Table of Contents

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 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 September 30, 2018

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 No. 001-38535

Aptinyx Inc.
(Exact name of registrant as specified in its charter)

Delaware	**45-4626057**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**

909 Davis Street, Suite 600
Evanston, IL 60201
(847) 871-0377
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

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, 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 November 13, 2018, the registrant had 33,497,344 shares of common stock, $0.01 par value per share, outstanding.

Table of Contents

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Quarterly Report on Form 10-Q contains forward-looking statements that involve risks, uncertainties, and other factors that may cause actual results, levels of activity, performance, or achievements to be materially different from the information expressed or implied by these forward-looking statements. All statements, other than statements of historical facts, contained in this Quarterly Report on Form 10-Q, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans and objectives of management and expected market growth are forward-looking statements. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "target," "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

These forward-looking statements include, among other things, statements about:

- the timing, progress, and results of preclinical studies and clinical studies for NYX-2925, NYX-783, NYX-458, and any future product candidates we may develop, including statements regarding the timing of initiation and completion of studies or trials and related preparatory work, the period during which the results of the studies will become available, and our research and development programs;
- the existence or absence of side effects or other properties relating to our product candidates which could delay or prevent their regulatory approval, limit their commercial potential, or result in significant negative consequences following any potential marketing approval;
- the potential for our identified research priorities to advance our technologies;
- the potential benefits of, and our ability to maintain our collaboration with, Allergan plc, and establish or maintain future collaborations or strategic relationships or obtain additional funding in connection with these relationships;
- the potential timelines for our clinical studies or our ability to demonstrate safety and efficacy of our product candidates to the satisfaction of applicable regulatory authorities;
- our ability to obtain and maintain regulatory approval of our product candidates, NYX-2925, NYX-783, NYX-458, and any other future product candidates, and any statements regarding the label of an approved product candidate, including any restrictions, limitations and/or warnings therein;
- our intellectual property position, including the scope of protection we are able to establish and maintain for intellectual property rights covering NYX-2925, NYX-783, NYX-458, and any additional product candidates we may develop, and any statements as to whether we do or do not infringe, misappropriate, or otherwise violate any third-party intellectual property rights;
- our ability and the potential to successfully manufacture our product candidates for clinical studies and for commercial use, if approved;
- our ability to commercialize our products in light of the intellectual property rights of others;
- our ability to obtain funding for our operations, including funding necessary to complete further development and commercialization of our product candidates;
- our plans to research, develop, and commercialize our product candidates;
- our ability to attract collaborators with development, regulatory, and commercialization expertise;
- the size and growth potential of the markets for our product candidates and our ability to serve those markets;
- the rate and degree of market acceptance and clinical utility of NYX-2925, NYX-783, NYX-458, and any future product candidates we may develop, if approved;
- the pricing and reimbursement of NYX-2925, NYX-783, NYX-458, and any future product candidates we may develop, if approved;
- regulatory developments in the United States and foreign countries;
- our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately;
- the success of competing therapies that are or may become available;
- our ability to retain the continued service of our key professionals and to identify, hire, and retain additional qualified professionals;
- the accuracy of our estimates regarding expenses, future revenue, capital requirements, and needs for additional financing;

- the impact of laws and regulations;
- the use of proceeds from our initial public offering, and
- our expectations regarding the time during which we will be an "emerging growth company" under the Jumpstart Our Business Startups Act.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this Quarterly Report on Form 10-Q, particularly in the "Risk Factors" section, that could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, collaborations, joint ventures or investments that we may make or into which we may enter.

You should read this Quarterly Report on Form 10-Q and the documents that we reference herein and have filed or incorporated by reference as exhibits hereto completely and with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

PART I—FINANCIAL INFORMATION

Item 1. Condensed Financial Statements.

Aptinyx Inc.
Condensed Balance Sheets
(unaudited)
(In thousands, except per share data)

	September 30, 2018	December 31, 2017
Assets		
Current assets:		
Cash and cash equivalents	$ 165,578	$ 92,136
Restricted cash	252	—
Accounts receivable	593	937
Prepaid expenses and other current assets	1,169	1,960
Total current assets	167,592	95,033
Other assets	674	473
Property and equipment, net	1,813	1,816
Total assets	$ 170,079	$ 97,322
Liabilities, convertible preferred stock, and stockholders' equity (deficit)		
Current liabilities:		
Accounts payable	$ 1,208	$ 1,537
Accrued expenses and other current liabilities	6,465	2,835
Total current liabilities	7,673	4,372
Other long-term liabilities	435	282
Total liabilities	$ 8,108	$ 4,654
Commitments and contingencies (see Note 10)		
Convertible preferred stock:		
Convertible preferred stock, Series A-1, $0.01 par value, no shares and 151,773 shares authorized, issued and outstanding at September 30, 2018 and December 31, 2017, respectively	—	22,650
Convertible preferred stock, Series A-2, $0.01 par value, no shares and 173,453 shares authorized, issued and outstanding at September 30, 2018 and December 31, 2017, respectively	—	39,979
Convertible preferred stock, Series B, $0.01 par value, no shares and 234,955 shares authorized, issued and outstanding as of September 30, 2018 and December 31, 2017, respectively	—	69,757
Stockholders' equity (deficit):		
Preferred stock, $0.01 par value, 10,000 and no shares authorized as of September 30, 2018 and December 31, 2017, respectively; no shares issued and outstanding as of September 30, 2018 and December 31, 2017, respectively	—	—
Common stock, $0.01 par value, 150,000 shares authorized, 33,229 issued and outstanding as of September 30, 2018 and 900,000 shares authorized, 5,342 issued and outstanding as of December 31, 2017	332	53
Additional paid-in capital	253,084	12,486
Accumulated deficit	(91,445)	(52,257)
Total stockholders' equity (deficit)	$ 161,971	$ (39,718)
Total liabilities, convertible preferred stock and stockholders' equity (deficit)	$ 170,079	$ 97,322

See accompanying notes to these unaudited condensed financial statements.

Aptinyx Inc.
Condensed Statements of Operations
(unaudited)
(In thousands, except per share data)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2018	**2017**	**2018**	**2017**
Collaboration and grant revenue	$ 943	$ 1,205	$ 5,535	$ 3,778
Operating expenses:				
Research and development	11,950	8,067	37,860	24,930
General and administrative	3,782	1,318	7,853	3,819
Total operating expenses	15,732	9,385	45,713	28,749
Loss from operations	(14,789)	(8,180)	(40,178)	(24,971)
Other income	608	35	990	129
Net loss and comprehensive loss	$ (14,181)	$ (8,145)	$ (39,188)	$ (24,842)
Net loss per share attributable to common stockholders, basic and diluted	$ (0.43)	$ (1.56)	$ (2.48)	$ (4.82)
Weighted-average number of common shares outstanding, basic and diluted	33,191	5,232	15,789	5,159

See accompanying notes to these unaudited condensed financial statements.

Aptinyx Inc.
Condensed Statements of Cash Flows
(unaudited)
(In thousands)

	Nine Months Ended September 30,	
	2018	**2017**
Cash flows from operating activities:		
Net loss	$ (39,188)	$ (24,842)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization expense	336	225
Stock-based compensation expense	1,984	653
Changes in operating assets and liabilities:		
Prepaid expenses and other assets	356	(613)
Accounts receivable	344	(262)
Accounts payable	(263)	839
Accrued expenses and other liabilities	3,966	(336)
Net cash used in operating activities	(32,465)	(24,336)
Cash flows from investing activities:		
Purchases of property and equipment	(391)	(1,338)
Net cash used in investing activities	(391)	(1,338)
Cash flows from financing activities:		
Proceeds from issuance of Series A-2 convertible preferred stock, net issuance of costs	—	39,979
Payment of deferred issuance costs associated with Series B convertible preferred stock financing	(232)	—
Proceeds from stock options exercised	2	—
Proceeds from initial public offering, net of underwriters discounts	109,517	—
Payment of deferred offering costs	(2,971)	—
Net cash provided by financing activities	106,316	39,979
Net increase in cash, cash equivalents, and restricted cash	73,460	14,305
Cash, cash equivalents and restricted cash at beginning of period	92,609	16,953
Cash, cash equivalents and restricted cash at end of period	$ 166,069	$ 31,258
Supplemental disclosure of non-cash investing and financing activities:		
Property and equipment purchases not yet paid	$ —	$ 34
Deferred initial public offering costs not yet paid	$ 41	$ —

See accompanying notes to these unaudited condensed financial statements.

Aptinyx Inc.
Statements of Convertible Preferred Stock and Stockholders' (Deficit) Equity
(unaudited)
(in thousands)

	Series A-1 convertible preferred stock		Series A-2 convertible preferred stock		Series B convertible preferred stock		Common stock		Additional paid-in capital	Accumulated deficit	Total stockholders' equity (deficit)
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount			
Balance at December 31, 2016	151,773	$ 22,650	—	$ —	—	$ —	5,049	$ 50	$ 11,588	$ (20,189)	$ (8,551)
Issuance of Series A-2 convertible preferred stock, net of issuance costs of $21	—	—	173,453	39,979	—	—	—	—	—	—	—
Issuance of Series B convertible preferred stock, net of issuance costs of $243	—	—	—	—	234,955	69,757	—	—	—	—	—
Issuance of common stock upon vesting of restricted stock awards	—	—	—	—	—	—	293	3	(3)	—	—
Stock-based compensation	—	—	—	—	—	—	—	—	901	—	901
Net loss	—	—	—	—	—	—	—	—	—	(32,068)	(32,068)
Balance at December 31, 2017	151,773	$ 22,650	173,453	$ 39,979	234,955	$ 69,757	5,342	$ 53	$ 12,486	$ (52,257)	$ (39,718)
Issuance of common stock upon vesting of restricted stock awards	—	—	—	—	—	—	220	2	(2)	—	—
Stock-based compensation	—	—	—	—	—	—	—	—	1,984	—	1,984
Conversion of preferred stock upon IPO	(151,773)	(22,650)	(173,453)	(39,979)	(234,955)	(69,757)	20,306	203	132,183	—	132,386
Issuance of common stock upon IPO, net of underwriters' discount and other offering costs of $2,902	—	—	—	—	—	—	7,360	74	106,431	—	106,505
Issuance of common stock upon exercise of stock options	—	—	—	—	—	—	1	—	2	—	2
Net loss	—	—	—	—	—	—	—	—	—	(39,188)	(39,188)
Balance at September 30, 2018	—	$ —	—	$ —	—	$ —	33,229	$ 332	$ 253,084	$ (91,445)	$ 161,971

See accompanying notes to financial statements

Aptinyx Inc.
Notes to Condensed Financial Statements
(Unaudited)

1. Organization

Description of business

Aptinyx Inc. (the "Company" or "Aptinyx") was incorporated in Delaware on June 24, 2015 and maintains its headquarters in Evanston, Illinois.

Aptinyx is a clinical-stage biopharmaceutical company focused on the discovery, development, and commercialization of novel, proprietary, synthetic small molecules for the treatment of brain and nervous system disorders. Aptinyx has a platform for discovering proprietary compounds that work through a novel mechanism: modulation of N-methyl-D-aspartate receptors ("NMDAr"), which are vital to normal and effective brain and nervous system functions. This mechanism has applicability across a number of brain and nervous system disorders.

Initial public offering

On June 20, 2018, the Company's registration statement on Form S‑1 (File No. 333-225150) relating to the initial public offering ("IPO") of its common stock became effective and on June 25, 2018, the IPO closed. Pursuant to the IPO, the Company issued and sold 7,359,998 shares of common stock at a public offering price of $16.00 per share, which included 959,999 shares sold pursuant to the exercise of the underwriters' option to purchase additional shares. The Company received net proceeds of $106.5 million after deducting underwriting discounts and commissions and other offering costs of $3.0 million. The shares began trading on the Nasdaq Global Select Market on June 21, 2018. Upon the closing of the IPO, all of the Company's outstanding shares of convertible preferred stock automatically converted into 20,306,497 shares of common stock at the applicable conversion ratio.

The Company is also authorized to issue 10 million shares of undesignated preferred stock, par value $0.01, in one or more series. As of September 30, 2018, no shares of preferred stock were issued or outstanding.

Liquidity and capital resources

As of September 30, 2018, the Company had cash and cash equivalents of $165.6 million which the Company believes will be sufficient to funds its planned operations for a period of at least twelve months from the date of issuance of these condensed financial statements.

2. Summary of significant accounting policies

Basis of presentation

The condensed financial statements of the Company included herein have been prepared pursuant to the rules and regulations of the Securities and Exchange Commission (the "SEC"). Certain information and footnote disclosures normally included in financial statements prepared in accordance with accounting principles generally accepted in the United States of America ("GAAP") have been condensed or omitted from this report, as is permitted by such rules and regulations. The accompanying condensed financial statements reflect all adjustments consisting of normal, recurring adjustments that are necessary for a fair presentation of the financial position results of operations and cash flows for the interim periods presented. Interim results are not necessarily indicative of results for a full year. Accordingly, these financial statements should be read in conjunction with the financial statements as of and for the year ended December 31, 2017, and notes thereto, included in the Company's final prospectus for the IPO filed with the SEC pursuant to Rule 424(b)(4) dated June 20, 2018 (the "Prospectus").

From time to time, new accounting pronouncements are issued by the Financial Accounting Standards Board ("FASB"), or other standard setting bodies and adopted by the Company as of the specified effective date. Unless otherwise

discussed, the impact of recently issued standards that are not yet effective will not have a material impact on the Company's financial statements upon adoption. Under the Jumpstart Our Business Startups Act of 2012, as amended (the "JOBS Act"), the Company meets the definition of an emerging growth company, and has elected the extended transition period for complying with new or revised accounting standards, which delays the adoption of these accounting standards until they would apply to private companies.

Reverse stock split

On June 7, 2018, the Company effected a one-for-27.58621 reverse stock split of the Company's issued and outstanding shares of common stock and a proportional adjustment to the existing conversion ratios for the Company's convertible preferred stock. The par value per share and authorized shares of common and convertible preferred stock were not adjusted as a result of the reverse stock split. All common stock and common stock per share amounts within the financial statements and notes thereto have been retroactively adjusted for all periods presented to give effect to this reverse stock split, including reclassifying an amount equal to the reduction in par value of common stock to additional paid-in capital.

Use of estimates

The financial statements are prepared in conformity with GAAP. This process requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities as of the date of the financial statements and the reported amounts of expenses during the reporting period. Actual results could differ from those estimates.

Significant accounting policies

The Company's significant accounting policies are described in Note 3, "Summary of significant accounting policies," in the Prospectus. There have been no material changes to the significant accounting policies during the period ended September 30, 2018.

Recently issued accounting pronouncements

In February 2016, the FASB issued ASU No. 2016-02, *Leases* ("ASU 2016-02"), which requires a lessee to recognize assets and liabilities on the balance sheet for operating leases and changes many key definitions, including the definition of a lease. The new standard includes a short-term lease exception for leases with a term of 12 months or less, as part of which a lessee can make an accounting policy election not to recognize lease assets and lease liabilities. Lessees will continue to differentiate between finance leases (previously referred to as capital leases) and operating leases using classification criteria that are substantially similar to the previous guidance. The new standard will be effective for the Company beginning after December 15, 2019, and early adoption is permitted. The Company is currently evaluating the potential impact ASU 2016-02 may have on its financial statements.

In May 2014, the FASB issued ASU No. 2014-09, *Revenue from Contracts with Customers* ("ASU 2014-09"), which supersedes nearly all existing revenue recognition guidance. The core principle of ASU 2014-09 is to recognize revenues when promised goods or services are transferred to customers in an amount that reflects the consideration to which an entity expects to be entitled for those goods or services. ASU 2014-09 defines a five step process to achieve this core principle and, in doing so, more judgment and estimates may be required within the revenue recognition process than are required under existing GAAP. The standard is effective for annual periods beginning after December 15, 2018, using either of the following transition methods: (i) a full retrospective approach reflecting the application of the standard in each prior reporting period with the option to elect certain practical expedients, or (ii) a retrospective approach with the cumulative effect of initially adopting ASU 2014-09 recognized at the date of adoption (which includes additional footnote disclosures). The Company is evaluating the impact of the pending adoption of ASU 2014-09 on the financial statements and has not yet determined the method by which the Company will adopt the standard when required.

3. Supplemental financial information

Cash, cash equivalents and restricted cash

Cash and cash equivalents consist of cash and, if applicable, highly liquid investments with an original maturity of three months or less when purchased. The following table provides a reconciliation of cash, cash equivalents, and restricted cash reported within the balance sheets that sum to the total of the same such amounts shown in the statements of cash flows (amounts in thousands).

	As of September 30, 2018	As of December 31, 2017
Cash and cash equivalents	$ 165,578	$ 92,136
Short-term and long-term restricted cash	491	473
Total cash, cash equivalents, and restricted cash shown in the statements of cash flows	$ 166,069	$ 92,609

Prepaid expenses and other current assets

Prepaid expenses and other current assets consist of the following (in thousands):

	As of September 30, 2018	As of December 31, 2017
Prepaid clinical	$ 173	$ 1,718
Prepaid insurance	791	137
Other prepaid expenses and current assets	205	105
Total prepaid expenses and other current assets	$ 1,169	$ 1,960

Accrued expenses and other current liabilities

Accrued expenses and other current liabilities consist of the following (in thousands):

	As of September 30, 2018	As of December 31, 2017
Employee-related expenses	$ 2,056	$ 1,435
Development costs and sponsored research	1,805	737
Clinical trials	2,282	69
Other	322	594
Total accrued expenses and other current liabilities	$ 6,465	$ 2,835

4. Research collaboration agreement with Allergan

On July 24, 2015, the Company entered into a Research Collaboration Agreement ("RCA") with Naurex Inc., a subsidiary of Allergan plc ("Allergan"), focused on the research and discovery of small molecules that modulate NMDArs. The collaboration is supervised by a Joint Steering Committee ("JSC") comprising an equal number of representatives from both the Company and Allergan. Under the terms of the agreement, Allergan will pay the Company $1.0 million for each option exercised by Allergan. Under the terms of the agreement, the RCA will terminate upon the earlier of a predetermined anniversary of the RCA or on the date on which Allergan exercises three options to acquire molecules from a pool of eligible compounds. On May 16, 2018, Allergan exercised its option to acquire exclusive rights to develop and commercialize AGN-241751 within a predefined set of indications. For the nine months ended September 30, 2018, the Company recognized the $1.0 million non-refundable milestone payment within collaboration

and grant revenue in the statements of operations as there were no remaining performance obligations associated with the optioned compound.

The Company accounts for the agreement as a joint risk-sharing collaboration in accordance with ASC 808, Collaboration Arrangements. Costs between the Company and Allergan with respect to each party's share of development costs that have been incurred pursuant to the RCA are substantially recorded within research and development in the accompanying statements of operations. Reimbursable expenses under the RCA include chemistry, discovery, screening, and profiling efforts around novel NMDAr modulators from the Company's discovery platform as well as salary of full-time employees at a fixed annual rate for each individual assigned to those efforts, consistent with oversight and guidance of the JSC. Such costs for each compound are considered reimbursable up until the point that the compound is selected by one of the collaboration parties. As such, none of the costs reimbursed by Allergan in any period presented were directly related to the Company's lead product candidates, NYX-2925, NYX-783, and NYX-458, which the Company selected under the collaboration.

During the three months ended September 30, 2018 and 2017, the Company recorded expenses of $1.9 million and $1.9 million, respectively, for certain development activities in accordance with the terms of the RCA of which 50% was reimbursed by Allergan. The Company received reimbursements of $0.9 million and $1.0 million during the three months ended September 30, 2018 and 2017, respectively. During the nine months ended September 30, 2018 and 2017, the Company recorded expenses of $5.8 million and $5.8 million, respectively, for certain development activities in accordance with the terms of the RCA of which 50% was reimbursed by Allergan. The Company received reimbursements of $2.9 and $2.9 million during the nine months ended September 30, 2018 and 2017, respectively. Such reimbursements were reported within collaboration and grant revenue in the statements of operations.

5. Fair value measurements

ASC 820, Fair Value Measurement ("ASC 820"), establishes a fair value hierarchy for instruments measured at fair value that distinguishes between assumptions based on market data (observable inputs) and the Company's own assumptions (unobservable inputs). ASC 820 identifies fair value as the exchange price, or exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As a basis for considering market participant assumptions in fair value measurements, ASC 820 establishes a three-tier fair value hierarchy that distinguishes between the following:

- Level 1 inputs are quoted prices (unadjusted) in active markets for identical assets or liabilities;
- Level 2 inputs are inputs other than quoted prices included within Level 1 that are observable for the asset or liability, either directly or indirectly; and
- Level 3 inputs are unobservable inputs that reflect the Company's own assumptions about the assumptions market participants would use in pricing the asset or liability. Financial assets and liabilities are classified in their entirety based on the lowest level of input that is significant to the fair value measurement.

To the extent that the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

The carrying values reported in the Company's balance sheets for cash and cash equivalents, restricted cash, accounts receivable, accounts payable, and accrued expenses are reasonable estimates of their fair values due to the short-term nature of these items.

Assets measured at fair value as of September 30, 2018 are as follows (in thousands):

	September 30, 2018	Level 1	Level 2	Level 3
Assets				
Money market funds, included in cash and cash equivalents	$ 163,705	$ 163,705	$ —	$ —
Money market funds, included in restricted cash	252	252	—	—
Money market funds, included in other assets	67	67	—	—
	$ 164,024	$ 164,024	$ —	$ —

Assets measured at fair value as of December 31, 2017 are as follows (in thousands):

	December 31, 2017	Level 1	Level 2	Level 3
Assets				
Money market funds, included in cash and cash equivalents	$ 89,553	$ 89,553	$ —	$ —
Money market funds, included in other assets	317	317	—	—
	$ 89,870	$ 89,870	$ —	$ —

6. Property and equipment

Property and equipment are as follows (in thousands):

	As of September 30, 2018	As of December 31, 2017
Computer software and equipment	$ 15	$ 15
Office equipment and furniture	160	92
Laboratory equipment	1,571	1,529
Leasehold improvements	1,051	748
Construction in progress	—	22
Less accumulated depreciation	(984)	(590)
Property and equipment, net	$ 1,813	$ 1,816

Depreciation expense was $0.1 million for each of the three months ended September 30, 2018 and 2017, and $0.4 million and $0.2 million for the nine months ended September 30, 2018 and 2017, respectively.

7. Stock incentive plans

On June 5, 2018, the Company's stockholders approved the 2018 Stock Option and Incentive Plan (the "2018 Plan"), which became effective on June 20, 2018. The number of shares available for grant under the Company's 2018 Plan as of September 30, 2018 was 3,878,940, which includes 505,046 shares of the Company's common stock reserved under the Company's 2015 Stock Option and Grant Plan (the "2015 Plan") that became available for issuance upon the effectiveness of the 2018 Plan. No future issuance will be made under the 2015 Plan.

Stock-based compensation expense

Non-cash stock-based compensation expense recognized in the accompanying statements of operations relating to both stock options and restricted stock awards for the three and nine months ended September 30, 2018 and 2017 was as follows (in thousands):

	Three months ended September 30,		Nine months ended September 30,	
	2018	2017	2018	2017
Research and development	$ 242	$ 91	$ 616	$ 233
General and administrative	478	151	1,368	420
Total stock-based compensation expense	$ 720	$ 242	$ 1,984	$ 653

Stock options

The table below summarizes activity related to stock options (in thousands, except per share amounts):

Options	Shares	Weighted-average exercise price	Weighted-average remaining contractual term	Aggregate intrinsic value
Outstanding, December 31, 2017	1,498	$ 2.48	8.93	$ 4,146
Granted	2,443	9.95		
Exercised	1	1.82		
Forfeited and canceled	(5)	2.77		
Outstanding, September 30, 2018	3,937	$ 7.07	8.94	$ 86,148
Vested and expected to vest at September 30, 2018	3,937	$ 7.07	8.94	$ 86,148
Exercisable at September 30, 2018	702	$ 2.28	8.08	$ 18,739

During the nine months ended September 30, 2018 and 2017, the Company granted 2.4 million and 1.2 million stock options, respectively and these options had a weighted-average grant-date fair value of $9.95 and $2.59 per share, respectively. As of September 30, 2018, there was $15.3 million of total unrecognized stock-based compensation expense related to non-vested stock options which is expected to be recognized over a weighted-average period of 3.16 years. The options have a ten-year life and generally vest over a period of four years, subject to continuous employment.

Restricted stock awards

Non-cash restricted stock award expense recognized in the accompanying statements of operations was $0.1 million for each of the three months ended September 30, 2018 and 2017 and $0.3 million for each of the nine months ended September 30, 2018 and 2017. The total fair value of shares that vested in the nine months ended September 30, 2018 was $1.4 million. At September 30, 2018, there was $0.3 million of unrecognized compensation cost related to 268,000 unvested restricted stock awards that will be recognized as expense over a weighted-average period of 0.91 years.

8. Net loss per share

Basic and diluted net loss per share attributable to common stockholders was calculated as follows for the three and nine months ended September 30, 2018 and 2017 (in thousands, except per share data):

	Three months ended September 30,		Nine months ended September 30,	
	2018	2017	2018	2017
Numerator:				
Net loss attributable to common stockholders	$ (14,181)	$ (8,145)	$ (39,188)	$ (24,842)
Denominator:				
Weighted-average common shares outstanding—basic and diluted	33,191	5,232	15,789	5,159
Net loss per share attributable to common stockholders—basic and diluted	$ (0.43)	$ (1.56)	$ (2.48)	$ (4.82)

The following common stock equivalents outstanding as of September 30, 2018 and 2017, were excluded from the computation of diluted net loss per share attributable to common stockholders for the periods presented because including them would have been anti-dilutive (in thousands):

	As of September 30,	
	2018	2017
Series A-1 convertible preferred stock	—	5,502
Series A-2 convertible preferred stock	—	6,288
Stock options issued and outstanding	3,937	1,497
Unvested restricted stock	268	655
Total	4,205	13,942

9. Income taxes

Deferred tax assets and liabilities are determined based on the difference between the financial statement and tax bases of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. Valuation allowances are provided if based upon the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized. The Company has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets, including its net operating losses. Based on its history of operating losses, the Company believes that it is more likely than not that the benefit of its deferred tax assets will not be realized. Accordingly, the Company has provided a full valuation allowance for deferred tax assets as of September 30, 2018 and December 31, 2017.

On December 22, 2017, the President of the United States signed into law the Tax Cuts and Jobs Act ("TCJA"). The TCJA makes significant changes in U.S. tax law including a reduction in the corporate tax rates, changes to net operating loss carryforwards and carrybacks, and a reduction of the amount of the orphan drug credit. As a result of the TCJA, the Company remeasured its ending deferred tax assets and liabilities at December 31, 2017 to the newly enacted U.S. federal corporate tax rate of 21%. The Company recognized the provisional tax impacts related to the remeasurement of the deferred tax assets and liabilities pursuant to SEC Staff Accounting Bulletin No. 118 and included these amounts in its financial statements for the year ended December 31, 2017. The Company did not record any adjustments to this provisional amount during the period ended September 30, 2018 and will continue to analyze and refine its calculations related to the remeasurement as the impact of TCJA is finalized.

10. Commitments and contingencies

Contingencies

From time to time, the Company is subject to occasional lawsuits, investigations and claims arising out of the normal conduct of business. The Company has no significant pending or threatened litigation as of September 30, 2018.

Indemnifications

In the normal course of business, the Company enters into contracts that contain a variety of indemnifications with its employees, licensors, suppliers and service providers. Further, the Company indemnifies its directors and officers who are, or were, serving at the Company's request in such capacities. The Company's maximum exposure under these arrangements is unknown at September 30, 2018. The Company does not anticipate recognizing any significant losses relating to these arrangements.

Leases

The Company enters into various non-cancelable, operating lease agreements for its facilities and equipment in order to conduct its operations. The Company expenses rent on a straight-line basis over the life of the lease and has recorded deferred rent on the Company's balance sheets within both accrued expenses and other current liabilities and other long-term liabilities.

On July 18, 2018, the Company entered into a sublease agreement for additional office space adjacent to the Company's existing headquarters in Evanston, Illinois, totaling approximately 6,172 square feet. The term of the lease commenced on July 18, 2018 and continues through September 30, 2022. The total aggregate estimated base rent payments over the term of the sublease approximate $0.9 million.

Total rent expense, inclusive of lease incentives, under all the operating lease agreements amounted to $0.2 million for each of the three months ended September 30, 2018 and 2017, and $0.5 million for each of the nine months ended September 30, 2018 and 2017.

11. Related party transactions

The Company received consulting services from PharmaKey, LLC ("PharmaKey") during the three and nine months ended September 30, 2018 and 2017, where the Company's Chief Development Officer is founder, owner, chairman, and former president. The transactions engaged between the Company and PharmaKey have been reviewed and approved by the Company's Board of Directors and transacted on an arm's length basis. As of September 30, 2018, the Company had a balance of approximately $1,000 recorded within accounts payable. The Company incurred consulting services from PharmaKey totaling approximately $1,000 and $34,000 for the three months ended September 30, 2018 and 2017, respectively, and approximately $13,000 and $76,000 for the nine months ended September 30, 2018 and 2017, respectively, which are included within research and development expenses in the statements of operations.

Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations.

The following discussion should be read in conjunction with our condensed financial statements and accompanying footnotes appearing elsewhere in this Quarterly Report on Form 10-Q and our audited financial statements and related footnotes included in our final prospectus for our initial public offering filed pursuant to Rule 424(b) under the Securities Act of 1933, as amended, or the Securities Act, with the Securities and Exchange Commission, or the SEC dated June 20, 2018, or the Prospectus.

Some of the information contained in this discussion and analysis or set forth elsewhere in this Quarterly Report on Form 10-Q , including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. See "Special Note Regarding Forward-Looking Statements." Because of many factors, including those factors set forth in the "Risk Factors" section of this Quarterly Report on Form 10- Q, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis. We do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

Overview

We are a clinical-stage biopharmaceutical company focused on the discovery, development, and commercialization of novel, proprietary, synthetic small molecules for the treatment of brain and nervous system disorders. We focus our efforts on targeting and modulating N-methyl-D-aspartate receptors, or NMDArs, which are vital to normal and effective function of the brain and nervous system. We believe leveraging the therapeutic advantages of the differentiated modulatory mechanism of our compounds will drive a paradigm shift in the treatment of disorders of the brain and nervous system.

We are advancing a pipeline of distinct product candidates derived from our NMDAr modulator discovery platform. We are currently studying our most advanced product candidate, NYX-2925, in two Phase 2 studies in chronic pain. The first is in subjects with painful diabetic peripheral neuropathy, or DPN, and the second is in subjects with fibromyalgia. We expect to report top-line data from these studies early in the first quarter of 2019. Our second product candidate, NYX-783, has been evaluated in Phase 1 clinical development. We intend to develop NYX-783 for the treatment of post-traumatic stress disorder, or PTSD, and plan to report data from a Phase 2 clinical study in the second half of 2019. We are currently evaluating the safety and tolerability of our third product candidate, NYX-458, in a Phase 1 study, which we expect to complete in the first half of 2019. We intend to develop NYX-458 for the treatment of cognitive impairment associated with Parkinson's disease.

Since our inception in June 2015, we have never generated revenue from the sale of our products and have incurred significant net losses. Our revenue has been primarily derived from a research collaboration agreement with Allergan plc, or Allergan, a development services agreement with Allergan, and research and development grants from the U.S. government. From our inception through September 30, 2018, we have raised an aggregate of $135 million of gross proceeds from sales of our convertible preferred stock and $117.8 million of gross proceeds from our IPO. Our net losses were $32.1 million and $15.5 million for the years ended December 31, 2017 and 2016, and $39.2 million and $24.8 million for the nine months ended September 30, 2018 and 2017, respectively. As of September 30, 2018, we had an accumulated deficit of $91.4 million. 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. We anticipate that our expenses will increase significantly in connection with our ongoing activities, as we:

- advance the clinical development of our lead product candidates;
- continue the research and development of our preclinical product candidates;
- seek to identify and develop additional product candidates;
- seek marketing approvals for any of our product candidates for which we successfully complete clinical development;
- develop and expand our sales, marketing, and distribution capabilities for our product candidates for which we obtain marketing approval;

- scale up our manufacturing processes and capabilities to support our ongoing preclinical activities and clinical studies of our product candidates and commercialization of any of our product candidates for which we obtain marketing approval;
- maintain, expand, and protect our intellectual property portfolio;
- expand our operational, financial, and management systems and increase personnel, including personnel to support our clinical development, manufacturing, and commercialization efforts; and
- increase our product liability and clinical trial insurance coverage as we initiate our clinical studies and commercialization efforts.

We do not expect to generate revenue from product sales unless and until we successfully complete clinical development and obtain regulatory approval for a product candidate, which we expect will take a number of years and the outcome of which is uncertain, or enter into collaborative agreements with third parties, the timing of which is largely beyond our control and may never occur. To fund our current and future operating plans, we will need additional capital, which we may obtain through one or more equity offerings, debt financings, or other third-party funding, including potential strategic alliances and licensing or collaboration arrangements. We may, however, be unable to raise additional funds or enter into such other arrangements when needed on favorable terms or at all. Our failure to raise capital or enter into such other arrangements as and when needed would have a negative impact on our financial condition and our ability to develop our current product candidates, or any additional product candidates, if developed. The amount and timing of our future funding requirements will depend on many factors, including the pace and results of our preclinical and clinical development efforts. We cannot assure you that we will ever be profitable or generate positive cash flow from operating activities.

Financial operations overview

Collaboration and grant revenue

We have not generated any revenue from product sales. Our revenue to date has been primarily derived from a research collaboration agreement with Allergan; a development services agreement with Allergan, which was put in place to continue certain development activities for a pre-determined period of time following Allergan's acquisition of Naurex Inc., or Naurex, prior to the spin-out of Aptinyx; and research and development grants from the U.S. government which have no repayment or royalty obligations. The development services agreement with Allergan was terminated in October 2016. Therefore, we have not generated any revenues under this agreement since October 2016 and do not expect to generate revenues in the future under this agreement.

Operating expenses

Research and development expenses

Research and development activities account for a significant portion of our operating expenses. We expense research and development costs as incurred. Research and development expenses consists of costs incurred in connection with the development of our product candidates, including:

- fees paid to consultants, sponsored researchers, and contract research organizations, or CROs, including in connection with our preclinical and clinical studies, and other related clinical study fees, such as for investigator grants, patient screening, laboratory work, clinical study database management, and statistical compilation and analysis;
- costs related to acquiring and maintaining preclinical and clinical study materials and facilities;
- costs related to compliance with regulatory requirements; and
- costs related to salaries, bonuses, and other compensation for employees in research and development functions.

At this time, we cannot reasonably estimate or know the nature, timing, and costs of the efforts that will be necessary to complete the development of our product candidates. We are also unable to predict when, if ever, material net cash

inflows will commence from sales of our products, if approved. This is due to the numerous risks and uncertainties associated with developing such product candidates, including the uncertainty related to:

- future clinical study results; the scope, rate of progress, and expense of our ongoing as well as any additional preclinical studies, clinical studies and other research and development activities;
- clinical study enrollment rate;
- clinical study design;
- the manufacturing of our product candidates;
- our ability to obtain and maintain intellectual property protection for our product candidates;
- significant and changing government regulation;
- the timing and receipt of any regulatory approvals; and
- the risks disclosed in the section entitled "Risk Factors" included elsewhere in this Quarterly Report on Form 10-Q.

A change in the outcome of any of these variables with respect to the development of any of our product candidates could significantly change the costs, timing, and viability associated with the development of that product candidate.

We expect our research and development expenses to increase over the next several years as we continue to implement our business strategy, which includes advancing our product candidates into and through clinical development, expanding our research and development efforts, seeking regulatory approvals for any product candidates for which we successfully complete clinical studies, accessing and developing additional product candidates, and hiring additional personnel to support our research and development efforts. In addition, product candidates in later stages of clinical development generally incur higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical studies. As such, we expect our research and development expenses to increase as our product candidates advance into later stages of clinical development.

General and administrative expenses

General and administrative expenses consist primarily of salaries and related costs, including stock-based compensation. General and administrative expenses also include rent as well as professional fees for legal, consulting, accounting, and audit services.

In the future, we expect that our general and administrative expenses will increase as we increase our headcount to support our continued research and development and the potential commercialization of our product candidates, if approved. We also anticipate that we will incur increased accounting, audit, legal, tax, regulatory, compliance, and director and officer insurance costs, as well as investor and public relations expenses associated with maintaining compliance with exchange listing and SEC requirements.

Other income

Other income consists primarily of the interest income earned on our cash and cash equivalents.

Results of operations

Comparison of the three months ended September 30, 2018 and 2017

The following table summarizes our results of operations for the three months ended September 30, 2018 and 2017 (in thousands):

	Three months ended September 30,		Increase
	2018	2017	(Decrease)
Collaboration and grant revenue	$ 943	$ 1,205	$ (262)
Operating expenses:			
Research and development	11,950	8,067	3,883
General and administrative	3,782	1,318	2,464
Total operating expenses	15,732	9,385	6,347
Loss from operations	(14,789)	(8,180)	6,609
Other income	608	35	573
Net loss and comprehensive loss	$ (14,181)	$ (8,145)	$ 6,036

Collaboration and grant revenue

Revenue was $0.9 million for the three months ended September 30, 2018, compared to $1.2 million for the three months ended September 30, 2017. The decrease of $0.3 million was primarily driven by a reduction in our research and development costs incurred under our grants from the U.S. government as our outstanding grants were completed in the first half of 2018, and accordingly, we did not generate any grant-related revenues for the three months ending September 30, 2018.

Research and development expenses

The following table summarizes our research and development expenses incurred during the three months ended September 30, 2018 and 2017 (in thousands):

	Three months ended September 30,		Increase
	2018	2017	(Decrease)
NYX-2925	$ 5,791	$ 2,392	$ 3,399
NYX-783	360	604	(244)
NYX-458	867	336	531
Preclinical research and discovery programs	1,710	2,077	(367)
Personnel and related costs	3,222	2,658	564
Total research and development expenses	$ 11,950	$ 8,067	$ 3,883

Research and development expenses were $12.0 million for the three months ended September 30, 2018, compared to $8.1 million for the three months ended September 30, 2017. The increase of $3.9 million was primarily due to the following:

- approximately $3.4 million increase for clinical, regulatory, and drug product costs related to NYX-2925, including the ongoing Phase 2 clinical study in subjects with painful DPN, the ongoing exploratory clinical study in subjects with fibromyalgia and two Phase 1 target pathway clinical studies that commenced in early 2018;
- approximately $0.2 million decrease for clinical costs related to our Phase 1 clinical study of NYX-783 for the treatment of PTSD;
- approximately $0.5 million increase for Phase 1 clinical study costs related to ongoing development of NYX-458 for the treatment of Parkinson's disease cognitive impairment;

- approximately $0.4 million decrease for costs associated with our preclinical research efforts with external research organizations; and
- approximately $0.6 million increase for costs related to employee compensation and related support, including $0.2 million of additional stock-based compensation expense, due to increased headcount.

General and administrative expenses

General and administrative expenses were $3.8 million for the three months ended September 30, 2018, compared to $1.3 million for the three months ended September 30, 2017. The increase of $2.5 million was primarily driven by $0.9 million for increased costs related to employee compensation, including $0.3 million of additional stock-based compensation expense, due to increased headcount, and $1.5 million of increased professional fees to support ongoing business operations and to comply with obligations associated with being a publicly traded company.

Other income

We recorded $0.6 million of other income for the three months ended September 30, 2018, compared to less than $0.1 million for the three months ended September 30, 2017. This was due to increased interest income earned on our cash and cash equivalents.

Comparison of the nine months ended September 30, 2018 and 2017

The following table summarizes our results of operations for the nine months ended September 30, 2018 and 2017 (in thousands):

	Nine months ended September 30,		Increase
	2018	2017	(Decrease)
Collaboration and grant revenue	$ 5,535	$ 3,778	$ 1,757
Operating expenses:			
Research and development	37,860	24,930	12,930
General and administrative	7,853	3,819	4,034
Total operating expenses	45,713	28,749	16,964
Loss from operations	(40,178)	(24,971)	15,207
Other income	990	129	861
Net loss and comprehensive loss	$ (39,188)	$ (24,842)	$ 14,346

Collaboration and grant revenue

Revenue was $5.5 million for the nine months ended September 30, 2018, compared to $3.8 million for the nine months ended September 30, 2017. The net increase of $1.8 million was primarily the result of the following changes:

- approximately $0.8 million increase reflecting incremental work performed under our research and development grants from the U.S. government associated with preclinical studies towards NYX-458. We do not expect to generate significant grant revenues in the future; and
- $1.0 million increase due to Allergan's exercise of its option in May 2018 to acquire exclusive rights to develop and commercialize AGN-241751.

Research and development expenses

The following table summarizes our research and development expenses incurred during the nine months ended September 30, 2018 and 2017 (in thousands):

	Nine months ended September 30,		Increase
	2018	2017	(Decrease)
NYX-2925	$ 17,355	$ 8,091	$ 9,264
NYX-783	2,654	2,501	153
NYX-458	2,385	940	1,445
Preclinical research and discovery programs	5,804	5,645	159
Personnel and related costs	9,662	7,753	1,909
Total research and development expenses	$ 37,860	$ 24,930	$ 12,930

Research and development expenses were $37.9 million for the nine months ended September 30, 2018, compared to $24.9 million for the nine months ended September 30, 2017. The increase of $12.9 million was primarily due to the following:

- approximately $9.3 million increase for clinical, regulatory, and drug product costs related to our advancement of NYX-2925, including ongoing enrollment in our Phase 2 clinical study in subjects with painful DPN, ongoing enrollment in an exploratory clinical study in subjects with fibromyalgia, and two Phase 1 exploratory pharmacodynamic clinical studies that commenced in the first quarter of 2018;
- approximately $0.2 million increase for clinical, regulatory, and drug product costs initiated in the fourth quarter of 2017 related to our Phase 1 clinical study of NYX-783 for the treatment of PTSD;
- approximately $1.4 million increase for external research and development costs, IND-enabling activities, and Phase 1 clinical study costs initiated in the fourth quarter of 2017 related to ongoing development of NYX-458 for the treatment of Parkinson's disease cognitive impairment;
- approximately $0.2 million increase for costs associated with our internal preclinical research efforts and sponsored research activities with academic institutions; and
- approximately $1.9 million increase for costs related to employee compensation and related support, including $0.4 million of additional stock-based compensation expense, due to increased headcount.

General and administrative expenses

General and administrative expenses were $7.9 million for the nine months ended September 30, 2018, compared to $3.8 million for the nine months ended September 30, 2017. The increase of $4.0 million was primarily driven by $2.2 million for increased costs related to employee compensation, including $0.9 million of additional stock-based compensation expense, due to increased headcount and $1.6 million of increased professional fees spent to support ongoing business operations and to comply with obligations associated with being a publicly traded company.

Other income

We recorded $1.0 million of other income for the nine months ended September 30, 2018, compared to $0.1 million for the nine months ended September 30, 2017. This was due to increased interest income earned on our cash and cash equivalents.

Liquidity and capital resources

From our inception through September 30, 2018, we have incurred significant operating losses. We have generated limited revenue to date from a research collaboration agreement with Allergan, a development services agreement with Allergan, and research and development grants from the U.S. government. There are no repayment or royalty obligations with respect to such grants.

On June 25, 2018, we completed an initial public offering, pursuant to which we issued and sold 7,359,998 shares of our common stock at a price of $16.00 per share, which included 959,999 shares sold pursuant to the exercise of the underwriters' option to purchase additional shares. We received $106.5 million of proceeds, net of underwriting discounts and commissions and other offering expenses.

As of September 30, 2018, we had cash and cash equivalents of $165.6 million. We invest our cash equivalents in liquid money market accounts.

Funding requirements

Our primary uses of capital are, and we expect will continue to be, research and development services, compensation and related expenses, laboratory and related supplies, legal and other regulatory expenses, patent prosecution filing and maintenance costs for our licensed intellectual property and general overhead costs. We expect to continue to incur significant expenses and operating losses for the foreseeable future. In addition, since the closing of our initial public offering, we have incurred, and expect to incur, additional costs associated with operating as a public company. We anticipate that our expenses will increase significantly in connection with our ongoing activities, as we:

- advance the clinical development of our lead product candidates;
- continue the research and development of our preclinical product candidates;
- seek to identify and develop additional product candidates;
- seek marketing approvals for any of our product candidates for which we successfully complete clinical development;
- develop and expand our sales, marketing, and distribution capabilities for our product candidates for which we obtain marketing approval;
- scale up our manufacturing processes and capabilities to support our ongoing preclinical activities and clinical studies of our product candidates and commercialization of any of our product candidates for which we obtain marketing approval;
- maintain, expand, and protect our intellectual property portfolio;
- expand our operational, financial, and management systems and increase personnel to support our clinical development, manufacturing and commercialization efforts; and
- increase our product liability and clinical trial insurance coverage as we initiate our clinical studies and commercialization efforts.

Outlook

Based on our research and development plans and our timing expectations related to the progress of our programs, we expect that our cash and cash equivalents as of September 30, 2018 will be sufficient to fund our operations for at least the next 12 months. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect.

We do not expect to generate revenue from product sales unless and until we successfully complete clinical development and obtain regulatory approval for a product candidate, which we expect will take a number of years and the outcome of which is uncertain, or enter into collaborative agreements with third parties, the timing of which is largely beyond our control and may never occur. We will continue to require additional capital to develop our product candidates and fund operations for the foreseeable future, which we may obtain through one or more equity offerings, debt financings, or other third-party funding, including potential strategic alliances and licensing or collaboration arrangements. We may, however, be unable to raise additional funds or enter into such other arrangements when needed on favorable terms or at all. Our failure to raise capital or enter into such other arrangements as and when needed would have a negative impact on our financial condition and our ability to develop our current product candidates, or any additional product candidates, if developed. The amount and timing of our future funding requirements will depend on many factors, including the pace and results of our preclinical and clinical development efforts. We cannot assure you that we will ever be profitable or generate positive cash flow from operating activities.

Cash flows

The following table summarizes our sources and uses of cash for each of the nine months ended September 30, 2018 and 2017 (in thousands):

	Nine months ended September 30,	
	2018	**2017**
Net cash provided by (used in):		
Operating activities	$ (32,465)	$ (24,336)
Investing activities	(391)	(1,338)
Financing activities	106,316	39,979
Net increase in cash, cash equivalents and restricted cash	$ 73,460	$ 14,305

Operating activities

During the nine months ended September 30, 2018, our cash used in operating activities was primarily due to our net loss of $39.2 million as we incurred increased external research and development costs with our clinical studies during the nine months ended September 30, 2018 and increased general and administrative costs, partially offset by non-cash charges of $2.3 million, consisting primarily of $2.0 million in stock-based compensation and $0.3 million in depreciation and amortization. Net cash provided by changes in our operating assets and liabilities consisted of a $1.0 million decrease in accounts receivable, prepaid expenses and other current assets, and accounts payable partially offset by a $4.0 million increase in accrued expenses.

During the nine months ended September 30, 2017, our cash used in operating activities was primarily due to our net loss of $24.8 million, partially offset by non-cash charges of $0.9 million, consisting primarily of $0.7 million in stock-based compensation and $0.2 million in depreciation and amortization. Net cash used in changes in our operating assets and liabilities consisted of a $1.5 million use of cash driven by increases in prepaid expenses and other current assets and accounts receivable, and decreases in accrued expenses and other current liabilities, partially offset by a $1.1 million increase in accounts payable and other liabilities.

Investing activities

Net cash used in investing activities was $0.4 million during the nine months ended September 30, 2018, consisting of purchases of property and equipment, primarily laboratory equipment and leasehold improvements.

Net cash used in investing activities was $1.3 million during the nine months ended September 30, 2017, consisting of purchases of property and equipment, primarily laboratory equipment and leasehold improvements.

Financing activities

Net cash provided by financing activities was $106.3 million during the nine months ended September 30, 2018, consisting of $109.5 million of IPO proceeds, net of underwriting discounts and commissions, offset by $3.0 million of offering costs related to our IPO and additional costs of $0.2 million related to our series B financing that closed in December 2017.

Net cash provided by financing activities was $40.0 million during the nine months ended September 30, 2017, consisting of gross proceeds of $40.0 million received from the issuance of Series A-2 convertible preferred stock.

Critical accounting policies and significant judgments and estimates

This discussion and analysis of our financial condition and results of operations is based on our financial statements, which we have prepared in accordance with United States generally accepted accounting principles. The preparation of our financial statements and related disclosures requires us to make estimates, assumptions and judgments that affect the

reported amount of assets, liabilities, revenue, costs and expenses, and related disclosures. Our critical accounting policies are described under the heading "Management's Discussion and Analysis of Financial Condition and Results of Operations — Critical Accounting Policies and Significant Judgments and Estimates" in our Prospectus, the notes to our audited financial statements appearing in the Prospectus and the notes to the financial statements appearing elsewhere in this Quarterly Report on Form 10-Q. There were no material changes to our critical accounting policies through September 30, 2018 from those discussed in our Prospectus.

Recent accounting pronouncements

See Note 2 to our condensed financial statements included elsewhere in this Quarterly Report on Form 10-Q.

Contractual obligations and other commitments

The following table summarizes our contractual obligations as of September 30, 2018 (in thousands):

	Payments due by period				
Contractual Obligations:	**Less than 1 year**	**1 to 3 years**	**3 to 5 years**	**More than 5 years**	**Total**
Operating leases(1)(2)	$ 824	$ 1,738	$ 831	$ —	$ 3,393
Total contractual obligations	$ 824	$ 1,738	$ 831	$ —	$ 3,393

(1) Operating leases include total future minimum rent payments under non-cancelable operating lease agreements.

(2) This includes the sublease agreement that we entered into on July 18, 2018 (see Note 10 to our condensed financial statements included elsewhere in this Quarterly Report on Form 10-Q).

We also enter into contracts in the normal course of business with contract research organizations for clinical studies, preclinical research studies and testing, manufacturing, and other services and products for operating purposes. These contracts generally are cancelable at any time by us, generally upon 30 days prior written notice. These payments are therefore not included in this table of contractual obligations. For a complete discussion of our contractual obligations, please refer to our Management's Discussion and Analysis of Financial Condition and Results of Operations in the Prospectus.

JOBS Act accounting election

Under Section 107(b) of the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, an "emerging growth company" can delay the adoption of new or revised accounting standards until such time as those standards would apply to private companies. We intend to rely on this exemption. There are other exemptions and reduced reporting requirements provided by the JOBS Act that we are currently evaluating. For example, as an "emerging growth company," we are exempt from Sections 14A(a) and (b) of the Exchange Act which would otherwise require us to (1) submit certain executive compensation matters to shareholder advisory votes, such as "say-on-pay," "say-on-frequency," and "golden parachutes;" and (2) disclose certain executive compensation related items such as the correlation between executive compensation and performance and comparisons of our chief executive officer's compensation to our median employee compensation. We also intend to rely on an exemption from the rule requiring us to provide an auditor's attestation report on our internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act. We will continue to remain an "emerging growth company" until the earliest of the following: (1) the last day of the fiscal year following the fifth anniversary of the date of the completion of our initial public offering; (2) the last day of the fiscal year in which our total annual gross revenue is equal to or more than $1.07 billion; (3) the date on which we have issued more than $1 billion in nonconvertible debt during the previous three years; or (4) the date on which we are deemed to be a large accelerated filer under the rules of the SEC.

Off-balance sheet arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined in the rules and regulations of the SEC.

Item 3. Quantitative and Qualitative Disclosures About Market Risk.

We are exposed to market risk related to changes in interest rates. As of September 30, 2018, we had cash and cash equivalents of $165.6 million, primarily comprised of money market mutual funds consisting of U.S. government-backed securities. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates. The primary objectives of our investment activities are to preserve principal, provide liquidity, and maximize income without significantly increasing risk. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, an immediate 100 basis point change in interest rates would not have a material effect on the fair market value of our portfolio.

We occasionally contract with vendors globally. We may be subject to fluctuations in foreign currency rates in connection with certain of these agreements. Transactions denominated in currencies other than the United States dollar are recorded based on exchange rates at the time such transactions arise. We have not engaged in the hedging of our foreign currency transactions to date. As of September 30, 2018, substantially all of our total liabilities were denominated in the United States dollar. We therefore believe that the risk of a significant impact on our operating income from foreign currency fluctuations is not substantial.

Inflation generally affects us by increasing our cost of labor. We do not believe that inflation had a material effect on our business, financial condition or results of operations during the nine months ended September 30, 2018 and September 30, 2017.

Item 4. Controls and Procedures.

The Company has established disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) designed to ensure that information required to be disclosed in the reports that the Company files or submits under the Securities Exchange Act of 1934, as amended, or Exchange Act, is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms and is accumulated and communicated to management, including the principal executive officer (our Chief Executive Officer) and principal financial officer (our Chief Financial Officer), to allow timely decisions regarding required disclosure. In addition, the design of disclosure controls and procedures must reflect the fact that there are resource constraints and that management is required to apply judgment in evaluating the benefits of possible controls and procedures relative to their costs.

Evaluation of disclosure controls and procedures

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, evaluated, as of the end of the period covered by this Quarterly Report on Form 10-Q, the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act). Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Our disclosure controls and procedures have been designed to provide reasonable assurance of achieving their objectives. Based on that evaluation, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) were effective at the reasonable assurance level as of September 30, 2018.

Changes in internal control over financial reporting

There were no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) that occurred during the three months ended September 30, 2018 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

PART II—OTHER INFORMATION

Item 1. Legal Proceedings.

From time to time, we may be involved in lawsuits, claims, investigations and proceedings, consisting of intellectual property, commercial, employment and other matters which arise in the ordinary course of business. While the outcome of any such proceedings cannot be predicted with certainty, as of September 30, 2018, we were not party to any legal proceedings that we would expect to have a material adverse impact on our financial position, results of operations or cash flow.

Item 1A. Risk Factors.

In evaluating the Company and our business, careful consideration should be given to the following risk factors, in addition to the other information set forth in this Quarterly Report on Form 10-Q and in other documents that we file with the SEC. Investing in our common stock involves a high degree of risk. If any of the following risks and uncertainties actually occurs, our business, prospects, financial condition or results of operations could be materially and adversely affected. The risks described below are not intended to be exhaustive and are not the only risks facing the Company. New risk factors can emerge from time to time, and it is not possible to predict the impact that any factor or combination of factors may have on our business, prospects, financial condition or results of operations.

Risks related to our business, financial position, and need for additional capital

We are a clinical-stage biopharmaceutical company with a very limited operating history and no products approved for commercial sale, which may make it difficult to evaluate our current business and predict our future success and viability.

We are a clinical-stage biopharmaceutical company with a limited operating history, focused on developing therapeutics for disorders of the brain and nervous system. We were incorporated in June 2015, have no products approved for commercial sale, and have not generated any revenue from product sales. Our operations to date have been limited primarily to organizing and staffing our company, raising capital, and conducting research and development activities for our product candidates.

To date, we have not obtained marketing approval for any product candidates, manufactured, on our own or through a third party, a commercial scale product, or conducted sales and marketing activities necessary for successful product commercialization. Our short operating history as a company makes any assessment of our future success and viability subject to significant uncertainty. We will encounter risks and difficulties frequently experienced by early-stage biopharmaceutical companies in rapidly evolving fields, and we have not yet demonstrated an ability to successfully overcome such risks and difficulties. If we do not address these risks and difficulties successfully, our business will suffer.

We have incurred significant operating losses since our inception and anticipate we will incur continued losses for the foreseeable future.

We have funded our operations to date through proceeds from collaborations, grants, sales of convertible preferred stock and our initial public offering. From our inception through September 30, 2018, we have received net proceeds of $267.6 million from such transactions. As of September 30, 2018, our cash and cash equivalents were $165.6 million. We have incurred net losses in each year since our inception, and we have an accumulated deficit of $91.4 million as of September 30, 2018.

Substantially all of our operating losses have resulted from costs incurred in connection with general and administrative costs associated with our operations, and our research and development programs, including for our preclinical and clinical product candidates and our discovery platform. We expect to incur increasing levels of operating losses over the next several years and for the foreseeable future. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' equity (deficit) and working capital. We expect our research and development expenses to significantly increase in connection with our clinical studies of our product candidates. In

addition, if we obtain marketing approval for our product candidates, we will incur significant sales and marketing, legal, and outsourced-manufacturing expenses. In addition, we will incur additional costs associated with operating as a public company. As a result, we expect to continue to incur significant and increasing operating losses for the foreseeable future. Because of the numerous risks and uncertainties associated with developing pharmaceutical products, we are unable to predict the extent of any future losses or when we will become profitable, if at all. Even if we do become profitable, we may not be able to sustain or increase our profitability on a quarterly or annual basis.

Drug development is a highly uncertain undertaking and involves a substantial degree of risk. We have never generated any revenue from product sales, and we may never generate revenue or be profitable.

Our ability to become profitable depends upon the ability of our product candidates to generate revenue. To date, we have not generated any revenue from our product candidates and we do not know when, or if, we will do so. We do not expect to generate significant revenue unless and until we obtain marketing approval of, and begin to sell, our current or future product candidates. Our ability to generate revenue depends on a number of factors, including, but not limited to:

- successfully completing preclinical and clinical development of our product candidates;
- identifying, assessing, and/or developing new product candidates from our discovery platform;
- developing a sustainable and scalable manufacturing process for our product candidates, as well as establishing and maintaining commercially viable supply relationships with third parties that can provide adequate products and services to support clinical activities and commercial demand for our product candidates;
- negotiating favorable terms in any collaboration, licensing, or other arrangements into which we may enter;
- obtaining regulatory approvals and marketing authorizations for product candidates for which we successfully complete clinical development;
- launching and successfully commercializing product candidates for which we obtain regulatory and marketing approval, either by establishing a sales, marketing, and distribution infrastructure or collaborating with a partner;
- negotiating and maintaining an adequate price for our product candidates, both in the United States and in foreign countries where our products are commercialized;
- obtaining market acceptance of our product candidates as viable treatment options;
- building out new facilities or expanding existing facilities to support our ongoing development activity;
- addressing any competing technological and market developments;
- maintaining, protecting, expanding, and enforcing our portfolio of intellectual property rights, including patents, trade secrets, and know-how; and
- attracting, hiring, and retaining qualified personnel.

Because of the numerous risks and uncertainties associated with drug development, we are unable to predict the timing or amount of our expenses, or when we will be able to generate any meaningful revenue or achieve or maintain profitability, if ever. In addition, our expenses could increase beyond our current expectations if we are required by the FDA, or foreign regulatory agencies, to perform studies in addition to those that we currently anticipate, or if there are any delays in any of our or our future collaborators' clinical studies or the development of any of our product candidates. Even if one or more of our product candidates is approved for commercial sale, absent our entering into a collaboration or partnership agreement, we anticipate incurring significant costs associated with commercializing any approved product candidate and ongoing compliance efforts.

Even if we are able to generate revenue from the sale of any approved products, we may not become profitable and may need to obtain additional funding to continue operations. Revenue from the sale of any product candidate for which regulatory approval is obtained will be dependent, in part, upon the size of the markets in the territories for which we gain regulatory approval, the accepted price for the product, the ability to get reimbursement at any price, and whether we own the commercial rights for that territory. The precise number of people with painful DPN, fibromyalgia, PTSD, and Parkinson's disease cognitive impairment is unknown. 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 drug candidates, are based on estimates. If the number of addressable patients is not as significant as we anticipate, the indication approved by regulatory authorities is narrower than we expect, or the reasonably accepted population for

treatment is narrowed by competition, physician choice, or treatment guidelines, we may not generate significant revenue from sales of our product candidates, even if approved. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis.

Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our pipeline of product candidates, or continue our operations and cause a decline in the value of our common stock, all or any of which may adversely affect our viability.

Due to the significant resources required for the development of our discovery platform and pipeline, and depending on our ability to access capital, we must prioritize development of certain product candidates. Moreover, we may fail to expend our limited resources on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

We currently have three lead product candidates, NYX-2925, NYX-783, and NYX-458, which are at various stages of clinical development. We seek to maintain a process of prioritization and resource allocation to maintain an optimal balance between aggressively advancing product candidates and ensuring replenishment of our portfolio.

In July 2015, we entered into a research collaboration agreement with Allergan, pursuant to which we and Allergan have research, development, and commercial rights to compounds discovered using our discovery platform. Under the research collaboration, both we and Allergan have the right, exercisable during a specified period, to select an eligible compound for further investigation. Due to the terms of the collaboration agreement, we may not have the opportunity to select a desired eligible compound. We may also choose not to select an eligible compound based on the preliminary information available to us. As a result of such incomplete information or incorrect analysis by us, we may select an eligible compound that later proves to have less commercial potential than an alternative or none at all.

Due to the significant resources required for the development of our product candidates, we must focus on specific diseases and disease pathways and decide which product candidates to pursue and advance and the amount of resources to allocate to each. Our decisions concerning the allocation of research, development, collaboration, management, and financial resources toward particular product candidates or therapeutic areas may not lead to the development of any viable commercial product and may divert resources away from better opportunities. If we make incorrect determinations regarding the viability or market potential of any of our product candidates or misread trends in the biopharmaceutical industry, in particular for disorders of the brain and nervous system, our business, financial condition, and results of operations could be materially adversely affected. As a result, we may fail to capitalize on viable commercial products or profitable market opportunities, be required to forego or delay pursuit of opportunities with other product candidates or other diseases and disease pathways that may later prove to have greater commercial potential than those we choose to pursue, or relinquish valuable rights to such product candidates through collaboration, licensing, or other royalty arrangements in cases in which it would have been advantageous for us to invest additional resources to retain sole development and commercialization rights.

We will need to raise additional funding to advance NYX-2925 through Phase 3 clinical studies, which funding may not be available on acceptable terms, or 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.

As of September 30, 2018, our cash and cash equivalents were $165.6 million. Based on our current plans, we expect that our existing cash and cash equivalents will be sufficient to fund our operations through the first half of 2020. We will require additional funding to advance NYX-2925 through Phase 3 clinical studies. Our ability to secure this additional funding may be adversely impacted by negative or ambiguous results in our Phase 2 clinical development of NYX-2925, our Phase 1 clinical development of NYX-783, or our Phase 1 study of NYX-458.

We are currently advancing our product candidates through clinical development, with one product candidate in Phase 2 clinical development, two product candidates in Phase 1 clinical development, and several other potential product candidates in early-stage discovery and screening. The clinical development of a product candidate is lengthy, complicated, and expensive. In particular, conducting a Phase 3 clinical study is a complex process that differs from

clinical studies conducted in earlier phases. While some of our employees have conducted Phase 3 clinical studies in the past while employed at different companies, we, as a company, have not conducted Phase 3 clinical studies before, and as a result, may require more time and incur greater costs than we anticipated. Moreover, developing small-molecule products is expensive, and we expect our discovery, research, and development expenses to increase substantially in connection with our ongoing activities, particularly as we advance our product candidates in clinical studies. We may also need to raise additional funds sooner if we choose to pursue additional indications and/or geographies for our product candidates or otherwise expand more rapidly than we presently anticipate.

In addition, 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. In any event, we will require additional capital to obtain regulatory approval for, and, if approved, to commercialize our product candidates. Raising funds in the current economic environment may present additional challenges. Even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital if market conditions are favorable or if we have specific strategic considerations.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and, if approved, commercialize our product candidates. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Moreover, the terms of any financing may adversely affect the holdings or the rights of our stockholders and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our shares to decline. The sale of additional equity or convertible securities would dilute all of our stockholders. The incurrence of indebtedness would result in increased fixed payment obligations and we may be required to agree to certain restrictive covenants, such as 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 collaborative partners or otherwise at an earlier stage than otherwise would be desirable and we may be required to relinquish rights to some of our technologies or product candidate or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, operating results, and prospects.

If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay, or discontinue one or more of our research or development programs or the commercialization of any product candidate or be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition, and results of operations.

Risks related to product development and commercialization

Research and development of biopharmaceutical products is inherently risky.

We are at an early stage of development of the product candidates currently in our pipeline and are continuing to discover additional potential product candidates leveraging our discovery platform. To date, we have devoted substantially all of our efforts and financial resources to identify, secure intellectual property for, and develop our discovery platform and our product candidates, including conducting multiple preclinical and clinical studies, and providing general and administrative support for these operations. Our business depends heavily on the successful preclinical and clinical development, regulatory approval, and commercialization of our lead product candidates, NYX-2925 which is in Phase 2 clinical development, NYX-783, which has been evaluated in a Phase 1 clinical study, and NYX-458, which is in Phase 1 clinical development. None of our product candidates have advanced into late-stage development or a pivotal clinical study and it may be years before any such study is initiated, if at all. NYX-2925, NYX-783, and NYX-458 will require substantial additional clinical development, testing, and regulatory approval before we are permitted to commence their commercialization. Further, we cannot be certain that any of our product candidates will be successful in clinical studies.

Our future success is dependent on our ability to successfully develop, obtain regulatory approval for, and then successfully commercialize our product candidates, and we may fail to do so for many reasons, including the following:

- our product candidates may not successfully complete preclinical or clinical studies;
- a product candidate may, upon further study, be shown to have harmful side effects or other characteristics that indicate it is unlikely to be effective or otherwise does not meet applicable regulatory criteria;
- our competitors may develop therapeutics that render our product candidates obsolete or less attractive;
- our competitors may develop platform technologies that render our platform technology obsolete or less attractive;
- the product candidates that we develop and our discovery platform may not be sufficiently covered by intellectual property for which we hold exclusive rights;
- the market for a product candidate may change so that the continued development of that product candidate is no longer reasonable or commercially attractive;
- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all;
- we may not be able to establish manufacturing capabilities or arrangements with third-party manufacturers for clinical and, if approved, commercial study;
- even if a product candidate obtains regulatory approval, we may be unable to establish sales and marketing capabilities, or successfully market such approved product candidate, to gain market acceptance; and
- a product candidate may not be accepted as safe or effective by patients, the medical community or third-party payors, if applicable.

If any of these events occur, we may be forced to abandon our development efforts for a product candidate or candidates, which would have a material adverse effect on our business and could potentially cause us to cease operations. For instance, if we observe harmful side effects or other characteristics that indicate one product candidate is unlikely to be effective or otherwise does not meet applicable regulatory criteria, these findings may implicate the discovery platform as a whole.

We may not be successful in our efforts to further develop our discovery platform technology and current product candidates. We are not permitted to market or promote any of our product candidates before we receive regulatory approval from the FDA or comparable foreign regulatory authorities, and we may never receive such regulatory approval for any of our product candidates. Each of our product candidates is in the early stages of development and will require significant additional clinical development, management of preclinical, clinical, and manufacturing activities, regulatory approval, adequate manufacturing supply, a commercial organization, and significant marketing efforts before we generate any revenue from product sales, if at all.

The nonclinical and clinical studies for our product candidates are, and the manufacturing and marketing of our product candidates will be, subject to extensive and rigorous review and regulation by numerous government authorities in the United States, and in other countries where we intend to test and, if approved, market any product candidate. Before obtaining regulatory approvals for the commercial sale of any product candidate, we must, among other requirements, demonstrate through preclinical studies and clinical studies that the product candidate is safe and effective for use in each target indication. Drug development is a long, expensive, and uncertain process, and delay or failure can occur at any stage of any of our clinical studies. This process can take many years and may include post-marketing studies and surveillance, which will require the expenditure of substantial resources. Of the large number of drugs in development in the United States, only a small percentage will successfully complete the FDA regulatory approval process and will be commercialized. Accordingly, even if we are able to obtain the requisite financing to continue to fund our development and preclinical studies and clinical studies, we cannot assure you that any of our product candidates will be successfully developed or commercialized.

If any of our product candidates successfully complete clinical studies, we generally plan to seek regulatory approval to market our product candidates in the United States, the European Union, or EU, and in additional foreign countries where we believe there is a viable commercial opportunity and significant patient need. We have never commenced, compiled, or submitted an application seeking regulatory approval to market any product candidate. We may never

receive regulatory approval to market any product candidates even if such product candidates successfully complete clinical studies, which would adversely affect our viability. To obtain regulatory approval in countries outside the United States, we must comply with numerous and varying regulatory requirements of such other countries regarding safety, efficacy, chemistry, manufacturing and controls, clinical studies, commercial sales, pricing, and distribution of our product candidates. We may also rely on collaborators or partners to conduct the required activities to support an application for regulatory approval, and to seek approval, for one or more of our product candidates. We cannot be sure that any collaborators or partners will conduct these activities or do so within the timeframe we desire. Even if we (or any collaborators or partners) are successful in obtaining approval in one jurisdiction, we cannot ensure that we will obtain approval in any other jurisdictions. If we are unable to obtain approval for our product candidates in multiple jurisdictions, our revenue and results of operations could be negatively affected.

Even if we receive regulatory approval to market any of our product candidates, we cannot assure you that any such product candidate will be successfully commercialized, widely accepted in the marketplace, or more effective than other commercially available alternatives.

Investment in biopharmaceutical product development involves significant risk that any product candidate will fail to demonstrate adequate efficacy or an acceptable safety profile, gain regulatory approval, and become commercially viable. We cannot provide any assurance that we will be able to successfully advance any of our product candidates through the development process or, if approved, successfully commercialize any of our product candidates.

We may not be successful in our efforts to continue to create a pipeline of product candidates or to develop commercially successful products. If we fail to successfully identify and develop additional product candidates, our commercial opportunity may be limited.

One of our strategies is to identify and pursue clinical development of additional product candidates. We currently have several compounds in the research, discovery, screening, and preclinical stages of development. Identifying, developing, obtaining regulatory approval, and commercializing additional product candidates for the treatment of disorders of the brain and nervous system will require substantial additional funding and is prone to the risks of failure inherent in drug development. We cannot provide you any assurance that we will be able to successfully identify or acquire additional product candidates, advance any of these additional product candidates through the development process, successfully commercialize any such additional product candidates, if approved, or assemble sufficient resources to identify, acquire, develop or, if approved, commercialize additional product candidates. If we are unable to successfully identify, acquire, develop, and commercialize additional product candidates, our commercial opportunity may be limited.

We may not be able to conduct, or contract others to conduct, animal testing in the future, which could harm our research and development activities.

Certain laws and regulations relating to drug development require us to test our product candidates on animals before initiating clinical studies involving humans. Animal testing activities have been the subject of controversy and adverse publicity. Animal rights groups and other organizations and individuals have attempted to stop animal testing activities by pressing for legislation and regulation in these areas and by disrupting these activities through protests and other means. To the extent the activities of these groups are successful, our research and development activities may be interrupted or delayed.

We have concentrated our research and development efforts on the treatment of disorders of the brain and nervous system, a field that has seen limited success in drug development. Further, our product candidates are based on new approaches and novel technology, which makes it difficult to predict the time and cost of product candidate development and subsequently obtaining regulatory approval.

We have focused our research and development efforts on addressing disorders of the brain and nervous system, including painful DPN, PTSD, and Parkinson's disease cognitive impairment. Efforts by biopharmaceutical companies in the field of disorders of the brain and nervous system have seen limited successes in drug development. There are few effective therapeutic options available for patients with painful DPN, PTSD, or Parkinson's disease cognitive impairment. Our future success is highly dependent on the successful development of our discovery platform technology

and our product candidates for treating disorders of the brain and nervous system. Developing and, if approved, commercializing our product candidates for treatment of disorders of the brain and nervous system subjects us to a number of challenges, including engineering product candidates and obtaining regulatory approval from the FDA and other regulatory authorities who have only a limited set of precedents to rely on.

Our approach to targeting the NMDAr is different from other antagonist and agonist agents currently being developed. Our proprietary compounds are designed to subtly modulate NMDArs. This strategy may not prove to be successful. We cannot be sure that our approach will yield satisfactory therapeutic products that are safe and effective, scalable, or profitable.

Moreover, public perception of drug safety issues, including adoption of new therapeutics or novel approaches to treatment, may adversely influence the willingness of subjects to participate in clinical studies, or if approved, of physicians to prescribe our products.

We may encounter difficulties in enrolling subjects in our clinical studies, thereby delaying or preventing development of our product candidates.

There is no precise method of establishing the actual number of people with disorders of the brain and nervous system in any geography over any time period. We estimate that neuropathic pain affects approximately 18 million people in the United States, and approximately 5.5 million of those suffer from painful DPN. It is estimated that over 8.5 million people suffer from PTSD. If the actual number of people with disorders of the brain and nervous system is lower than we believe, we may experience difficulty in enrolling subjects in our clinical studies, thereby delaying development of our product candidates. Furthermore, we may experience difficulties in subject enrollment in our clinical studies for a variety of other reasons, including:

- the subject eligibility criteria defined in the protocol, including biomarker-driven identification and/or certain highly-specific criteria related to stage of disease progression, which may limit the patient populations eligible for our clinical studies to a greater extent than competing clinical studies for the same indication that do not have biomarker-driven patient eligibility criteria;
- eligibility requirements mandated by regulatory agencies which may limit the number of eligible patients in a given disorder;
- the size of the study population required for analysis of the study's primary endpoints;
- the proximity of subjects to a study site;
- the design of the study;
- our use of academic sites, which are less accustomed to running clinical studies and managing enrollment;
- public perception of drug safety issues;
- our ability to recruit clinical study investigators with the appropriate competencies and experience;
- competing clinical studies for similar therapies or targeting patient populations meeting our patient eligibility criteria;
- clinicians' and patients' perceptions as to the potential advantages and side effects of the product candidate being studied in relation to other available therapies and product candidates;
- our ability to obtain and maintain patient consents; and
- the risk that subjects enrolled in clinical studies will not complete such studies, for any reason.

For instance, we have experienced and may continue to experience slower than what may be considered typical durations for subject enrollment as a result of our strict enrollment criteria in our painful DPN and fibromyalgia studies. If we are unable to successfully enroll subjects in a timely way for the clinical studies for our product candidates, our clinical studies could be significantly delayed, which could materially affect our financial condition and results of operations.

Our clinical studies may fail to demonstrate adequate safety and efficacy of our product candidates, which would prevent, delay, or limit the scope of regulatory approval and commercialization.

Before obtaining regulatory approvals for the commercial sale of any of our product candidates, we must, among other requirements, demonstrate through lengthy, complex, and expensive preclinical studies and clinical studies that our product candidates are both safe and effective for use in each target indication. Each product candidate must demonstrate an adequate risk versus benefit profile in its intended patient population and for its intended use.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical study process. The results of preclinical studies of our product candidates may not be predictive of the results of early-stage or later-stage clinical studies, and results of early-stage clinical studies of our product candidates may not be predictive of the results of later-stage clinical studies. The results of clinical studies in one set of subject or disease indications may not be predictive of those obtained in another. In some instances, there can be significant variability in safety or efficacy results between different clinical studies of the same product candidate due to numerous factors, including changes in study procedures set forth in protocols, differences in the size and type of the patient populations, changes in and lack of adherence to the dosing regimen and other clinical study protocols, and the rate of dropout among clinical study participants. Product candidates in later stages of clinical studies may fail to show the desired safety and efficacy profile despite having progressed through preclinical studies and initial clinical studies. A number of companies in the biopharmaceutical industry have suffered significant setbacks in later-stage clinical studies due to lack of efficacy or safety issues, notwithstanding promising results in early-stage studies. This is particularly true in disorders of the brain and nervous system, where failure rates historically have been higher than in other disease areas. Most product candidates that begin clinical studies are never approved by regulatory authorities for commercialization.

We have limited experience in designing clinical studies and may be unable to design and execute a clinical study to support marketing approval. We cannot be certain that our current clinical studies or any other future clinical studies will be successful. Additionally, any safety concerns observed in any one of our clinical studies in our targeted indications could limit the prospects for regulatory approval of our product candidates in those, and other indications, which could have a material adverse effect on our business, financial condition, and results of operations.

In addition, even if such clinical studies are successfully completed, we cannot guarantee that the FDA or foreign regulatory authorities will interpret the results as we do, and more studies could be required before we submit our product candidates for approval. To the extent that the results of the studies are not satisfactory to the FDA or foreign regulatory authorities for support of a marketing application, we may be required to expend significant resources, which may not be available to us, to conduct additional studies in support of potential approval of our product candidates. Even if regulatory approval is secured for any of our product candidates, the terms of such approval may limit the scope and use of our product candidates, which may also limit their commercial potential.

Our product candidates may cause serious adverse events or other undesirable side effects that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any.

Serious adverse events or other undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay, or halt clinical studies, and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other regulatory authorities.

Further, clinical studies by their nature utilize a sample of the potential patient population for a limited duration of exposure. Rare and severe side effects of a product candidate may only be uncovered with a significantly larger number of patients exposed to the product candidate. If our product candidates receive marketing approval and we or others identify undesirable side effects caused by such product candidates (or any other similar products) after such approval, a number of potentially significant negative consequences could result, including:

- regulatory authorities may suspend, withdraw, or limit their approval of such products;
- regulatory authorities may require the addition of labeling statements, such as a "boxed" warning or a contraindication;

- we may be required to change the way such products are distributed or administered;
- we may be required to conduct additional post-marketing studies and surveillance;
- we may be required to implement a risk evaluation and mitigation strategy, or REMS, or create a medication guide outlining the risks of such side effects for distribution to patients;
- we may be subject to regulatory investigations and government enforcement actions;
- subjects in a clinical study may experience severe or unexpected drug-related side effects;
- we may decide, or regulatory authorities may require us, to conduct additional clinical studies or abandon product development programs;
- we may decide to remove such products from the marketplace;
- we could be sued and held liable for injury caused to individuals exposed to or taking our products;
- the product may become less competitive; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the affected product candidates, could substantially increase the costs of commercializing our product candidates, and could significantly impact our ability to successfully commercialize our product candidates and generate revenues.

Failures or delays in the commencement or completion of, or ambiguous or negative results from, our ongoing or planned clinical studies of our product candidates could result in increased costs to us and could delay, prevent, or limit our ability to generate revenue and continue our business.

We do not know whether any of our ongoing or planned clinical studies will begin or be completed on schedule, if at all, as the commencement and completion of clinical studies can be delayed or prevented for a number of reasons, including, among others:

- the FDA or other regulatory bodies may not authorize us or our investigators to commence our planned clinical studies or any other clinical studies we may initiate, or may suspend our clinical studies, for example, through imposition of a clinical hold;
- delays in filing or receiving clearance of additional INDs that may be required;
- lack of adequate funding to continue our clinical studies and preclinical studies;
- negative results from our ongoing preclinical studies;
- delays in reaching or failing to reach agreement on acceptable terms with CROs, and clinical study sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and study sites;
- inadequate quantity or quality of a product candidate or other materials necessary to conduct clinical studies, for example delays in the manufacturing of sufficient supply of finished drug product;
- difficulties obtaining ethics committee or Institutional Review Board, or IRB, approval to conduct a clinical study at a prospective site or sites;
- challenges in recruiting and enrolling subjects to participate in clinical studies, the proximity of subjects to study sites, eligibility criteria for the clinical study, the nature of the clinical study protocol, the availability of approved effective treatments for the relevant disease, and competition from other clinical study programs for similar indications;
- severe or unexpected drug-related side effects experienced by subjects in a clinical study;
- we may decide, or regulatory authorities may require us, to conduct additional clinical studies or abandon product development programs;
- delays in validating, or inability to validate, any endpoints utilized in a clinical study;
- the FDA may disagree with our clinical study design and our interpretation of data from clinical studies, or may change the requirements for approval even after it has reviewed and commented on the design for our clinical studies;
- reports from preclinical or clinical testing of other NMDAr-dependent therapies that raise safety or efficacy concerns; and
- difficulties retaining subjects who have enrolled in a clinical study but may be prone to withdraw due to rigors of the clinical studies, lack of efficacy, side effects, personal issues, or loss of interest.

Clinical studies may also be delayed or terminated as a result of ambiguous or negative interim results. In addition, a clinical study may be suspended or terminated by us, the FDA, the IRBs at the sites where the IRBs are overseeing a clinical study, a data and safety monitoring board, or DSMB, overseeing the clinical study at issue or other regulatory authorities due to a number of factors, including, among others:

- failure to conduct the clinical study in accordance with regulatory requirements or our clinical protocols;
- inspection of the clinical study operations or study sites by the FDA or other regulatory authorities that reveals deficiencies or violations that require us to undertake corrective action, including in response to the imposition of a clinical hold;
- unforeseen safety issues, including any that could be identified in our ongoing preclinical or clinical studies, adverse side effects or lack of effectiveness;
- changes in government regulations or administrative actions;
- problems with clinical supply materials; and
- lack of adequate funding to continue clinical studies.

Changes in regulatory requirements, FDA guidance, or unanticipated events during our nonclinical studies and clinical studies of our product candidates may occur, which may result in changes to nonclinical or clinical study protocols or additional nonclinical or clinical study requirements, which could result in increased costs to us and could delay our development timeline.

Changes in regulatory requirements, FDA guidance, or unanticipated events during our nonclinical studies and clinical studies may force us to amend nonclinical studies and clinical study protocols or the FDA may impose additional nonclinical studies and clinical study requirements. Amendments or changes to our clinical study protocols would require resubmission to the FDA and IRBs for review and approval, which may adversely impact the cost, timing, or successful completion of clinical studies. Similarly, amendments to our nonclinical studies may adversely impact the cost, timing, or successful completion of those nonclinical studies. If we experience delays completing, or if we terminate, any of our nonclinical studies or clinical studies, or if we are required to conduct additional nonclinical or clinical studies, the commercial prospects for our product candidates may be harmed and our ability to generate product revenue will be delayed.

If, in the future, we are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell and market any product candidates we may develop, we may not be successful in commercializing those product candidates if and when they are approved.

We do not currently have an infrastructure for the sales, marketing, and distribution of pharmaceutical products. In order to market our product candidates, if approved by the FDA or any other regulatory body, we must build our sales, marketing, managerial, and other non-technical capabilities, or make arrangements with third parties to perform these services. There are risks involved with both establishing our own commercial capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force or reimbursement specialists is expensive and time-consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing and other commercialization capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our commercialization personnel.

If we enter into arrangements with third parties to perform sales, marketing, commercial support, and distribution services, our product revenue or the profitability of product revenue may be lower than if we were to market and sell any products we may develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to commercialize our product candidates or may be unable to do so on terms that are favorable to us. We may have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish commercialization capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates if approved.

If we are unable to establish adequate sales, marketing, and distribution capabilities, whether independently or with third parties, or if we are unable to do so on commercially reasonable terms, our business, results of operations, financial condition, and prospects will be materially adversely affected.

Even if we receive marketing approval for our product candidates, our product candidates may not achieve broad market acceptance by physicians, patients, healthcare payors, or others in the medical community, which would limit the revenue that we generate from their sales.

The commercial success of our product candidates, if approved by the FDA or other applicable regulatory authorities, will depend upon the awareness and acceptance of our product candidates among the medical community, including physicians, patients, and healthcare payors. If any of our product candidates are approved but do not achieve an adequate level of acceptance by physicians, patients, healthcare payors, and others in the medical community, we may not generate sufficient revenue to become or remain profitable. Market acceptance of our product candidates, if approved, will depend on a number of factors, including, among others:

- the safety, efficacy, and other potential advantages of our approved product candidates compared to other available therapies;
- limitations or warnings contained in the labeling approved for our product candidates by the FDA or other applicable regulatory authorities;
- any restrictions on the use of our products together with other medications;
- the prevalence and severity of any adverse effects associated with our product candidates;
- inability of certain types of patients to take our products;
- the clinical indications for which our product candidates are approved;
- availability of alternative treatments already approved or expected to be commercially launched in the near future;
- the potential and perceived advantages of our approved product candidates over current treatment options or alternative treatments, including future alternative treatments;
- the size of the target patient population, and the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support and timing of market introduction of competitive products;
- publicity concerning our products or competing products and treatments;
- pricing and cost effectiveness;
- the effectiveness of our sales and marketing strategies;
- our ability to increase awareness of our product candidates through sales and marketing efforts;
- our ability to obtain sufficient third-party payor coverage or reimbursement; or
- the willingness of patients to pay out-of-pocket in the absence of third-party payor coverage.

If our product candidates are approved but do not achieve an adequate level of acceptance by patients, physicians, and payors, we may not generate sufficient revenue from our product candidates to become or remain profitable. Before granting reimbursement approval, healthcare payors may require us to demonstrate that our product candidates, in addition to treating these target indications, also provide incremental health benefits to patients. Our efforts to educate the medical community and third-party payors about the benefits of our product candidates may require significant resources and may never be successful.

Even if we obtain regulatory approval for our product candidates, our products will remain subject to extensive regulatory scrutiny.

Even if we receive marketing approval for our product candidates, regulatory authorities may still impose significant restrictions on our product candidates, indicated uses or marketing, or impose ongoing requirements for potentially costly post-approval studies. If any of our product candidates are approved, they will be subject to ongoing regulatory requirements, including for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping, conduct of post-marketing studies, and submission of safety, efficacy, and other post-marketing information,

including both federal and state requirements in the United States and requirements of comparable foreign regulatory authorities.

Manufacturers and manufacturers' facilities are required to comply with extensive requirements imposed by the FDA and comparable foreign regulatory authorities, including, for example, ensuring that quality control and manufacturing procedures conform to current Good Manufacturing Practice, or cGMP, regulations. As such, we and our contract manufacturers will be subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made in any new drug application, or NDA, or comparable marketing approval. Accordingly, we and others with whom we work must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production, and quality control.

The FDA has significant post-marketing authority, including, for example, the authority to require labeling changes based on new safety information and to require post-marketing studies or clinical studies to evaluate serious safety risks related to the use of a drug. The FDA also has the authority to require, as part of an NDA or post-approval, the submission of a REMS. Many chronic pain therapies have been recognized as drugs of abuse and require REMS. While NYX-2925 has been well tolerated in clinical studies to date and has shown low abuse potential in preclinical drug discrimination and abuse liability studies, the FDA may still determine that NYX-2925 requires a REMS program. Any REMS required by the FDA may lead to increased costs to assure compliance with new post-approval regulatory requirements and potential requirements or restrictions on the sale of approved products, all of which could lead to lower sales volume and revenue.

Any regulatory approvals that we receive for our product candidates will be subject to limitations on the approved indicated uses for which the product may be marketed and promoted or to the conditions of approval (including the requirement to implement a REMS), or contain requirements for potentially costly post-marketing testing. We will be required to report certain adverse reactions and production problems, if any, to the FDA and comparable foreign regulatory authorities. Any new legislation addressing drug safety issues could result in delays in product development or commercialization, or increased costs to assure compliance. The FDA and other agencies, including the U.S. Department of Justice, closely regulate and monitor the post-approval marketing and promotion of products to ensure that they are manufactured, marketed, and distributed only for the approved indications and in accordance with the provisions of the approved labeling. We will have to comply with requirements concerning advertising and promotion for our products. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved label. As such, we may not promote our products for indications or uses for which they do not have approval. The holder of an approved NDA or comparable marketing approval must submit new or supplemental applications and obtain approval for certain changes to the approved product, product labeling, or manufacturing process. We could also be asked to conduct post-marketing studies or clinical studies to verify the safety and efficacy of our products in general or in specific patient subsets.

If a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, or disagrees with the promotion, marketing or labeling of a product, such regulatory agency may impose restrictions on that product or us, including requiring withdrawal of the product from the market. If we fail to comply with applicable regulatory requirements, a regulatory agency or enforcement authority may, among other things:

- issue warning or untitled letters that would result in adverse publicity;
- impose civil or criminal penalties;
- suspend or withdraw regulatory approvals;
- suspend any of our ongoing clinical studies;
- refuse to approve pending applications or supplements to approved applications submitted by us;
- impose restrictions on our operations, including closing our contract manufacturers’ facilities;
- seize or detain products; or
- request that we initiate a product recall.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response, and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may

significantly and adversely affect our ability to commercialize and generate revenue from our products. If regulatory sanctions are applied or if regulatory approval is withdrawn, the value of our company and our operating results will be adversely affected.

We face significant competition in an environment of rapid technological and scientific change, and there is a possibility that our competitors may achieve regulatory approval before us or develop therapies that are safer, more advanced, or more effective than ours, which may negatively impact our ability to successfully market or commercialize any product candidates we may develop and ultimately harm our financial condition.

The development and commercialization of new drug products is highly competitive. Moreover, treating brain and nervous system disorders is characterized by strong and increasing competition, with a strong emphasis on intellectual property. We may face competition with respect to any product candidates that we seek to develop or commercialize in the future from major pharmaceutical companies, specialty pharmaceutical companies, and biotechnology companies worldwide. Potential competitors also include academic institutions, government agencies, and other public and private research organizations that conduct research, seek patent protection, and establish collaborative arrangements for research, development, manufacturing, and commercialization.

Companies that we are aware are developing or commercializing NMDAr-targeted therapies include companies with significant financial and/or scientific resources, such as Adamas Pharmaceuticals Inc., Allergan plc, AmKor Pharma, Inc., Avanir Pharmaceuticals Inc., Axsome Therapeutics, Inc., Biohaven Pharmaceutical Holding Co. Ltd., Cadent Therapeutics, Inc., Cerecor Inc., Eli Lilly and Company, Genentech Inc., Immune Pharmaceuticals Inc., Intra-Cellular Therapies, Inc., Janssen Pharmaceuticals, Inc., NeuroRx, Inc., NeuroOp, Inc., Newron Pharmaceuticals S.p.A., Osmotica Pharmaceuticals US LLC, Otonomy, Inc., Relmada Therapeutics, Inc., Sage Therapeutics, Inc., UCB S.A., and Vistagen Therapeutics, Inc.

Many of our current or potential competitors, either alone or with their strategic partners, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical studies, obtaining regulatory approvals, and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical study sites and patient registration for clinical studies, as well as in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products 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. Furthermore, currently approved products could be discovered to have application for treatment of disorders of the brain and nervous system indications, which could give such products significant regulatory and market timing advantages over any of our product candidates. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours and may obtain orphan product exclusivity from the FDA for indications our product candidates are targeting, which could result in our competitors establishing a strong market position before we are able to enter the market. Additionally, products or technologies developed by our competitors may render our potential product candidates uneconomical or obsolete, and we may not be successful in marketing any product candidates we may develop against competitors.

In addition, we could face litigation or other proceedings with respect to the scope, ownership, validity and/or enforceability of our patents relating to our competitors' products and our competitors may allege that our products infringe, misappropriate, or otherwise violate their intellectual property. The availability of our competitors' products could limit the demand, and the price we are able to charge, for any products that we may develop and commercialize. See "Risks related to our intellectual property rights."

Even if we receive marketing approval for our product candidates in the United States, we may never receive regulatory approval to market our product candidates outside of the United States.

In order to market any product outside of the United States, we must establish and comply with the numerous and varying safety, efficacy, and other regulatory requirements of other countries. Approval procedures vary among countries and can involve additional product candidate testing and additional administrative review periods. The time required to obtain approvals in other countries might differ from that required to obtain FDA approval. The marketing approval processes in other countries may implicate all of the risks detailed above regarding FDA approval in the United States as well as other risks. In particular, in many countries outside of the United States, products must receive pricing and reimbursement approval before the product can be commercialized. Obtaining this approval can result in substantial delays in bringing products to market in such countries. Marketing approval in one country does not ensure marketing approval in another, but a failure or delay in obtaining marketing approval in one country may have a negative effect on the regulatory process in others. Failure to obtain marketing approval in other countries or any delay or other setback in obtaining such approval would impair our ability to market our product candidates in such foreign markets. Any such impairment would reduce the size of our potential market, which could have a material adverse impact on our business, results of operations, and prospects.

Risks related to regulatory approval and other legal compliance matters

The regulatory approval processes of the FDA and comparable foreign regulatory authorities are lengthy, time-consuming, and inherently unpredictable. If we are ultimately unable to obtain regulatory approval for our product candidates, we will be unable to generate product revenue and our business will be substantially harmed.

The time required to obtain approval by the FDA and comparable foreign regulatory authorities is unpredictable, typically takes many years following the commencement of clinical studies, and depends upon numerous factors, including the type, complexity, and novelty of the product candidates involved. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions, which may cause delays in the approval or the decision not to approve an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. Moreover, the FDA or other regulatory authorities may fail to approve companion diagnostics that we contemplate using with our therapeutic product candidates. We have not submitted for, or obtained regulatory approval for any product candidate, and it is possible that none of our existing product candidates or any product candidates we may seek to develop in the future will ever obtain regulatory approval.

Applications for our product candidates could fail to receive regulatory approval for many reasons, including but not limited to the following:

- the FDA or comparable foreign regulatory authorities may disagree with the design, implementation, or results of our clinical studies;
- the FDA or comparable foreign regulatory authorities may determine that our product candidates are not safe and effective, only moderately effective, or have undesirable or unintended side effects, toxicities, or other characteristics that preclude our obtaining marketing approval or prevent or limit commercial use;
- the population studied in the clinical program may not be sufficiently broad or representative to assure efficacy and safety in the full population for which we seek approval;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical studies;
- the data collected from clinical studies of our product candidates may not be sufficient to support the submission of an NDA or other submission, or to obtain regulatory approval in the United States or elsewhere;
- we may be unable to demonstrate to the FDA or comparable foreign regulatory authorities that a product candidate's risk-benefit ratio for its proposed indication is acceptable;
- the FDA or comparable foreign regulatory authorities may find deficiencies with or fail to approve the manufacturing processes, test procedures and specifications, or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and

- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

This lengthy approval process, as well as the unpredictability of the results of clinical studies, may result in our failing to obtain regulatory approval to market any of our product candidates, which would significantly harm our business, results of operations, and prospects.

We are subject to healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, and diminished profits and future earnings.

Although we do not currently have any products on the market, once we begin commercializing our products, we may be subject to additional healthcare statutory and regulatory requirements and enforcement by the federal government and the states and foreign governments in which we conduct our business. Healthcare providers, physicians, and others will play a primary role in the recommendation and prescription of our product candidates, if approved. Our future arrangements with third-party payors will expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell, and distribute our product candidates, if we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- the federal Anti-Kickback Statute, or AKS, 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 healthcare programs such as Medicare and Medicaid;
- the federal False Claims Act imposes criminal and civil penalties, including those from civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease, or conceal an obligation to pay money to the federal government;
- the federal Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security, and transmission of individually identifiable health information;
- the federal false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact, or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items, or services;
- the federal transparency requirements, sometimes referred to as the "Sunshine Act," under the Patient Protection and Affordable Care Act, or the ACA, require manufacturers of drugs, devices, biologics, and medical supplies that are reimbursable under Medicare, Medicaid, or the Children's Health Insurance Program to report to the Department of Health and Human Services information related to physician payments and other transfers of value and physician ownership and investment interests; and
- analogous state laws and regulations, such as state anti-kickback and false claims laws and transparency laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, and some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures and drug pricing.

Ensuring that our future business arrangements with third parties comply with applicable healthcare laws and regulations could be costly. It is possible that governmental authorities will conclude that our business practices do 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, including anticipated activities to be conducted by our sales team, were 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, damages, fines, and exclusion from government funded

healthcare programs, such as Medicare and Medicaid, any of which could substantially disrupt our operations. If any of the physicians or other providers or entities with whom we expect to do business is found not to be in compliance with applicable laws, they may be subject to criminal, civil, or administrative sanctions, including exclusions from government funded healthcare programs.

If any of our product candidates obtain regulatory approval, additional competitors could enter the market with generic versions of such drugs, which may result in a material decline in sales of affected products.

Under the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, a pharmaceutical manufacturer may file an abbreviated new drug application, or ANDA, seeking approval of a generic copy of an approved, small-molecule innovator product. Under the Hatch-Waxman Act, a manufacturer may also submit an NDA, under Section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act that references the FDA's prior approval of the small-molecule innovator product. A 505(b)(2) NDA product may be for a new or improved version of the original innovator product. The Hatch-Waxman Act also provides for certain periods of regulatory exclusivity, which preclude FDA approval (or in some circumstances, FDA filing and reviewing) of an ANDA or 505(b)(2) NDA. These include, subject to certain exceptions, the period during which an FDA-approved drug is subject to orphan drug exclusivity. For example, a drug that is granted regulatory approval may be eligible for five years of marketing exclusivity in the United States following regulatory approval if that drug is classified as a new chemical entity, or NCE. A drug can be classified as a NCE if the FDA has not previously approved any other drug containing the same active moiety. While we believe there is a likelihood that the FDA would grant NCE status to both NYX-2925 and NYX-783 if both are granted regulatory approval, NYX-2925 and NYX-783 have the same structural formula but differ in spatial orientation, i.e., are separate stereoisomers of each other, and there can be no assurance that both will be granted NCE exclusivity.

In addition to the benefits of regulatory exclusivity, an innovator NDA holder may have patents claiming the active ingredient, product formulation or an approved use of the drug, which would be listed with the product in the FDA publication, "Approved Drug Products with Therapeutic Equivalence Evaluations," known as the "Orange Book." If there are patents listed in the Orange Book, a generic or 505(b)(2) applicant that seeks to market its product before expiration of the patents must include in the ANDA a "Paragraph IV certification," challenging the validity or enforceability of, or claiming non-infringement of, the listed patent or patents. Appropriate notice of the certification must be given to the innovator, too, and if within 45 days of receiving such notice the innovator sues to protect its patents, approval of the ANDA is stayed for 30 months, or as lengthened or shortened by the court.

Accordingly, if any of our product candidates are approved, competitors could file ANDAs for generic versions of our small-molecule drug products or 505(b)(2) NDAs that reference our small-molecule drug products, respectively. If there are patents listed for our small-molecule drug products in the Orange Book, those ANDAs and 505(b)(2) NDAs would be required to include a certification as to each listed patent indicating whether the ANDA applicant does or does not intend to challenge the patent. We cannot predict which, if any, patents in our current portfolio or patents we may obtain in the future will be eligible for listing in the Orange Book, how any generic competitor would address such patents, whether we would sue on any such patents, or the outcome of any such suit.

We may not be successful in securing or maintaining proprietary patent protection for products and technologies we develop or license. Moreover, if any of our owned or in-licensed patents that are listed in the Orange Book are successfully challenged by way of a Paragraph IV certification and subsequent litigation, the affected product could immediately face generic competition and its sales would likely decline rapidly and materially. See "Risks related to our intellectual property rights."

The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. If we are found to have improperly promoted off-label uses, we may become subject to significant liability.

The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about prescription products, such as NYX-2925, NYX-783, and NYX-458, if approved. In particular, a product may not be promoted for uses that are not approved by the FDA or such other regulatory agencies as reflected in the product's approved labeling. For example, if we receive marketing approval for NYX-2925 as a treatment for painful DPN, physicians may

nevertheless prescribe NYX-2925 to their patients in a manner that is inconsistent with the approved label. If we are found to have promoted such off-label uses, we may become subject to significant liability. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off-label promotion. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed. If we cannot successfully manage the promotion of our product candidates, if approved, we could become subject to significant liability, which would materially adversely affect our business and financial condition.

Even if approved, reimbursement policies could limit our ability to sell our product candidates.

Market acceptance and sales of our product candidates will depend on reimbursement policies and may be affected by healthcare reform measures. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels for those medications. Cost containment is a primary concern in the U.S. healthcare industry and elsewhere. Government authorities and these third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. We cannot be sure that reimbursement will be available for our product candidates and, if reimbursement is available, the level of such reimbursement. Reimbursement may impact the demand for, or the price of, our product candidates. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize our product candidates.

In some foreign countries, particularly in Canada and European countries, the pricing of prescription pharmaceuticals is subject to strict governmental control. In these countries, pricing negotiations with governmental authorities can take six to 12 months or longer after the receipt of regulatory approval and product launch. To obtain favorable reimbursement for the indications sought or pricing approval in some countries, we may be required to conduct a clinical study that compares the cost-effectiveness of our product candidates with other available therapies. If reimbursement for our product candidates is unavailable in any country in which we seek reimbursement, if it is limited in scope or amount, if it is conditioned upon our completion of additional clinical studies, or if pricing is set at unsatisfactory levels, our operating results could be materially adversely affected.

Recently enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and affect the prices we may obtain.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay regulatory approval of our product candidates, restrict or regulate post-approval activities, and affect our ability to profitably sell any product candidates for which we obtain marketing approval.

Among policy makers and payors in the United States 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 United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. In March 2010, President Obama signed into law the ACA, a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for the healthcare and health insurance industries, impose new taxes and fees on the health industry, and impose additional health policy reforms.

Among the provisions of the ACA of importance to our product candidates are the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted, or injected;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13.0% of the average manufacturer price for branded and generic drugs, respectively;

- expansion of healthcare fraud and abuse laws, including the False Claims Act and the AKS, which include, among other things, new government investigative powers and enhanced penalties for non-compliance;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals, thereby potentially increasing manufacturers' Medicaid rebate liability;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- the requirements under the federal open payments program and its implementing regulations;
- a requirement to annually report drug samples that manufacturers and distributors provide to physicians; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

Since its enactment, some of the provisions of the ACA have yet to be fully implemented, while certain provisions have been subject to judicial, congressional, and executive challenges. As a result, there have been delays in the implementation of, and action taken to repeal or replace, certain aspects of the ACA. The U.S. Supreme Court has upheld certain key aspects of the legislation, including a tax-based shared responsibility payment imposed on certain individuals who fail to maintain qualifying health coverage for all or part of a year, which is commonly known as the requirement that all individuals maintain health insurance coverage or pay a penalty, referred to as the "individual mandate." However, as a result of tax reform legislation passed in late December 2017, the individual mandate has been eliminated effective January 1, 2019. According to the Congressional Budget Office, the repeal of the individual mandate will cause 13 million fewer Americans to be insured in 2027 and premiums in insurance markets may rise.

Since January 2017, President Trump has signed two Executive Orders designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. One Executive Order directs federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. The second Executive Order terminates the cost-sharing subsidies, or CSR, that reimburse insurers under the ACA. Several state Attorneys General filed suit to stop the administration from terminating the subsidies, but their request for a restraining order was denied by a federal judge in California on October 25, 2017. The loss of the CSR payments is expected to increase premiums on certain policies issued by qualified health plans under the ACA. In addition, the Centers for Medicare & Medicaid Services, or CMS, has recently proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results. We continue to evaluate the effect that the ACA and its possible repeal and replacement has on our business.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. These changes included aggregate reductions to Medicare payments to providers of 2% per fiscal year through 2027. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. We expect that the ACA, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and in additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payers. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our products.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for approved products. In addition, there have been several recent Congressional inquiries and proposed bills designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the cost of drugs under Medicare and reform government program reimbursement methodologies for drugs. 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 labeling and post-marketing testing and other requirements.

It is likely that federal and state legislatures within the United States and foreign governments will continue to consider changes to existing health care legislation. We cannot predict the reform initiatives that may be adopted in the future or whether initiatives that have been adopted will be repealed or modified. The continuing efforts of the government, insurance companies, managed care organizations, and other health care payors of to contain or reduce costs of health care may adversely affect the demand for any product candidates for which we may obtain regulatory approval, our ability to set a price that we believe is fair for our products, our ability to obtain coverage and reimbursement approval for a product, our ability to generate revenue and achieve or maintain profitability; and the level of taxes that we are required to pay.

Our future growth may depend, in part, on our ability to commercialize our product candidates in foreign markets, where we would be subject to additional regulatory burdens and other risks and uncertainties.

Our future profitability may depend, in part, on our ability to commercialize our product candidates in foreign markets for which we may rely on collaboration with third parties. If we commercialize our product candidates in foreign markets, we would be subject to additional risks and uncertainties, including:

- our customers' ability to obtain reimbursement for our product candidates in foreign markets;
- our inability to directly control commercial activities because we are relying on third parties;
- the burden of complying with complex and changing foreign regulatory, tax, accounting, and legal requirements;
- different medical practices and customs in foreign countries affecting acceptance in the marketplace;
- import or export licensing requirements;
- longer accounts receivable collection times;
- longer lead times for shipping;
- language barriers for technical training;
- reduced protection of intellectual property rights in some foreign countries;
- the existence of additional potentially relevant third-party intellectual property rights;
- foreign currency exchange rate fluctuations; and
- the interpretation of contractual provisions governed by foreign laws in the event of a contract dispute.

Foreign sales of our product candidates could also be adversely affected by the imposition of governmental controls, political and economic instability, trade restrictions, and changes in tariffs.

Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not mean that we will be successful in obtaining regulatory approval of our product candidates in other jurisdictions.

In order to market any product outside of the United States, however, we must establish and comply with the numerous and varying safety, efficacy, and other regulatory requirements of other countries. Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain regulatory approval in any other jurisdiction, but a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory approval process in others. For example, even if the FDA or other comparable foreign regulatory authority grants marketing approval of a product candidate, comparable regulatory authorities in foreign jurisdictions must also approve the manufacturing, marketing, and promotion of the product

candidate in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from those in the United States, including additional preclinical studies or clinical studies as clinical studies conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. The marketing approval processes in other countries may implicate all of the risks detailed above regarding FDA approval in the United States, as well as other risks. In many jurisdictions outside the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we intend to charge for our products is also subject to approval.

Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties, and costs for us and could delay or prevent the introduction of our products in certain countries. Failure to obtain marketing approval in other countries or any delay or other setback in obtaining such approval would impair our ability to market our product candidates in such foreign markets. Any such impairment would reduce the size of our potential market, which could have a material adverse impact on our business, results of operations, and prospects.

Our employees, independent contractors, consultants, commercial partners, and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk of fraud, misconduct, or other illegal activity by our employees, independent contractors, consultants, commercial partners, and vendors. Misconduct by these parties could include intentional, reckless, and negligent conduct that fails to: comply with the laws of the FDA and other comparable foreign regulatory authorities; provide true, complete and accurate information to the FDA and other comparable foreign regulatory authorities; comply with manufacturing standards we have established; comply with healthcare fraud and abuse laws in the United States and similar foreign fraudulent misconduct laws; or report financial information or data accurately or to disclose unauthorized activities to us. If we obtain FDA approval of any of our product candidates and begin commercializing those products in the United States, our potential exposure under such laws will increase significantly, and our costs associated with compliance with such laws are also likely to increase. In particular, sales, marketing, and other business arrangements in the healthcare industry are subject to extensive laws designed to prevent fraud, kickbacks, self-dealing, and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales and commission, certain customer incentive programs, and other business arrangements generally. Activities subject to these laws also involve the improper use of information obtained in the course of patient recruitment for clinical studies, which could result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of business conduct and ethics, but it is not always possible to identify and deter misconduct by employees and third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws. 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.

If we or any contract manufacturers and suppliers we engage 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.

We and any contract manufacturers and suppliers we engage are subject to numerous federal, state, and local environmental, health, and safety laws, regulations, and permitting requirements, including those governing laboratory procedures; the generation, handling, use, storage, treatment, and disposal of hazardous and regulated materials and wastes; the emission and discharge of hazardous materials into the ground, air, and water; and employee health and safety. Under certain environmental laws, we could be held responsible for costs relating to any contamination at our current or past facilities and at third-party facilities. We also could incur significant costs associated with civil or criminal fines and penalties.

We could be adversely affected by violations of the U.S. Foreign Corrupt Practices Act, or FCPA, and other worldwide anti-bribery laws.

We are subject to the FCPA, which prohibits companies and their intermediaries from making payments in violation of law to non-U.S. government officials for the purpose of obtaining or retaining business or securing any other improper advantage. We have an ongoing relationship with Sai Life Sciences Ltd., or Sai, a non-U.S. company, as a third-party supplier of custom chemical synthesis of the compounds used in our product candidates such as spiro-beta lactam. Our significant reliance on a foreign supplier demands a high degree of vigilance in preventing our employees and consultants from participation in corrupt activity, because this supplier could be deemed our agent, and we could be held responsible for its actions. The FCPA and similar anti-bribery laws to which we may be subject are complex and far-reaching in nature, and, as a result, we cannot assure you that we would not be required in the future to alter one or more of our practices to be in compliance with these laws or any changes in these laws or the interpretation thereof. Any violations of these laws, or allegations of such violations, could disrupt our operations, involve significant management distraction, and involve significant costs and expenses, including legal fees. We could also suffer severe penalties, including criminal and civil penalties, disgorgement, and other remedial measures.

Risks related to collaborations with third parties

We depend on our collaboration with Allergan and may depend on collaborations with third parties for the research, development, and commercialization of certain of the product candidates we may develop. If any such collaborations are not successful, we may not be able to realize the market potential of those product candidates.

In July 2015, we entered into a research collaboration agreement with Allergan, focused on the research and discovery of small molecules that modulate NMDArs. Under the research collaboration agreement, Allergan and we may exercise the right to pick certain product candidates from a pool of eligible compounds (which were selected based upon the results of a mutually agreed set of screening assays of molecules from our drug discovery platform) in alternating fashion. On May 16, 2018, Allergan exercised its option to acquire the compound designated AGN-241751, triggering payment of a $1.0 million option fee in connection with such exercise. Allergan may also exercise its option to acquire up to two more of its selected compounds and must pay an option exercise fee for each such compound. The collaboration involves a complex allocation of rights. Under this agreement, each time Allergan exercises its option right with respect to a particular compound, Allergan will exclusively own the intellectual property rights specific to such compound and we will not be permitted to develop or commercialize such compound. When Allergan exercises one of its options with respect to a particular compound, we will not be entitled to any milestones, royalties, or other downstream revenue with respect to that compound other than the $1.0 million exercise fee. When Allergan exercises its option on a compound that ultimately generates any revenue, we are not entitled to receive any of the resulting revenue from such product candidate and, as a result, may not realize the economic benefits of a compound we generated from our discovery platform. We cannot provide any assurance that this collaboration will enhance our business or that we will achieve significant benefits from the collaboration. Moreover, we cannot provide any assurance with respect to the success of the collaboration.

We may seek third-party collaborators for the research, development, and commercialization of certain of the product candidates we plan to develop. Our likely collaborators for any other collaboration arrangements include large and mid-size pharmaceutical companies, biotechnology companies, or academic institutions. If we enter into any such arrangements with any third parties, we will likely have shared or limited control over the amount and timing of resources that our collaborators dedicate to the development or potential commercialization of any product candidates we may seek to develop with them. Our ability to generate revenue from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. We cannot predict the success of any collaboration that we enter into.

Collaborations involving our research programs, or any product candidates we may develop, pose the following risks to us:

- collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaborations. For example, under our collaboration agreement with Allergan, Allergan funds a certain amount for costs associated with our medicinal chemistry, screening, and profiling efforts;
- collaborators may not properly obtain, maintain, enforce, or defend intellectual property or proprietary rights relating to our product candidates or research programs or may use our proprietary information in such a way as to expose us to potential litigation or other intellectual property related proceedings, including proceedings challenging the scope, ownership, validity, and enforceability of our intellectual property;
- collaborators may own or co-own intellectual property covering our product candidates or research programs that results from our collaboration with them, and in such cases, we may not have the exclusive right or any right to commercialize such intellectual property or such product candidates or research programs;
- we may need the cooperation of our collaborators to enforce or defend any intellectual property we contribute to or that arises out of our collaborations, which may not be provided to us;
- disputes may arise between the collaborators and us that result in the delay or termination of the research, development, or commercialization of our product candidates or research programs or that result in costly litigation or arbitration that diverts management attention and resources;
- collaborators may decide not to pursue development and commercialization of any product candidates we develop or may elect not to continue or renew development or commercialization programs based on clinical study results, changes in the collaborator's strategic focus or available funding, or external factors such as an acquisition that diverts resources or creates competing priorities;
- collaborators may delay clinical studies, provide insufficient funding for a clinical study program, stop a clinical study or abandon a product candidate, repeat or conduct new clinical studies, or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates or research programs if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- collaborators with marketing and distribution rights to one or more product candidates may not commit sufficient resources to the marketing and distribution of such product candidates;
- we may lose certain valuable rights under circumstances identified in our collaborations, including if we undergo a change of control;
- collaborators may undergo a change of control and the new owners may decide to take the collaboration in a direction which is not in our best interest;
- collaborators may become bankrupt, which may significantly delay our research or development programs, or may cause us to lose access to valuable technology, know-how, or intellectual property of the collaborator relating to our products, product candidates, or research programs;
- key personnel at our collaborators may leave, which could negatively impact our ability to productively work with our collaborators;
- collaborations may require us to incur short and long-term expenditures, issue securities that dilute our stockholders, or disrupt our management and business;
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates or our discovery platform; and
- collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If a present or future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our development or commercialization program under such collaboration could be delayed, diminished, or terminated.

In addition, the terms and conditions of collaboration agreements, including our research collaboration with Allergan, involve complex legal, business and scientific issues, and certain provisions may be susceptible to multiple interpretations. As with any complex contractual arrangement, disputes may arise between us and our collaborators regarding the terms and conditions of these agreements, including with respect to the scope of rights granted to, or

restrictions placed on, each party under these agreements. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights under the agreement, or increase what we believe to be our obligations under the relevant agreement, either of which could materially harm our business, financial condition, results of operations, and prospects.

Moreover, we may face significant competition in seeking appropriate collaborations. Recent business combinations among biotechnology and pharmaceutical companies have resulted in a reduced number of potential collaborators. In addition, the negotiation process is time-consuming and complex, and we may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop product candidates or bring them to market and generate product revenue.

If we enter into collaborations to develop and potentially commercialize any product candidates, we may not be able to realize the benefit of such transactions if we or our collaborator elects not to exercise the rights granted under the agreement or if we or our collaborator are unable to successfully integrate a product candidate into existing operations and company culture. In addition, if our agreement with any of our collaborators terminates, our access to technology and intellectual property licensed to us by that collaborator may be restricted or terminate entirely, which may delay our continued development of our product candidates utilizing the collaborator's technology or intellectual property or require us to stop development of those product candidates completely. We may also find it more difficult to find a suitable replacement collaborator or attract new collaborators, and our development programs may be delayed or the perception of us in the business and financial communities could be adversely affected. Many of the risks relating to product development, regulatory approval, and commercialization described in this "Risk factors" section also apply to the activities of our collaborators and any negative impact on our collaborators may adversely affect us.

Our drug development programs and the potential commercialization of our product candidates will require substantial additional cash to fund expenses. For some of our product candidates, we may decide to collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates.

Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical studies, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. The terms of any collaborations or other arrangements that we may establish may not be favorable to us.

In addition, any future collaborations that we enter into may not be successful. The success of our collaboration arrangements will depend heavily on the efforts and activities of our collaborators. Collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaborations. Disagreements between parties to a collaboration arrangement regarding clinical development and commercialization matters can lead to delays in the development process or commercializing the applicable product candidate and, in some cases, termination of the collaboration arrangement. These disagreements can be difficult to resolve if neither of the parties has final decision-making authority. Collaborations with pharmaceutical or biotechnology companies and other third parties often are terminated or allowed to expire by the other party. Any such termination or expiration would adversely affect us financially and could harm our business reputation.

Exclusivity and other governance provisions within our agreements with Allergan may prevent us from pursuing alternative product candidates and exercising complete control over our product candidates' development.

Pursuant to our research collaboration agreement with Allergan, during the research term defined therein, we cannot, directly or indirectly, whether alone, or with a third party, engage in any activities to identify, generate, discover, or develop small-molecule compounds that modulate NMDArs, including any collaboration compounds, except as set forth in the agreement. In addition, during the exclusivity period defined in the research collaboration agreement, we may not alone, or with a third party, directly or indirectly engage in (a) the research or preclinical development of any compound or any product for the purpose of the treatment, prevention or diagnosis of any disorders or conditions in a specified field, which is defined as any therapeutic, prophylactic, or diagnostic use for certain delineated psychiatric or neurocognitive disorders or conditions, and which we refer to as Allergan's Field, (b) the clinical development of any compound or any product for the treatment, prevention or diagnosis of any disorders and conditions in Allergan's Field, or the manufacture of such compound or product for such purpose, or (c) the commercialization of any compound or any product labelled, or approved or licensed by any regulatory authority, for the treatment, prevention, or diagnosis of any disorders or conditions in Allergan's Field, or the manufacture of such compound or product. We are bound by a similar set of restrictions on our research, development, and commercialization activities with respect to compounds and products in Allergan's Field under an asset contribution agreement that we entered into with Allergan in connection with Allergan's acquisition of Naurex. Except with respect to the compounds for which Allergan exercises its option under the Allergan Research Collaboration Agreement, Allergan is not precluded under the Allergan Research Collaboration Agreement or the asset contribution agreement from competing with us outside of Allergan's Field.

Further, our collaboration with Allergan is supervised by a joint steering committee, or JSC. Subject to limitations specified in the agreement, if the JSC is unable to make a decision by consensus and the parties are unable to resolve the issue after referring the matter to designated executive officers of the parties, then such disputed matter shall remain deadlocked until mutual agreement, provided that each party will have the right to make the final decision with respect to any matter concerning its respective selected compounds. These exclusivity and governance provisions may inhibit our development efforts and may materially harm our business, financial condition, results of operations, and prospects.

Risks related to our reliance on third parties

We rely, and expect that we will continue to rely, on third parties to conduct any clinical studies for our product candidates. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our product candidates and our business could be substantially harmed.

We do not have the ability to independently conduct clinical studies. We rely on medical institutions, clinical investigators, contract laboratories, and other third parties, such as CROs, to conduct clinical studies on our product candidates. For example, we have entered into a sponsored research agreement with Northwestern University through which Northwestern University furnishes the laboratory facilities and equipment necessary to conduct certain research projects and related clinical studies. We enter into agreements with third-party CROs to provide monitors for and to manage data for our ongoing clinical studies. We rely heavily on these parties for execution of clinical studies for our product candidates and control only certain aspects of their activities. As a result, we have less direct control over the conduct, timing, and completion of these clinical studies and the management of data developed through clinical studies than would be the case if we were relying entirely upon our own staff. Communicating with outside parties can also be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. Outside parties may:

- have staffing difficulties;
- fail to comply with contractual obligations;
- experience regulatory compliance issues;
- undergo changes in priorities or become financially distressed; or
- form relationships with other entities, some of which may be our competitors.

These factors may materially adversely affect the willingness or ability of third parties to conduct our clinical studies and may subject us to unexpected cost increases that are beyond our control. Nevertheless, we are responsible for ensuring

that each of our clinical studies is conducted in accordance with the applicable protocol, legal, regulatory, and scientific requirements and standards, and our reliance on CROs does not relieve us of our regulatory responsibilities. We and our CROs are required to comply with regulations and guidelines, including Good Clinical Practices, or GCPs, for conducting, monitoring, recording, and reporting the results of clinical studies to ensure that the data and results are scientifically credible and accurate, and that the study patients are adequately informed of the potential risks of participating in clinical studies. These regulations are enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area and comparable foreign regulatory authorities for any products in clinical development. The FDA enforces GCP regulations through periodic inspections of clinical study sponsors, principal investigators and study sites. If we or our CROs fail to comply with applicable GCPs, the clinical data generated in our clinical studies may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical studies before approving our marketing applications. We cannot assure you that, upon inspection, the FDA will determine that any of our clinical studies comply with GCPs. In addition, our clinical studies must be conducted with product candidates produced under cGMP regulations and will require a large number of test patients. Our failure or the failure of our CROs to comply with these regulations may require us to repeat clinical studies, which would delay the regulatory approval process and could also subject us to enforcement action up to and including civil and criminal penalties.

Although we do design our clinical studies for our product candidates, CROs conduct all of the clinical studies. As a result, many important aspects of our drug development programs are outside of our direct control. In addition, the CROs may not perform all of their obligations under arrangements with us or in compliance with regulatory requirements, but we remain responsible and are subject to enforcement action that may include civil penalties and criminal prosecution for any violations of FDA laws and regulations during the conduct of our clinical studies. If the CROs do not perform clinical studies in a satisfactory manner, breach their obligations to us, or fail to comply with regulatory requirements, the development and commercialization of our product candidates may be delayed or our development program materially and irreversibly harmed. We cannot control the amount and timing of resources these CROs devote to our program or our clinical products. If we are unable to rely on clinical data collected by our CROs, we could be required to repeat, extend the duration of, or increase the size of our clinical studies and this could significantly delay commercialization and require significantly greater expenditures.

If any of our relationships with these third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs. For example, the sponsored research agreement with Northwestern University may be terminated by either party upon 60 days' written notice to the other party. If our collaboration is delayed or terminated or our ability to continue to use the current research space is terminated as a result of conflicts of interest, we may not be able to continue our planned research projects and related clinical studies on the expected timeline and may need to spend significant time and efforts to secure alternative lab facilities and equipment. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, any clinical studies such CROs are associated with may be extended, delayed, or terminated, and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. As a result, we believe that our financial results and the commercial prospects for our product candidates in the subject indication would be harmed, our costs could increase and our ability to generate revenue could be delayed.

The manufacture of our product candidates, particularly those that utilize our discovery platform, is complex and we may encounter difficulties in production. If we or any of our third-party manufacturers encounter such difficulties, or fail to meet rigorously enforced regulatory standards, our ability to provide supply of our product candidates for clinical studies or our products for patients, if approved, could be delayed or stopped, or we may be unable to maintain a commercially viable cost structure.

The processes involved in manufacturing our drug product candidates, particularly those that utilize our discovery platform, are complex, expensive, highly-regulated, and subject to multiple risks. Further, as product candidates are developed through preclinical studies to late-stage clinical studies towards approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods, are altered along the way in an effort to optimize processes and results. Such changes carry the risk that they will not achieve these intended

objectives, and any of these changes could cause our product candidates to perform differently and affect the results of planned clinical studies or other future clinical studies.

In addition, the manufacturing process for any products that we may develop is subject to FDA and other comparable foreign regulatory authority approval processes and continuous oversight, and we will need to contract with manufacturers who can meet all applicable FDA and foreign regulatory authority requirements, including, for example, complying with cGMPs, on an ongoing basis. If we or our third-party manufacturers are unable to reliably produce products to specifications acceptable to the FDA or other regulatory authorities, we may not obtain or maintain the approvals we need to commercialize such products. Even if we obtain regulatory approval for any of our product candidates, there is no assurance that either we or our contract manufacturers will be able to manufacture the approved product to specifications acceptable to the FDA or other regulatory authorities, to produce it in sufficient quantities to meet the requirements for the potential launch of the product, or to meet potential future demand. Any of these challenges could delay completion of clinical studies, require bridging clinical studies or the repetition of one or more clinical studies, increase clinical study costs, delay approval of our product candidate, impair commercialization efforts, increase our cost of goods, and have an adverse effect on our business, financial condition, results of operations, and growth prospects.

We rely completely on third-party suppliers to manufacture our clinical drug supplies for our product candidates, and we intend to rely on third parties to produce preclinical, clinical, and commercial supplies of any future product candidates.

We do not currently have, nor do we plan to acquire, the infrastructure or capability to internally manufacture our clinical drug supply of our product candidates, or any future product candidates, for use in the conduct of our preclinical studies and clinical studies, and we lack the internal resources and the capability to manufacture any product candidates on a clinical or commercial scale. The facilities used by our contract manufacturers to manufacture the active pharmaceutical ingredient and final drug product must complete a pre-approval inspection by the FDA and other comparable foreign regulatory agencies to assess compliance with applicable requirements, including cGMPs, after we submit our NDA or relevant foreign regulatory submission to the applicable regulatory agency.

We do not control the manufacturing process of, and are completely dependent on, our contract manufacturers to comply with cGMPs for manufacture of both active drug substances and finished drug products. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or applicable foreign regulatory agencies, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. In addition, we have no direct control over our contract manufacturers' ability to maintain adequate quality control, quality assurance, and qualified personnel. Furthermore, all of our contract manufacturers are engaged with other companies to supply and/or manufacture materials or products for such companies, which exposes our manufacturers to regulatory risks for the production of such materials and products. For example, our product candidates are spiro-beta lactams which may require our manufacturers to manufacture them in specifically isolated facilities. If our contract manufacturers cannot successfully manufacture material, such as spiro-beta lactams, that conforms to our specifications and the strict regulatory requirements of the FDA or applicable foreign regulatory agencies, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. As a result, failure to satisfy the regulatory requirements for the production of those materials and products may affect the regulatory clearance of our contract manufacturers' facilities generally. If the FDA or an applicable foreign regulatory agency determines now or in the future that these facilities for the manufacture of our product candidates are noncompliant, we may need to find alternative manufacturing facilities, which would adversely impact our ability to develop, obtain regulatory approval for or market our product candidates. Our reliance on contract manufacturers also exposes us to the possibility that they, or third parties with access to their facilities, will have access to and may appropriate our trade secrets or other proprietary information.

We do not have long-term supply agreements in place with our contractors, and each batch of our product candidates is individually contracted under a quality and supply agreement. If we engage new contractors, such contractors must complete an inspection by the FDA and other applicable foreign regulatory agencies. We plan to continue to rely upon contract manufacturers and, potentially, collaboration partners to manufacture commercial quantities of our product

candidates, if approved. Our current scale of manufacturing is adequate to support all of our needs for preclinical studies and clinical study supplies.

We are dependent on single-source suppliers for some of the components and materials used in, and the processes required to develop, our product candidates.

We currently depend on single-source suppliers for our active ingredients used in, and processes required to develop, our product candidates. In particular, we rely on Sai to produce custom chemical synthesis of the compounds used in our product candidates such as spiro-beta lactam. We cannot ensure that our suppliers will remain in business, have sufficient capacity or supply to meet our needs, or that they will not be purchased by one of our competitors or another company that is not interested in continuing to work with us. Our use of single-source suppliers of raw materials, components, key processes, and finished goods exposes us to several risks, including disruptions in supply, price increases, or late deliveries. There are, in general, relatively few alternative sources of supply for substitute components. In particular, given our use of the compound spiro-beta lactam, Sai will need to comply with certain regulatory and contractual requirements which significantly limit our ability to find alternative sources of supply. There are a limited number of suppliers that have the requisite facilities that comply with the required regulatory standards, which may lead to a supply gap in the unexpected event that Sai is unable to provide our products. These new vendors may be unable or unwilling to meet our future demands for our clinical studies or commercial sale. Any disruption in supply from Sai or any other single-source supplier or service provider could lead to supply delays or interruptions which would damage our business, financial condition, results of operations, and prospects. If we have to switch to a replacement supplier, the manufacture and delivery of our compounds could be interrupted for an extended period, adversely affecting our business.

Establishing additional or replacement suppliers for the components or processes used in our product candidates, if required, may not be accomplished quickly. If we are able to find a replacement supplier, the replacement supplier would need to be qualified and may require additional regulatory authority approval, which could result in further delay. For example, the FDA could require additional supplemental data and clinical study data if we rely upon a new supplier for the compounds used in our product candidates. While we seek to maintain adequate inventory of the single-source components and materials used in our products, any interruption or delay in the supply of components or materials, or our inability to obtain components or materials from alternate sources at acceptable prices in a timely manner, could impair our ability to meet the demand of our customers and cause them to cancel orders.

In addition, as part of the FDA's approval of our product candidates, submission of manufacturing information and a satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities where our product candidates are produced is required to assess compliance with cGMPs and assure that the facilities, methods, and controls are adequate to preserve the product candidates' identity, strength, quality, and purity. Such inspections may include inspection of the manufacturers of the individual components of our process, which include the manufacturing processes and facilities of our single-source suppliers. Our current single-source suppliers have not undergone this process nor have they had any components included in any product approved by the FDA.

Our reliance on single-source suppliers subjects us to a number of risks that could harm our reputation, business, and financial condition, including, among other things:

- delays to the development timelines for our product candidates;
- interruption of supply resulting from modifications to or discontinuation of a supplier's operations;
- delays in product shipments resulting from uncorrected defects, reliability issues, or a supplier's variation in a component;
- a lack of long-term supply arrangements for key components with our suppliers;
- inability to obtain adequate supply in a timely manner, or to obtain adequate supply on commercially reasonable terms;
- difficulty and cost associated with locating and qualifying alternative suppliers for our components in a timely manner;
- production delays related to the evaluation and testing of products from alternative suppliers, and corresponding regulatory qualifications;

- delay in delivery due to our suppliers prioritizing other customer orders over ours;
- damage to our reputation caused by defective components produced by our suppliers;
- increased cost of our warranty program due to product repair or replacement based upon defects in components produced by our suppliers; and
- fluctuation in delivery by our suppliers due to changes in demand from us or their other customers.

If any of these risks materialize, costs could significantly increase and our ability to meet demand for our products could be impacted.

Risks related to our intellectual property rights

If we are unable to adequately protect our proprietary technology, or obtain and maintain issued patents that are sufficient to protect our product candidates, others could compete against us more directly by developing and commercializing products similar or identical to ours, which would have a material adverse impact on our business, results of operations, financial condition, and prospects.

Our success will depend significantly on our ability to obtain and maintain patent and other proprietary protection in the United States and other countries for commercially important technology, inventions, and know-how related to our business, defend and enforce our patents, should they issue, preserve the confidentiality of our trade secrets, and operate without infringing the valid and enforceable patents and proprietary rights of third parties. We strive to protect and enhance the proprietary technologies that we believe are important to our business, including seeking patents intended to cover our products and compositions, their methods of use, and any other inventions that are important to the development of our business. Our owned patents and patent applications relate to NYX-2925, NYX-783, NYX-458, and other NMDAr modulators. We also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

We currently have no issued patents covering our clinical-stage product candidate NYX-458. We cannot provide any assurances that any of our pending patent applications will mature into issued patents in any particular jurisdiction and, if they do, that such patents will include claims with a scope sufficient to protect our product candidates or otherwise provide any competitive advantage. The patent application and approval process is expensive, complex, and time-consuming. We may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output in time to obtain patent protection. If we are unable to obtain or maintain patent protection with respect to any of our proprietary products and technology we develop, our business, financial condition, results of operations, and prospects could be materially harmed.

The patent positions of biotechnology and pharmaceutical companies, including our patent position, involve complex legal and factual questions, which in recent years have been the subject of much litigation, and, therefore, the issuance, scope, validity, enforceability, and commercial value of any patent claims that we may obtain cannot be predicted with certainty. No consistent policy regarding the breadth of claims allowed in biotechnology and pharmaceutical patents has emerged to date in the United States or in many foreign jurisdictions. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. The laws of some foreign countries do not protect our proprietary rights to the same extent as the laws of the United States, and we may encounter significant problems in protecting our proprietary rights in these countries.

Patent applications are generally maintained in confidence until publication. In the United States, for example, patent applications are typically maintained in secrecy for up to 18 months after their filing. Similarly, publication of discoveries in scientific or patent literature often lags behind actual discoveries. Consequently, we cannot be certain that we were the first to file patent applications on our product candidates. There is also no assurance that all of the potentially relevant prior art relating to our patents and patent applications has been found, which could be used by a third party to challenge the validity of our patents, should they issue, or prevent a patent from issuing from a pending patent application. Any of the foregoing could harm our competitive position, business, financial condition, results of operations, and prospects.

Moreover, our patents, if issued, may be challenged, deemed unenforceable, invalidated, or circumvented in the United States and abroad. U.S. patents and patent applications may also be subject to interference, derivation, *ex parte* reexamination, post-grant review, or *inter partes* review proceedings, supplemental examination and challenges in district court. Patents may also be subjected to opposition, post-grant review, or comparable proceedings lodged in various foreign, both national and regional, patent offices or courts. An adverse determination in any such proceeding could result in either loss of the patent or denial of the patent application, or loss or reduction in the scope of one or more of the claims of the patent or patent application, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. In addition, such proceedings may be costly. Thus, any patents, should they issue, that we may own or exclusively license may not provide any protection against competitors. Furthermore, an adverse decision in an interference proceeding can result in a third party receiving the patent right sought by us, which in turn could affect our ability to develop, market, or otherwise commercialize our product candidates.

Furthermore, though a patent, if it were to issue, is presumed valid and enforceable, its issuance is not conclusive as to its validity or its enforceability and it may not provide us with adequate proprietary protection or competitive advantages against competitors with similar products. Even if a patent issues and is held to be valid and enforceable, competitors may be able to design around or circumvent our patents, such as using pre-existing or newly developed technology or products in a non-infringing manner. Other parties may develop and obtain patent protection for more effective technologies, designs, or methods. If these developments were to occur, they could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Our ability to enforce our patent rights depends on our ability to detect infringement. It is difficult to detect infringers who do not advertise the components that are used in their products. Moreover, it may be difficult or impossible to obtain evidence of infringement in a competitor's or potential competitor's product. Any litigation to enforce or defend our patent rights, even if we were to prevail, could be costly and time-consuming and would divert the attention of our management and key personnel from our business operations. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded if we were to prevail may not be commercially meaningful.

In addition, proceedings to enforce or defend our patents, if and when issued, could put our patents at risk of being invalidated, held unenforceable, or interpreted narrowly. Such proceedings could also provoke third parties to assert claims against us, including that some or all of the claims in one or more of our patents are invalid or otherwise unenforceable. If any of our patents, if and when issued, covering our product candidates are invalidated or found unenforceable, our financial position and results of operations would be materially and adversely impacted. In addition, if a court found that valid, enforceable patents held by third parties covered our product candidates, our financial position and results of operations would also be materially and adversely impacted.

We will incur significant ongoing expenses in maintaining our patent portfolio. Should we lack the funds to maintain our patent portfolio or to enforce our rights against infringers, we could be adversely impacted.

The degree of future protection for our proprietary rights is uncertain, and we cannot ensure that:

- any of our pending patent applications, if issued, will include claims having a scope sufficient to protect our product candidates or any other products or product candidates;
- any of our pending patent applications will issue as patents at all;
- we will be able to successfully commercialize our product candidates, if approved, before our relevant patents expire;
- we were the first to make the inventions covered by each of our patents and pending patent applications;
- we were the first to file patent applications for these inventions;
- others will not develop similar or alternative technologies that do not infringe our patents;
- others will not use pre-existing technology to effectively compete against us;
- any of our patents, if issued, will be found to ultimately be valid and enforceable;
- any patents issued to us will provide a basis for an exclusive market for our commercially viable products, will provide us with any competitive advantages or will not be challenged by third parties;

- we will develop additional proprietary technologies or product candidates that are separately patentable; or
- that our commercial activities or products will not infringe upon the patents or proprietary rights of others.

Moreover, some of our future owned and licensed patents may be co-owned with third parties. If we are unable to obtain an exclusive license to any such third-party co-owner's interest in such patents or patent applications, such co-owners may be able to license their rights to other third parties, including our competitors, and our competitors could market competing products and technology. In addition, we may need the cooperation of any such co-owners of our patents in order to enforce such patents against third parties, and such cooperation may not be provided to us.

If we breach any of the agreements under which we license rights, we could lose license rights that are important to our business. For example, in connection with Allergan's acquisition of Naurex, we entered into a license agreement with Allergan, pursuant to which, among other things, Allergan granted us a non-exclusive license to certain intellectual property rights retained by Allergan in connection with such acquisition. In addition, we are party to a sublicense agreement with Allergan, pursuant to which Allergan granted us a sublicense for certain intellectual property rights that Allergan licenses from Northwestern University. We may also need to obtain additional licenses to advance the development and commercialization of other product candidates we may develop. Our existing sublicense agreement with Northwestern University imposes, and we expect that future license agreements will impose upon us various development and commercial diligence obligations, payment of milestones and/or royalties and other obligations. If we fail to comply with our obligations under certain of these agreements, we may be liable for damages, and the licensor may have the right to terminate the license, in which event we would not be able to develop, market, or otherwise commercialize products covered by the license. Our business could suffer, for example, if any current or future licenses terminate, if the licensors fail to abide by the terms of the license, if the licensed patents or other rights are found to be invalid or unenforceable, or if we are unable to enter into necessary licenses on acceptable terms.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position may be harmed.

We also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection. Additionally, we rely on unpatented know-how, continuing technological innovation to develop, strengthen, and maintain the proprietary and competitive position of our product candidates, which we seek to protect, in part, by confidentiality agreements with our employees and our collaborators and consultants. However, trade secrets are difficult to protect. For example, we may be required to share our trade secrets with third-party licensees, collaborators, consultants, contractors, or other advisors and we have limited control over the protection of trade secrets used by such third parties. Although we use reasonable efforts to protect our trade secrets, including by entering into confidentiality agreements, our employees, consultants, contractors, outside scientific collaborators, and other advisors may unintentionally or willfully disclose our trade secrets and proprietary information to competitors and we may not have adequate remedies for any such disclosure. Enforcing a claim that a third party illegally obtained and used, disclosed, or misappropriated any of our trade secrets is difficult, expensive, and time-consuming, and the outcome is unpredictable. Furthermore, we may not obtain these agreements in all circumstances, and the employees and consultants who are parties to these agreements may breach or violate the terms of these agreements, thus we may not have adequate remedies for any such breach or violation, and we could lose our trade secrets through such breaches or violations. In addition, trade secret laws in the United States vary, and some U.S. courts as well as courts outside the United States are sometimes less willing or unwilling to protect trade secrets. Moreover, it is possible that technology relevant to our business will be independently developed by a person that is not a party to such an agreement. Further, our trade secrets could otherwise become known or be independently discovered by our competitors or other third parties. We may not be able to prevent the unauthorized disclosure or use of our technical knowledge or trade secrets by consultants, vendors, former employees, and current employees. If our trade secrets or confidential or proprietary information is divulged to or acquired by third parties, including our competitors, our competitive position in the marketplace, business, financial condition, results of operations, and prospects may be materially adversely affected.

We may be sued for infringing the intellectual property rights of others, which may be costly and time-consuming and may prevent or delay our product development efforts and stop us from commercializing or increase the costs of commercializing our product candidates, if approved.

Our success will depend in part on our ability to operate without infringing, misappropriating, or otherwise violating the intellectual property and proprietary rights of third parties. We cannot assure you that our business, products, and methods do not or will not infringe the patents or other intellectual property rights of third parties. We may in the future become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our product candidates and technologies we use in our business.

The pharmaceutical industry is characterized by extensive litigation regarding patents and other intellectual property rights. Other parties may allege that our product candidates or the use of our technologies infringes or otherwise violates patent claims or other intellectual property rights held by them or that we are employing their proprietary technology without authorization. As we continue to develop and, if approved, commercialize our current product candidates and future product candidates, competitors may claim that our technology infringes their intellectual property rights as part of business strategies designed to impede our successful commercialization. There may be third-party patents or patent applications with claims to compositions, materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. Because patent applications can take many years to issue and may be confidential for 18 months or more after filing, and because patent claims can be revised before issuance, third parties may have currently pending patent applications which may later result in issued patents that our product candidates may infringe, or which such third parties claim are infringed by our technologies. If a patent holder believes one or more of our product candidates infringes its patent rights, the patent holder may sue us even if we have received patent protection for our technology. Moreover, we may face patent infringement claims from non-practicing entities that have no relevant drug revenue and against whom our own patent portfolio may thus have no deterrent effect.

The outcome of intellectual property litigation is subject to uncertainties that cannot be adequately quantified in advance. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. If we are sued for patent infringement, we would need to demonstrate that our product candidates, products or methods either do not infringe the patent claims of the relevant patent or that the patent claims are invalid or unenforceable, and we may not be able to do this. Even if we are successful in these proceedings, we may incur substantial costs and the time and attention of our management and scientific personnel could be diverted in pursuing these proceedings, which could have a material adverse effect on our business and results of operations. In addition, we may not have sufficient resources to bring these actions to a successful conclusion.

Patent and other types of intellectual property litigation can involve complex factual and legal questions, and their outcome is uncertain. If we are found to infringe a third party's intellectual property rights, we could be required to obtain a license from such third party to continue developing and marketing our product candidates and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were to obtain a license, it could be granted on non-exclusive terms, thereby providing our competitors and other third parties access to the same technologies licensed to us. In addition, if any such claim were successfully asserted against us and we could not obtain such a license, we may be forced to stop or delay developing, manufacturing, selling or otherwise commercializing our product candidates. Any claim relating to intellectual property infringement that is successfully asserted against us may require us to pay substantial damages, including treble damages and attorney's fees if we are found to be willfully infringing another party's patents, for past use of the asserted intellectual property and royalties and other consideration going forward if we are forced to take a license.

Even if we are successful in these proceedings, we may incur substantial costs and divert management time and attention in pursuing these proceedings, which could have a material adverse effect on us. There could also be public announcements of the results of the hearing, motions, or other interim proceedings or developments and if securities analysts or investors perceive those results to be negative, it could cause the price of shares of our common stock to decline. If we are unable to avoid infringing the patent rights of others, we may be required to seek a license, defend an infringement action, or challenge the validity of the patents in court, or redesign our products. Patent litigation is costly

and time-consuming. We may not have sufficient resources to bring these actions to a successful conclusion. In addition, intellectual property litigation or claims could force us to do one or more of the following:

- cease developing, selling or otherwise commercializing our product candidates;
- pay substantial damages for past use of the asserted intellectual property;
- obtain a license from the holder of the asserted intellectual property, which license may not be available on reasonable terms, if at all; and
- in the case of trademark claims, redesign, or rename, some or all of our product candidates to avoid infringing the intellectual property rights of third parties, which may not be possible and, even if possible, could be costly and time-consuming.

Any of these risks coming to fruition could have a material adverse effect on our business, results of operations, financial condition, and prospects.

We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property.

We enter into confidentiality and intellectual property assignment agreements with our employees, consultants, outside scientific collaborators, sponsored researchers, and other advisors. These agreements generally provide that inventions conceived by the party in the course of rendering services to us will be our exclusive property. However, these agreements may not be honored and may not effectively assign intellectual property rights to us. The assignment of intellectual property rights under these agreements may not be automatic upon the creation of the intellectual property or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. For example, even if we have a consulting agreement in place with an academic advisor pursuant to which such academic advisor is required to assign any inventions developed in connection with providing services to us, such academic advisor may not have the right to assign such inventions to us, as it may conflict with his or her obligations to assign all such intellectual property to his or her employing institution.

Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment, and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees, and various other government fees on our owned and in-licensed patents and patent applications are or will be due to be paid to the U.S. Patent and Trademark Office, or USPTO, in several stages and various government patent agencies outside of the United States over the lifetime of such patents and patent applications and any patent rights we may own or license in the future. We have systems in place to remind us to pay these fees, and we employ outside firms to remind us or our licensors to pay annuity fees due to foreign governmental patent agencies on our foreign patents and pending foreign patent applications. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment, and other similar provisions over the lifetime of our owned patents and applications. 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, competitors or other third parties might be able to enter the market earlier than would otherwise have been the case and this circumstance could have a material adverse effect on our business, financial condition, results of operations, and prospects.

We may be involved in lawsuits or other proceedings to protect or enforce our intellectual property, which could be expensive, time-consuming, and unsuccessful.

Even if our patent applications are issued, competitors and other third parties may infringe, misappropriate, or otherwise violate our patents and other intellectual property rights. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming and divert the attention of our management and key personnel from our business operations. Furthermore, many of our adversaries in these proceedings may have the ability to dedicate substantially greater resources to prosecuting these legal actions than we can. Our ability to enforce our patent rights also depends on our ability to detect infringement. It is difficult to detect infringers who do not advertise the components that are used in their products. Moreover, it may be difficult or impossible to obtain evidence of infringement in a competitor's or potential competitor's product.

In an infringement proceeding, a court may disagree with our allegations and refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question, or may decide that a patent of ours is invalid, or unenforceable. An adverse result in any litigation, defense or post-grant proceedings could result in one or more of our patents being invalidated or interpreted narrowly and could put our patent applications at risk of not issuing. If any of our patents, if and when issued, covering our product candidates are invalidated or found unenforceable, our financial position and results of operations would be materially and adversely impacted. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded if we were to prevail may not be commercially meaningful.

Interference proceedings provoked by third parties or brought by us may be necessary to determine the priority of inventions with respect to our patents or 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. Our involvement in 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 infringement, misappropriation of, or other violations of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States.

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. There could also 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 material adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing, or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

Issued patents covering our product candidates could be found invalid or unenforceable if challenged.

If we initiated legal proceedings against a third party to enforce a patent, if and when issued, covering one of our product candidates, the defendant could counterclaim that the patent covering our product candidate is invalid and/or unenforceable. The outcome of any such proceeding is generally unpredictable.

In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge include alleged failures to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for unenforceability assertions of a patent include allegations that someone connected with prosecution of the patent application that matured into the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution of the patent application. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the

context of litigation. Such mechanisms include re-examination, *inter partes* review, post grant review and equivalent proceedings in foreign jurisdictions, e.g., opposition proceedings. Such proceedings could result in revocation or amendment of our patents in such a way that they no longer cover our product candidates or competitive products. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to validity, for example, we cannot be certain that there is no 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 our product candidates. Such a loss of patent protection would have a material adverse impact on our business.

We may not seek to protect our intellectual property rights in all jurisdictions throughout the world and we may not be able to adequately enforce our intellectual property rights even in the jurisdictions where we seek protection.

Filing and prosecuting patent applications, and defending patents on product candidates in all countries and jurisdictions throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States could be less extensive than those in the United States, assuming that rights are obtained in the United States. 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 United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. In addition, the statutory deadlines for pursuing patent protection in individual foreign jurisdictions are based on the priority date of each of our patent applications and we may not timely file foreign patent applications. For the patent families related to NYX-458, as well as for many of the patent families that we own, the relevant statutory deadlines have not yet expired. Thus, for each of the patent families that we believe provide coverage for our lead product candidates, we will need to decide whether and where to pursue protection outside the United States. For patent families relating to NYX-2925 and NYX-783, we have chosen to pursue patent protection in only the United States, Mexico, Canada, and certain jurisdictions in Europe, Asia, Australia, and South America.

Competitors may use our technologies in jurisdictions where we do not pursue and obtain 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 United States. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. Even if we pursue and obtain issued patents in particular jurisdictions, our patent claims or other intellectual property rights may not be effective or sufficient to prevent third parties from so competing.

The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the United States. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property protection, especially those relating to biotechnology or pharmaceuticals. This could make it difficult for us to stop the infringement of our patents, if obtained, or the misappropriation of or marketing of competing products in violation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. In addition, many countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit. Patent protection must ultimately be sought on a country-by-country basis, which is an expensive and time-consuming process with uncertain outcomes. Accordingly, we may choose not to seek patent protection in certain countries, and we will not have the benefit of patent protection in such countries.

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, could put 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.

If we do not obtain additional protection under the Hatch-Waxman Act and similar foreign legislation by extending the patent terms and obtaining data exclusivity for our product candidates, our business may be materially harmed.

Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional patent application filing date in its chain of priority. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired for a product candidate, we may be open to competition from competitive products, including generic products. Given the amount of time required for the development, testing, and regulatory review of new product candidates, patents protecting such product candidates might expire before or shortly after such product candidates are commercialized. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing product candidates similar or identical to ours.

Depending upon the timing, duration, and specifics of FDA marketing approval of our product candidates, one or more of the U.S. patents we own may be eligible for a limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Act. The Hatch-Waxman Act permits a patent term extension of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. However, we may not be granted an extension because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain a patent term extension or the term of any such extension is less than we request, the duration of patent protection we obtain for our product candidates may not provide us with any meaningful commercial or competitive advantage, our competitors may obtain approval of competing products earlier than they would otherwise be able to do so, and our ability to generate revenues could be materially adversely affected.

Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our products.

As is the case with other biotechnology and pharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology and pharmaceutical industries involve both technological and legal complexity, and is therefore costly, time-consuming, and inherently uncertain. In addition, the United States has enacted and implemented wide-ranging patent reform legislation: the Leahy-Smith America Invents Act. The America Invents Act includes a number of significant changes to U.S. patent law. After March 2013, under the America Invents Act, the United States transitioned to a first-inventor-to-file system in which, assuming that other requirements for patentability are met, the first-inventor-to-file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. The America Invents Act also includes provisions that affect the way patent applications will be prosecuted and that may also affect patent litigation. It is not yet clear what, if any, impact the America Invents Act will have on the operation of our business. However, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of any patents that may issue from our patent applications, all of which could have a material adverse effect on our business and financial condition.

In addition, U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. The full impact of these decisions is not yet known. For example, on March 20, 2012, in *Mayo Collaborative Services, DBA Mayo Medical Laboratories, et al. v. Prometheus Laboratories, Inc.*, the Court held that several claims drawn to measuring drug metabolite levels from patient samples and correlating them to drug doses were not patent eligible subject matter. The decision appears to impact diagnostics patents that merely apply a law of nature via a series of routine steps and it has created uncertainty around the ability to obtain patent protection for certain inventions. Additionally, on June 13, 2013, in *Association for Molecular Pathology v. Myriad Genetics, Inc.*, the Court held that claims to isolated genomic DNA are not patent eligible, but claims to complementary DNA molecules are patent eligible because they are not a natural product. The effect of the decision on patents for other isolated natural products is uncertain. However, on March 4, 2014, the USPTO issued a memorandum to patent examiners providing guidance for examining claims that recite laws of nature, natural phenomena or natural

products under the *Myriad* and *Prometheus* decisions. This guidance did not limit the application of *Myriad* to DNA but rather applied the decision to other natural products.

In addition to increasing uncertainty with regard to our ability to obtain future patents, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on these and other decisions by the U.S. Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could weaken our ability to obtain new patents or to enforce any patents that may issue in the future.

We may be subject to damages resulting from claims that we or our employees, consultants, or advisors have wrongfully used or disclosed alleged trade secrets of their current or former employers.

Our employees have been previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. We also engage advisors and consultants who are concurrently employed at universities or who perform services for other entities.

Although we try to ensure that our employees, consultants, and advisors do not use the proprietary information or know-how of others in their work for us, and although we are not aware of any claims currently pending against us, we may be subject to claims that we or our employees, advisors, or consultants have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of a former employer or other third party. We have and may in the future also be subject to claims that an employee, advisor, or consultant performed work for us that conflicts with that person's obligations to a third party, such as an employer, and thus, that the third party has an ownership interest in the intellectual property arising out of work performed for us. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management. If we fail in defending such claims, in addition to paying money claims, we may lose valuable intellectual property rights or personnel. A loss of key personnel or their work product could hamper or prevent our ability to commercialize our product candidates, which would materially adversely affect our commercial development efforts.

Numerous factors may limit any potential competitive advantage provided by our intellectual property rights.

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, provide a barrier to entry against our competitors or potential competitors, or permit us to maintain our competitive advantage. Moreover, if a third party has intellectual property rights that cover the practice of our technology, we may not be able to fully exercise or extract value from our intellectual property rights. The following examples are illustrative:

- others may be able to develop and/or practice technology that is similar to our technology or aspects of our technology but that is not covered by the claims of patents, should such patents issue from our patent applications;
- we might not have been the first to make the inventions covered by a pending patent application that we own;
- we might not have been the first to file patent applications covering an invention;
- others may independently develop similar or alternative technologies without infringing our intellectual property rights;
- pending patent applications that we own or license may not lead to issued patents;
- patents, if issued, that we own or license may not provide us with any competitive advantages, or may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- third parties may compete with us in jurisdictions where we do not pursue and obtain patent protection;
- we may not be able to obtain and/or maintain necessary or useful licenses on reasonable terms or at all;
- third parties may assert an ownership interest in our intellectual property and, if successful, such disputes may preclude us from exercising exclusive rights over that intellectual property;
- we may not develop or in-license additional proprietary technologies that are patentable; and
- the patents of others may have an adverse effect on our business.

Should any of these events occur, they could significantly harm our business and results of operations.

General company-related risks

We will need to develop and expand our company, and we may encounter difficulties in managing this development and expansion, which could disrupt our operations.

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of technology research, product development and manufacturing, clinical affairs, regulatory affairs and, if any of our product candidates are submitted for or receive marketing approval, sales, marketing and distribution. To manage our anticipated development and expansion, we must continue to implement and improve our managerial, operational, and financial systems, expand our facilities, and continue to recruit and train additional qualified personnel. Also, our management may need to divert a disproportionate amount of its attention away from its day-to-day activities and devote a substantial amount of time to managing these development activities. Due to our limited resources, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. This may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees, and reduced productivity among remaining employees. The physical expansion of our operations may lead to significant costs and may divert financial resources from other projects, such as the development of our product candidates. If our management is unable to effectively manage our expected development and expansion, our expenses may increase more than expected, our ability to generate or increase our revenue could be reduced and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize our product candidates, if approved, and compete effectively will depend, in part, on our ability to effectively manage the future development and expansion of our company.

Our future success depends on our ability to retain our management team and to attract, retain, and motivate qualified personnel.

Our ability to compete in the highly competitive biotechnology and biopharmaceuticals industries depends upon our ability to attract and retain highly qualified managerial, scientific, and medical personnel. In order to induce valuable employees to continue their employment with us, we have provided stock options that vest over time. The value to employees of stock options that vest over time is significantly affected by movements in our stock price that are beyond our control, and may at any time be insufficient to counteract more lucrative offers from other companies.

We are highly dependent on our management, scientific and medical personnel, including our Chief Executive Officer, Norbert G. Riedel, Ph.D. Despite our efforts to retain valuable employees, members of our management, scientific, and development teams may terminate their employment with us on short notice. The loss of the services of any of our executive officers, including Dr. Riedel, other key employees and other scientific and medical advisors, and an inability to find suitable replacements could result in delays in product development and harm our business. Pursuant to their employment arrangements, each of our executive officers, and other employees may voluntarily terminate their employment at any time, with or without notice. Our success also depends on our ability to continue to attract, retain, and motivate highly skilled junior, mid-level, and senior managers as well as junior, mid-level, and senior scientific and medical personnel.

We may not be able to attract or retain qualified management and scientific personnel in the future due to the intense competition for a limited number of qualified personnel among biopharmaceutical, biotechnology, pharmaceutical, and other businesses. Many of the other pharmaceutical companies that we compete against for qualified personnel have greater financial and other resources, different risk profiles, and a longer history in the industry than we do. They also may provide more diverse opportunities and better chances for career advancement. Some of these characteristics may be more appealing to high quality candidates than what we may be able to offer. We also experience competition for the hiring of scientific personnel from universities and research institutions. If we are unable to continue to attract and retain high quality personnel, the rate and success at which we can develop and commercialize product candidates will be limited.

We face potential product liability exposure, and, if claims are brought against us, we may incur substantial liability.

The use of our product candidates in clinical studies and the sale of our product candidates, if approved, exposes us to the risk of product liability claims. Product liability claims might be brought against us by patients, healthcare providers, or others selling or otherwise coming into contact with our product candidates. For example, we may be sued if any product we develop 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, including as a result of interactions with alcohol or other drugs, negligence, strict liability, and a breach of warranties. Claims could also be asserted under state consumer protection acts. If we become subject to product liability claims and cannot successfully defend ourselves against them, we could incur substantial liabilities. In addition, regardless of merit or eventual outcome, product liability claims may result in, among other things:

- withdrawal of subjects from our clinical studies;
- substantial monetary awards to patients or other claimants;
- decreased demand for our product candidates or any future product candidates following marketing approval, if obtained;
- damage to our reputation and exposure to adverse publicity;
- increased FDA warnings on product labels;
- litigation costs;
- distraction of management's attention from our primary business;
- loss of revenue; and
- the inability to successfully commercialize our product candidates or any future product candidates, if approved.

We maintain product liability insurance coverage for our clinical studies with a $5.0 million annual aggregate coverage limit. Nevertheless, our insurance coverage may be insufficient to reimburse us for any expenses or losses we may suffer. Moreover, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses, including if insurance coverage becomes increasingly expensive. If and when we obtain marketing approval for our product candidates, we intend to expand our insurance coverage to include the sale of commercial products; however, we may not be able to obtain this product liability insurance on commercially reasonable terms. Large judgments have been awarded in class action lawsuits based on drugs that had unanticipated side effects. The cost of any product liability litigation or other proceedings, even if resolved in our favor, could be substantial, particularly in light of the size of our business and financial resources. A product liability claim or series of claims brought against us could cause our stock price to decline and, if we are unsuccessful in defending such a claim or claims and the resulting judgments exceed our insurance coverage, our financial condition, business, and prospects could be materially adversely affected.

We incur increased costs as a result of operating as a public company, and our management team is required to devote substantial time to new compliance initiatives.

As a public company, we incur significant legal, accounting, and other expenses that we did not incur as a private company and these costs will further increase if and once we are no longer an "emerging growth company." In addition, the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, and rules subsequently implemented by the SEC and The Nasdaq Stock Market have imposed various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations increase our legal and financial compliance costs and make some activities more time-consuming and costly.

Pursuant to Section 404 of the Sarbanes-Oxley Act, or Section 404, we will be required to furnish a report by our management on our internal control over financial reporting, including an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. However, while we remain an "emerging growth company," we will not be required to include an attestation report on internal control over financial

reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants, and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented, and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that neither we nor our independent registered public accounting firm will be able to conclude within the prescribed timeframe that our internal control over financial reporting is effective as required by Section 404. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

If we fail to maintain proper and effective internal controls, our ability to produce accurate and timely financial statements could be impaired, which could result in sanctions or other penalties that would harm our business.

We are subject to the reporting requirements of the Securities Exchange Act of 1934, or the Exchange Act, the Sarbanes-Oxley Act, and the rules and regulations of The Nasdaq Stock Market. The Sarbanes-Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal controls over financial reporting. Commencing with our fiscal year ending the year after our initial public offering was completed, we must perform system and process design evaluation and testing of the effectiveness of our internal controls over financial reporting to allow management to report on the effectiveness of our internal controls over financial reporting in our Form 10-K filing for that year, as required by Section 404 of the Sarbanes-Oxley Act. This will require that we incur substantial additional professional fees and internal costs to expand our accounting and finance functions and that we expend significant management efforts. Prior to our initial public offering, we were never required to test our internal controls within a specified period and, as a result, we may experience difficulty in meeting these reporting requirements in a timely manner.

We may discover weaknesses in our system of internal financial and accounting controls and procedures that could result in a material misstatement of our financial statements. Our internal control over financial reporting will not prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud will be detected.

If we are not able to comply with the requirements of Section 404 of the Sarbanes-Oxley Act in a timely manner, or if we are unable to maintain proper and effective internal controls over financial reporting, we may not be able to produce timely and accurate financial statements. If that were to happen, our investors could lose confidence in our reported financial information, the market price of our stock could decline and we could be subject to sanctions or investigations by the SEC or other regulatory authorities.

In order to satisfy our obligations as a public company, we will need to hire additional qualified accounting and financial personnel with appropriate public company experience.

As a public company, we need to establish and maintain effective disclosure and financial controls and make changes in our corporate governance practices. We will need to hire additional accounting and financial personnel with appropriate public company experience and technical accounting knowledge, and it may be difficult to recruit and maintain such personnel. Even if we are able to hire appropriate personnel, our existing operating expenses and operations will be impacted by the direct costs of their employment and the indirect consequences related to the diversion of management resources from product development efforts.

Changes in tax law, including the recently passed comprehensive tax reform bill, could adversely affect our business and financial condition.

The rules dealing with U.S. federal, state, and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service and the U.S. Treasury Department. Changes to tax laws

(which changes may have retroactive application) could adversely affect us or holders of our common stock. In recent years, many such changes have been made and changes are likely to continue to occur in the future. On December 22, 2017, President Trump signed into law the Tax Cuts and Jobs Act, or the TCJA, which significantly reforms the Internal Revenue Code of 1986, as amended, or the Code. The TCJA, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, limitation of the tax deduction for net interest expense to 30% of adjusted earnings (except for certain small businesses), limitation of the deduction for net operating losses to 80% of current year taxable income and elimination of net operating loss carrybacks, in each case, for losses arising in taxable years beginning after December 31, 2017 (though any such net operating losses may be carried forward indefinitely), and modifying or repealing many business deductions and credits (including reducing the business tax credit for certain clinical testing expenses incurred in the testing of certain drugs for rare diseases or conditions generally referred to as "orphan drugs"). We continue to examine the impact this tax reform legislation may have on our business. However, the effect of the TCJA on our business, whether adverse or favorable, is uncertain, and may not become evident for some period of time. We urge investors to consult with their legal and tax advisers regarding the implications of the TCJA and other changes in tax laws on an investment in our common stock.

Our ability to use our net operating loss carryforwards and certain tax credit carryforwards may be subject to limitation.

As of December 31, 2017, we had federal and state net operating loss, or NOL, carryforwards of $48.8 million and $4.6 million, respectively, which begin to expire in 2027. Under Section 382 of the Code changes in our ownership may limit the amount of our net operating loss carryforwards and research and development tax credit carryforwards that could be utilized annually to offset our future taxable income, if any. This limitation would generally apply in the event of a cumulative change in ownership of our company of more than 50% within a three-year period. Any such limitation may significantly reduce our ability to utilize our net operating loss carryforwards and research and development tax credit carryforwards before they expire. The completion of our initial public offering, together with private placements and other transactions that have occurred since our inception, may trigger such an ownership change pursuant to Section 382. Any such limitation, whether as the result of our initial public offering, prior private placements, sales of our common stock by our existing stockholders, or additional sales of our common stock by us, could have a material adverse effect on our results of operations in future years. We have not yet completed a Section 382 analysis, and therefore, there can be no assurances that the NOL is already not limited. In addition, the reduction of the corporate tax rate under the TCJA may cause a reduction in the economic benefit of our NOL carryforwards and other deferred tax assets available to us.

Unfavorable global economic conditions could adversely affect our business, financial condition, or results of operations.

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. A global financial crisis can cause extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn, such as the global financial crisis years ago, could result in a variety of risks to our business, including, weakened demand for our product candidates and our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption, or cause our customers to delay making payments for our services. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

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 a serious disaster.

Earthquakes or other natural disasters could severely disrupt our operations, and have a material adverse effect on our business, results of operations, financial condition, and prospects. If a natural disaster, power outage, or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as the manufacturing facilities of our third-party contract manufacturers and suppliers, 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. The disaster recovery and business continuity plans we have in place may prove inadequate in

the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which, particularly when taken together with our lack of earthquake insurance, could have a material adverse effect on our business.

Our internal computer systems, or those of our third-party CROs or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product candidates' development programs.

Despite the implementation of security measures, our internal computer systems and those of our third-party CROs and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war, and telecommunication and electrical failures. While we have not experienced any such system failure, accident, or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our programs. For example, the loss of clinical study data for our product candidates could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of or damage to our data or applications or other data or applications relating to our technology or product candidates, or inappropriate disclosure of confidential or proprietary information, we could incur liabilities and the further development of our product candidates could be delayed.

We may acquire businesses or products, or form strategic alliances, in the future, and we may not realize the benefits of such acquisitions.

We may acquire additional businesses or products, form strategic alliances, or create joint ventures with third parties that we believe will complement or augment our existing business. If we acquire businesses with promising markets or technologies, we may not be able to realize the benefit of acquiring such businesses if we are unable to successfully integrate them with our existing operations and company culture. We may encounter numerous difficulties in developing, manufacturing, and marketing any new products resulting from a strategic alliance or acquisition that delay or prevent us from realizing their expected benefits or enhancing our business. We cannot provide assurance that, following any such acquisition, we will achieve the synergies expected in order to justify the transaction.

Risks related to our common stock

An active trading market for our common stock may not develop, and you may not be able to resell your shares at or above the initial public offering price.

Our IPO recently closed on June 25, 2018. Although our common stock has been listed on The Nasdaq Global Select Market, an active trading market for our shares may never develop or be sustained. If an active market for our common stock does not continue, it may be difficult for our stockholders to sell their shares without depressing the market price for the shares or sell their shares at or above the prices at which they acquired their shares or sell their shares at the time they would like to sell. Any inactive trading market for our common stock may also impair our ability to raise capital to continue to fund our operations by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration.

Market volatility may affect our stock price and the value of your investment.

The market price for our common stock is likely to be volatile, in part because our common stock has not been previously traded publicly prior to our IPO. In addition, the market price of our common stock may fluctuate significantly in response to a number of factors, most of which we cannot control, including, among others:

- plans for, progress of, or results from preclinical studies and clinical studies of our product candidates;
- the failure of the FDA to approve our product candidates;
- announcements of new products, technologies, commercial relationships, acquisitions, or other events by us or our competitors;
- the success or failure of other therapies for disorders of the brain and nervous system;

- regulatory or legal developments in the United States and other countries;
- failure of our product candidates, if approved, to achieve commercial success;
- fluctuations in stock market prices and trading volumes of similar companies;
- general economic, industry, and market conditions and overall fluctuations in U.S. equity markets;
- variations in our quarterly operating results or those of companies that are perceived to be similar to us;
- changes in our financial guidance or securities analysts' estimates of our financial performance;
- changes in accounting principles;
- our ability to raise additional capital and the terms on which we can raise it;
- sales of large blocks of our common stock, including sales by our executive officers, directors, and significant stockholders;
- additions or departures of key personnel;
- discussion of us or our stock price by the press and by online investor communities;
- market conditions in the pharmaceutical and biotechnology sectors; and
- other risks and uncertainties described in these risk factors.

In recent years, the stock market in general, and the market for pharmaceutical and biotechnology companies in particular, has experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to changes in the operating performance of the companies whose stock is experiencing those price and volume fluctuations. Broad market and industry factors may seriously affect the market price of our common stock, regardless of our actual operating performance. Following periods of such volatility in the market price of a company's securities, securities class action litigation has often been brought against that company. Because of the potential volatility of our stock price, we may become the target of securities litigation in the future. Securities litigation could result in substantial costs and divert management's attention and resources from our business.

A significant portion of our total outstanding shares are eligible to be sold into the market in the near future, which could cause the market price of our common stock to drop significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. As of June 2018 closing of our initial public offering, we had outstanding 33,496,224 shares of common stock, of which 24,916,842 shares are subject to restrictions on transfer under 180-day lock-up arrangements with the underwriters of our initial public offering. These restrictions are due to expire in December 2018, resulting in the majority of these shares becoming eligible for public sale if they are registered under the Securities Act or if they qualify for an exemption from registration under the Securities Act including under Rules 144 or 701.

In addition, 8,132,506 shares of common stock as of September 30, 2018 that are either subject to outstanding options or reserved for future issuance under our equity incentive plans will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules, the lock-up agreements and Rule 144 and Rule 701 under the Securities Act. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the market price of our common stock could decline.

The holders of approximately 20,306,497 shares of our common stock as of September 30, 2018 will be entitled to rights with respect to the registration of their shares under the Securities Act, subject to the lock-up agreements described above. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares purchased by affiliates. Any sales of securities by these stockholders could have a material adverse effect on the market our common stock.

Our principal stockholders and management own a significant percentage of our stock and, if they choose to act together, will be able to control or exercise significant influence over matters subject to stockholder approval, which will limit your ability to influence corporate matters and could delay or prevent a change in corporate control.

Our executive officers, directors, principal stockholders, and their affiliates, including investment funds affiliated with Bain Capital Life Sciences, Adams Street, New Leaf Ventures, Longitude, and Frazier, beneficially held, as of

September 30, 2018, in the aggregate of approximately 60% of our outstanding common stock. As a result, these stockholders, if they act together, will be able to influence our management and affairs and control the outcome of matters submitted to our stockholders for approval, including the election of directors and any sale, merger, consolidation, or sale of all or substantially all of our assets. The concentration of voting power among these stockholders may have an adverse effect on the price of our common stock. In addition, this concentration of ownership might adversely affect the market price of our common stock by:

- delaying, deferring, or preventing a change of control of us;
- impeding a merger, consolidation, takeover, or other business combination involving us; or
- discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of us.

We have broad discretion in how we use the cash and cash equivalents and may not use them effectively, which could affect our results of operations and cause our stock price to decline.

Our management has broad discretion to use our cash and cash equivalents to fund our operations and could spend these funds in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our common stock to decline and delay the development of our product candidates. Pending our use to fund operations, we may invest our cash and cash equivalents in a manner that does not produce income or that loses value.

We may be at an increased risk of securities class action litigation.

Historically, 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 and pharmaceutical companies have experienced significant stock price volatility in recent years. If we were to be sued, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of us, even one that may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our amended and restated certificate of incorporation and amended and restated bylaws may delay or prevent an acquisition of us or a change in our management. These provisions include a classified board of directors, a prohibition on actions by written consent of our stockholders, and the ability of our board of directors to issue preferred stock without stockholder approval. In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which limits the ability of stockholders owning in excess of 15% of our outstanding voting stock to merge or combine with us. Although we believe these provisions collectively provide for an opportunity to obtain greater value for stockholders by requiring potential acquirers to negotiate with our board of directors, they would apply even if an offer rejected by our board were considered beneficial by some stockholders. In addition, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for appointing the members of our management.

Our bylaws contain an exclusive forum provision, which may limit a stockholder's ability to bring a claim in a judicial forum it finds favorable and may discourage lawsuits with respect to such claims.

Our amended and restated bylaws provide that the United States District Court for the Northern District of Illinois is the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. In addition, our amended and restated bylaws provide that any person or entity purchasing or otherwise acquiring any interest in shares of our common stock is deemed to have notice of and consented to the foregoing provisions. We have chosen the United States District Court for the Northern District of Illinois as the exclusive forum for such causes of action because our principal executive offices are located in Evanston, Illinois. Some companies that have adopted similar federal district court forum selection provisions are currently subject to a suit in the Court of Chancery of the State of Delaware brought

by stockholders who assert that the federal district court forum selection provision is not enforceable. We recognize that the federal district court forum selection clause may impose additional litigation costs on stockholders who assert the provision is not enforceable and may impose more general additional litigation costs in pursuing any such claims, particularly if the stockholders do not reside in or near the State of Illinois. Additionally, the forum selection clauses in our amended and restated bylaws may limit our stockholders' ability to obtain a favorable judicial forum for disputes with us. Alternatively, if the federal district court forum selection provision is found inapplicable to, or unenforceable in respect of, one or more of the specified types of actions or proceedings, we may incur additional costs associated with resolving such matters in other jurisdictions, which could have an adverse effect on our business, financial condition or results of operations. The United States District Court for the Northern District of Illinois may also reach different judgments or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments may be more or less favorable to us than our stockholders.

We are an "emerging growth company," and as a result of the reduced disclosure and governance requirements applicable to emerging growth companies, our common stock may be less attractive to investors.

We are an "emerging growth company," as defined in the JOBS Act, and we intend to take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies including, but not limited to, not being required to comply with the auditor attestation requirements of Section 404, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. If we choose not to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act, our auditors will not be required to attest to the effectiveness of our internal control over financial reporting. As a result, investors may become less comfortable with the effectiveness of our internal controls and the risk that material weaknesses or other deficiencies in our internal controls go undetected may increase. If we choose to provide reduced disclosures in our periodic reports and proxy statements while we are an "emerging growth company," investors would have access to less information and analysis about our executive compensation, which may make it difficult for investors to evaluate our executive compensation practices. We cannot predict if investors will find our common stock less attractive because we will rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile. We may take advantage of these reporting exemptions until we are no longer an "emerging growth company." We will continue to remain an "emerging growth company" until the earliest of the following: (1) the last day of the fiscal year following the fifth anniversary of the date of the completion of our initial public offering, (2) the last day of the fiscal year in which our total annual gross revenue is equal to or more than $1.07 billion, (3) the date on which we have issued more than $1 billion in nonconvertible debt during the previous three years, or (4) the date on which we are deemed to be a large accelerated filer under the rules of the SEC.

In addition, as an "emerging growth company" the JOBS Act allows us to delay adoption of new or revised accounting pronouncements applicable to public companies until such pronouncements are made applicable to private companies. We have elected to use this extended transition period under the JOBS Act. As a result, our financial statements may not be comparable to the financial statements of issuers who are required to comply with the effective dates for new or revised accounting standards that are applicable to public companies, which may make comparison of our financials to those of other public companies more difficult.

We do not intend to pay dividends on our common stock and, consequently, your ability to achieve a return on your investment will depend on appreciation in the price of our common stock.

We have never declared or paid any cash dividend on our common stock and do not currently intend to do so in the foreseeable future. We currently anticipate that we will retain future earnings for the development, operation, and expansion of our business, and do not anticipate declaring or paying any cash dividends in the foreseeable future. Therefore, the success of an investment in shares of our common stock will depend upon any future appreciation in their value. There is no guarantee that shares of our common stock will appreciate in value or even maintain the price at which you purchased them.

If securities or industry analysts do not publish or cease publishing research or reports or publish misleading, inaccurate, or unfavorable research about us, our business or our market, our stock price, and trading volume could decline.

The trading market for our common stock will be influenced by the research and reports that securities or industry analysts publish about us, our business, our market, or our competitors. If one or more of the analysts who covers us downgrades our stock or publishes inaccurate or unfavorable research about our business, or provides more favorable relative recommendations about our competitors, our stock price would likely decline. If one or more of these analysts ceases coverage of us or fails to publish reports on us regularly, demand for our stock could decrease, which could cause our stock price or trading volume to decline.

Item 2. Unregistered Sales of Equity Securities and Use of Proceeds.

None.

Use of Proceeds from our Public Offering of Common Stock

On June 25, 2018, we closed our initial public offering, in which we issued and sold 6,399,999 shares of common stock at a public offering price of $16.00 per share, and issued an additional 959,999 shares of common stock at a price of $16.00 per share pursuant to the exercise of the underwriters' over-allotment option. All of the shares of common stock issued and sold in our initial public offering were registered under the Securities Act pursuant to a registration statement on Form S-1 (Registration No. 333-225150), which was declared effective by the SEC on June 20, 2018. J.P. Morgan, Cowen, Leerink Partners, and BMO Capital Markets acted as joint book-running managers for the offering. The aggregate gross proceeds to us from our initial public offering, inclusive of the over-allotment exercise, were $117.8 million.

The aggregate net proceeds to us from the public offering, inclusive of the over-allotment exercise, were approximately $106.5 million, after deducting underwriting discounts and commissions and other offering expenses payable by us of approximately $3.0 million. No offering expenses were paid directly or indirectly to any of our directors or officers (or their associates) or persons owning 10% or more of any class of our equity securities or to any other affiliates.

As of September 30, 2018, none of the net offering proceeds from the IPO had been used. We are holding the net proceeds from the IPO in cash and cash equivalents. As described in the Prospectus, we expect to use the net proceeds from our IPO to fund our ongoing Phase 2 clinical studies of NYX-2925 through completion, to advance NYX-783 through completion of Phase 1 clinical development and our planned Phase 2 clinical study, to advance NYX-458 for the treatment of Parkinson's disease cognitive impairment through completion of Phase 1 clinical development and into our planned Phase 2 clinical study, and to explore NMDAr-dependent biomarkers and develop any additional product candidates.

Item 3. Defaults Upon Senior Securities.

Not applicable.

Item 4. Mine Safety Disclosures.

Not applicable.

Item 5. Other Information.

None.

Item 6. Exhibits.

EXHIBIT INDEX

Exhibit Number	Description
3.1	Amended and Restated Certificate of Incorporation of the Registrant (Incorporated by reference to Exhibit 3.1 to our Current Report on Form 8-K (File No. 001-38535) filed with the SEC on June 25, 2018)
3.2	Amended and Restated Bylaws of the Registrant (as currently in effect) (Incorporated by reference to Exhibit 3.2 to our Current Report on Form 8-K (File No. 001-38535) filed with the SEC on June 25, 2018)
31.1*	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as amended
31.2*	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as amended
32.1+	Certification of Principal Executive Officer and Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
101.INS*	XBRL Instance Document
101.SCH*	XBRL Taxonomy Extension Schema Document
101.CAL*	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF*	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB*	XBRL Taxonomy Extension Label Linkbase Document
101.PRE*	XBRL Taxonomy Extension Presentation Linkbase Document

* Filed herewith.

\+ The certifications furnished in Exhibit 32.1 hereto are deemed to be furnished with this Quarterly Report on Form 10-Q and will not be deemed to be "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, except to the extent that the Registrant specifically incorporates it by reference.

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.

APTINYX INC.

Date: November 13, 2018

By: /s/ Norbert G. Riedel
Norbert G. Riedel
President and Chief Executive Officer
(Principal executive officer)

Date: November 13, 2018

By: /s/ Ashish Khanna
Ashish Khanna
Chief Financial Officer and Chief Business Officer
(Principal financial and accounting officer)

EXHIBIT 31.1

CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER PURSUANT TO RULE 13a-14(a) / 15d-14(a) OF THE SECURITIES EXCHANGE ACT OF 1934, AS AMENDED

I, Norbert G. Riedel, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q for the period ended September 30, 2018 of Aptinyx 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)) 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. (Paragraph omitted pursuant to SEC Release Nos. 33-8238/34-47986 and 33-8392/34-49313);

    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 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.

Dated: November 13, 2018

/s/ Norbert G. Riedel

Norbert G. Riedel
President and Chief Executive Officer
(Principal Executive Officer)

EXHIBIT 31.2

CERTIFICATION OF PRINCIPAL FINANCIAL OFFICER PURSUANT TO RULE 13a-14(a) / 15d-14(a) OF THE SECURITIES EXCHANGE ACT OF 1934, AS AMENDED

I, Ashish Khanna, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q for the period ended September 30, 2018 of Aptinyx 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)) 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. (Paragraph omitted pursuant to SEC Release Nos. 33-8238/34-47986 and 33-8392/34-49313);

    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 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.

Dated: November 13, 2018

/s/ Ashish Khanna

Ashish Khanna
Chief Financial Officer and Chief Business Officer
(Principal Financial and Accounting Officer)

EXHIBIT 32.1*

CERTIFICATIONS OF PRINCIPAL EXECUTIVE OFFICER AND PRINCIPAL FINANCIAL OFFICER 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 on Form 10-Q of Aptinyx Inc. (the "Company") for the quarter ended September 30, 2018 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned hereby certify, pursuant to 18 U.S.C. Section 1350, that, to the best of their knowledge:

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

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

/s/ Norbert G. Riedel
Norbert G. Riedel
President and Chief Executive Officer
(Principal Executive Officer)

Dated: November 13, 2018

/s/ Ashish Khanna
Ashish Khanna
Chief Financial Officer and Chief Business Officer
(Principal Financial and Accounting Officer)

Dated: November 13, 2018

* This certification shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, or otherwise subject to the liability of that section, nor shall it be deemed to be incorporated by reference into any filing under the Securities Act of 1933 or the Securities Exchange Act of 1934.