar companies; and
- the other factors described in this "Risk Factors" section.

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

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

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

In addition, in the future, we may issue additional common shares, preferred shares, or other equity or debt securities convertible into common shares in connection with a financing, collaboration agreement, acquisition, litigation settlement, employee arrangements or otherwise. Any such issuance, including any issuances pursuant to our "at-the-market" equity offering program under our August 2020 sales agreement with Jefferies and Stifel, could result in substantial dilution to our existing shareholders and could cause the market price of our common shares to decline.

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

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

- shareholders cannot amend our articles unless such amendment is approved by shareholders holding at least two-thirds of the shares entitled to vote on such approval;
- shareholders must give advance notice to nominate directors or to submit proposals for consideration at shareholders' meetings; and

- applicable Canadian securities laws generally require, subject to certain exceptions, a tender offer to remain open for 105 days and that more than 50% of the outstanding securities not owned by the offeror be tendered before the offeror may take up the securities.

Any provision in our articles, by-laws, under the CBCA or under any applicable Canadian securities law that has the effect of delaying or deterring a change in control could limit the opportunity for our shareholders to receive a premium for their common shares, and could also affect the price that some investors are willing to pay for our common shares.

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

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

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

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

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

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

We will remain a smaller reporting company so long as, as of June 30 of the preceding year, (i) the market value of our common shares held by non-affiliates, or our public float, is less than $250 million; or (ii) we have annual revenues less than $100 million and either we have no public float or our public float is less than $700 million.

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

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

As of March 31, 2021, stock options to purchase 5,742,608 of our common shares with a weighted-average exercise price of $11.35 per common share were outstanding, a warrant to purchase 40,000 of our common shares with a weighted-average exercise price of $9.79 per common share was outstanding, 1,016,000 of our Series 1 Preferred Shares were outstanding, which are convertible into our common shares on a one-for-one basis at the option of the holder, subject to certain ownership limitations following a requested conversion, and pre-funded warrants to purchase 1,081,081 of our common shares with an exercise price of $0.0001 per share. The exercise of any of these stock options or warrants or conversion of the remaining Series 1 Preferred Shares would result in dilution to current common shareholders. Further, because we anticipate the need to raise additional capital to fund our clinical development programs, we may in the future sell substantial amounts of common shares, preferred shares, pre-funded warrants, or other securities convertible into or exchangeable for common shares. Pursuant to our equity incentive plans, our compensation committee (or a subset or delegate thereof) is authorized to grant equity-based incentive awards to our employees, directors and consultants. Future stock option grants and issuances of common shares under our share-based compensation plans may have an adverse effect on the market price of our common shares.

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

We are at risk of securities class action litigation.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology companies have experienced significant share price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business. In addition, an increase in litigation against biotechnology companies may make it more difficult and more expensive for us to obtain director and officer liability insurance, and we may be required to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage.

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

We have broad discretion in the application of any net proceeds we have received or may receive pursuant to our March 2021 public offering of common shares and pre-funded warrants to purchase common shares, our August 2020 "at-the-market" equity offering program with Jefferies and Stifel, any net proceeds we have received pursuant to our January 2020 public offering of common shares, as well as the net proceeds to us from previous equity and debt financings. Shareholders may not agree with our decisions, and our use of the proceeds and our existing cash and cash equivalents and marketable securities may not improve our results of operation or enhance the value of our common shares. Our failure to apply these funds effectively could have a material adverse effect on our business, delay the development of our product candidates and cause the market price of our common shares to decline. In addition, until the net proceeds are used, they may be placed in investments that do not produce significant income or that may lose value.

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

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

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

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

General Risk Factors

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

Global credit and financial markets have at times experienced extreme disruptions, including most recently in connection with the novel coronavirus, or COVID-19 pandemic, characterized by increased market volatility, declines in consumer confidence, declines in economic growth, increases in unemployment rates, and uncertainty about economic stability. If another such disruption in credit and financial markets and deterioration of confidence in economic conditions occurs, our business may be adversely affected. If the equity and credit markets were to deteriorate significantly in the future, it may make any necessary equity or debt financing more difficult to complete, more costly, and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our growth strategy, financial performance and the market price of our common shares could require us to delay or abandon development or commercialization plans. In addition, there is a risk that one or more of our current collaborators, service providers, manufacturers and other partners would not survive or be able to meet their commitments to us under such circumstances, which could directly affect our ability to attain our operating goals on schedule and on budget.

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

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

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

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

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

A variety of organizations measure the performance of companies on such ESG topics, and the results of these assessments are widely publicized. In addition, investment in funds that specialize in companies that perform well in such assessments are increasingly popular, and major institutional investors have publicly emphasized the importance of such ESG measures to their investment decisions. Topics taken into account in such assessments include, among others, the role of the company's board of directors in supervising various ESG issues and board diversity.

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

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

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

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

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

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

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

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

Item 2. Recent Sales of Unregistered Securities

On February 18, 2021, we issued 41,152 common shares that were not registered under the Securities Act of 1933, as amended, to Genworks Inc., a consultant, pursuant to the exercise of stock options for cash consideration with exercise proceeds of approximately CAD$120,884.

The common shares issued pursuant to the exercise of options were offered, sold and issued pursuant to the Canadian prospectus exemption under section 2.42 of National Instrument 45-106—Prospectus Exemptions, or NI 45-106, as such securities were offered, sold and issued in accordance with the terms and conditions of securities that we had previously issued. The options described above were offered, sold and issued pursuant to the Canadian prospectus exemption under section 2.24 of NI 45-106 as such securities were offered, sold and issued by us to our directors, officers, employees and consultants.

This issuance of common shares upon exercise of stock options was exempt from registration under the Securities Act of 1933, as amended, under Section 4(a)(2) thereof as a transaction by an issuer not involving a public offering. The recipient acquired the securities for investment only and not with a view to or for sale in connection with any distribution of the securities and appropriate legends were affixed thereto.

Item 6. Exhibits

(a) Exhibits.

Exhibit Number	Description of Document	Incorporated by Reference			
		Form	File No.	Exhibit	Filing Date
4.1	Form of Pre-Funded Warrant.	8-K	001-36687	4.1	March 10, 2021
10.1†	Amendment #1, dated January 13, 2021, to the License and Collaboration Agreement, dated December 2, 2019, by and between Xenon Pharmaceuticals Inc. and Neurocrine Biosciences, Inc.	8-K	001-36687	10.1	January 14, 2021
10.2#	Employment Agreement, dated January 13, 2021, by and between the Company and Ian Mortimer.	8-K	001-36687	10.2	January 14, 2021
10.3#	Employment Agreement, dated January 13, 2021, by and between the Company and Simon Pimstone.	8-K	001-36687	10.3	January 14, 2021
10.4#	Employment Agreement, dated January 13, 2021, by and between the Company and Sherry Aulin.	8-K	001-36687	10.4	January 14, 2021
31.1	Certification of Chief Executive Officer pursuant to Rule 13a-14(a).				
31.2	Certification of Chief Financial Officer pursuant to Rule 13a-14(a).				
32.1*	Certification of Chief Executive Officer pursuant to 18 U.S.C Section 1350.				
32.2*	Certification of Chief Financial Officer pursuant to 18 U.S.C Section 1350.				
101.INS	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because XBRL tags are embedded within the Inline XBRL document				
101.SCH	Inline XBRL Taxonomy Extension Schema Document				
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document				
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document				
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document				
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document				
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)				

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

† Certain portions of this exhibit have been omitted in accordance with Item 601(b)(10) of Regulation S-K.

\# Indicates management contract or compensatory plan.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Date: May 11, 2021

XENON PHARMACEUTICALS INC.

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

Date: May 11, 2021

By: /s/ Ian Mortimer
Ian Mortimer
President and Chief Financial Officer

Exhibit 31.1

CERTIFICATIONS

I, Simon Pimstone, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Xenon Pharmaceuticals Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d–15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: May 11, 2021

By: /s/ Simon Pimstone
Simon Pimstone
Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATIONS

I, Ian Mortimer, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Xenon Pharmaceuticals Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d–15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: May 11, 2021

By: /s/ Ian Mortimer
Ian Mortimer
President and Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 32.1

XENON PHARMACEUTICALS INC.
CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Quarterly Report of Xenon Pharmaceuticals Inc. (the "Company") on Form 10-Q for the quarter ended March 31, 2021, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Simon Pimstone, Chief Executive Officer (Principal Executive Officer) of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to my knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: May 11, 2021

By: /s/ Simon Pimstone
Simon Pimstone
Chief Executive Officer
(Principal Executive Officer)

A signed original of this written statement required by Section 906 of the Sarbanes-Oxley Act of 2002 has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request.

This certification accompanies the Report to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of Xenon Pharmaceuticals Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Report), irrespective of any general incorporation language contained in such filing.

Exhibit 32.2

XENON PHARMACEUTICALS INC.
CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Quarterly Report of Xenon Pharmaceuticals Inc. (the "Company") on Form 10-Q for the quarter ended March 31, 2021, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Ian Mortimer, President and Chief Financial Officer (Principal Financial and Accounting Officer) of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to my knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: May 11, 2021

By: /s/ Ian Mortimer
Ian Mortimer
President and Chief Financial Officer
(Principal Financial and Accounting Officer)

A signed original of this written statement required by Section 906 of the Sarbanes-Oxley Act of 2002 has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request.

This certification accompanies the Report to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of Xenon Pharmaceuticals Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Report), irrespective of any general incorporation language contained in such filing.