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

FORM 10-Q

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

For the quarterly period ended September 30, 2019

OR

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

For the transition period from _____ to _____

Commission File Number 001-37635

AXSOME THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction of incorporation or organization)

45-4241907
(I.R.S. Employer Identification No.)

200 Broadway
3rd Floor
New York, New York
(Address of principal executive offices)

10038
(Zip Code)

Registrant's telephone number, including area code: (212) 332-3241

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

None

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 and posted pursuant to Rule 405 of Regulation S-T during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes No

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

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

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

<u>Title of each class:</u>	<u>Trading Symbol(s)</u>	<u>Name of each exchange on which registered:</u>
Common Stock, Par Value \$0.0001 Per Share	AXSM	The Nasdaq Global Market

There were 34,508,626 shares of the registrant's common stock, \$0.0001 par value, outstanding as of November 1, 2019.

**AXSOME THERAPEUTICS, INC.
QUARTERLY REPORT ON FORM 10-Q
FOR THE QUARTER ENDED SEPTEMBER 30, 2019**

TABLE OF CONTENTS

	<u>Page</u>
CAUTIONARY NOTE REGARDING FORWARD LOOKING STATEMENTS	3
PART I — FINANCIAL INFORMATION	
ITEM 1 Financial Statements	4
ITEM 2 Management’s Discussion and Analysis of Financial Condition and Results of Operations	22
ITEM 3 Quantitative and Qualitative Disclosure About Market Risk	35
ITEM 4 Controls and Procedures	35
PART II — OTHER INFORMATION	
ITEM 1 Legal Proceedings	36
ITEM 1A Risk Factors	36
ITEM 6 Exhibits	97
Signatures	99

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

Certain matters discussed in this report, including matters discussed under the caption “Management’s Discussion and Analysis of Financial Condition and Results of Operations,” may constitute forward-looking statements for purposes of the Securities Act of 1933, as amended, or the Securities Act, and the Securities Exchange Act of 1934, as amended, or the Exchange Act, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from the future results, performance or achievements expressed or implied by such forward-looking statements. The words “anticipate,” “believe,” “estimate,” “may,” “expect” and similar expressions are generally intended to identify forward-looking statements. Our actual results may differ materially from the results anticipated in these forward-looking statements due to a variety of factors, including, without limitation, those discussed under the captions “Risk Factors,” “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and elsewhere in this report, as well as other factors which may be identified from time to time in our other filings with the Securities and Exchange Commission, or the SEC, or in the documents where such forward-looking statements appear. All written or oral forward-looking statements attributable to us are expressly qualified in their entirety by these cautionary statements. Such forward-looking statements include, but are not limited to, statements about:

- our expectations for increases or decreases in expenses;
- our expectations for the clinical and preclinical development, manufacturing, regulatory approval, and commercialization of our pharmaceutical product candidates or any other products that we may acquire or in-license;
- our estimates of the sufficiency of our existing capital resources combined with future anticipated cash flows to finance our operating requirements;
- our expectations for incurring capital expenditures to expand our research and development and manufacturing capabilities;
- our expectations for generating revenue or becoming profitable on a sustained basis;
- our expectations or ability to enter into marketing and other partnership agreements;
- our expectations or ability to enter into product acquisition and in-licensing transactions;
- our expectations or ability to build our own commercial infrastructure to manufacture, market and sell our product candidates;
- our expected losses;
- our ability to obtain and maintain intellectual property protection for our product candidates;
- the acceptance of our products by doctors, patients, or payors;
- our stock price and its volatility;
- our ability to attract and retain key personnel;
- the performance of our third-party manufacturers;
- our expectations for future capital requirements; and
- our ability to successfully implement our strategy.

The forward-looking statements contained in this report reflect our views and assumptions only as of the date that this report is signed. Except as required by law, we assume no responsibility for updating any forward-looking statements.

We qualify all of our forward-looking statements by these cautionary statements. In addition, with respect to all of our forward-looking statements, we claim the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995.

PART I. FINANCIAL INFORMATION

ITEM 1. FINANCIAL STATEMENTS

Axsome Therapeutics, Inc.
Consolidated Balance Sheets

	September 30, 2019 (Unaudited)	December 31, 2018
Assets		
Current assets:		
Cash and cash equivalents	\$ 43,641,861	\$ 13,968,742
Prepaid and other current assets	594,345	1,246,360
Total current assets	44,236,206	15,215,102
Equipment, net	34,554	51,832
Other assets	168,969	112,345
Total assets	<u>\$ 44,439,729</u>	<u>\$ 15,379,279</u>
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	\$ 9,447,359	\$ 3,687,245
Accrued expenses and other current liabilities	8,413,107	3,843,299
Loan payable, current portion	648,523	3,291,394
Total current liabilities	18,508,989	10,821,938
Loan payable, long-term	19,108,144	3,619,420
Total liabilities	<u>37,617,133</u>	<u>14,441,358</u>
Stockholders' equity:		
Preferred stock, \$0.0001 par value per share (10,000,000 shares authorized, none issued and outstanding at September 30, 2019 and December 31, 2018, respectively)	—	—
Common stock, \$0.0001 par value per share (150,000,000 shares authorized, 34,496,846 and 30,087,213 shares issued and outstanding at September 30, 2019 and December 31, 2018, respectively)	3,450	3,009
Additional paid-in capital	157,907,655	108,485,219
Accumulated deficit	(151,088,509)	(107,550,307)
Total stockholders' equity	6,822,596	937,921
Total liabilities and stockholders' equity	<u>\$ 44,439,729</u>	<u>\$ 15,379,279</u>

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

Axsome Therapeutics, Inc.
Consolidated Statements of Operations
(Unaudited)

	Three months ended September 30,		Nine months ended September 30,	
	2019	2018	2019	2018
Operating expenses:				
Research and development	\$ 15,835,573	\$ 6,040,780	\$ 34,441,796	\$ 16,343,823
General and administrative	3,111,662	2,202,679	8,375,131	7,052,439
Total operating expenses	18,947,235	8,243,459	42,816,927	23,396,262
Loss from operations	(18,947,235)	(8,243,459)	(42,816,927)	(23,396,262)
Interest and amortization of debt discount (expense)	(327,825)	(270,933)	(860,723)	(878,605)
Tax credit	139,448	217,418	139,448	217,418
Change in fair value of warrant liability	—	15,000	—	2,689,000
Net loss	\$ (19,135,612)	\$ (8,281,974)	\$ (43,538,202)	\$ (21,368,449)
Net loss per common share, basic and diluted	\$ (0.56)	\$ (0.31)	\$ (1.29)	\$ (0.83)
Weighted average common shares outstanding, basic and diluted	34,445,489	26,325,904	33,771,671	25,875,783

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

Axsome Therapeutics, Inc.
Consolidated Statements of Stockholders' Equity
(Unaudited)

	Common stock		Additional paid-in capital	Accumulated deficit	Total stockholders' equity
	Shares	Amount			
Balance at December 31, 2017	25,492,992	2,549	93,299,517	(76,584,843)	16,717,223
Stock-based compensation	—	—	534,570	—	534,570
Issuance of common stock upon financing	56,900	6	139,914	—	139,920
Net loss	—	—	—	(4,805,559)	(4,805,559)
Balance at March 31, 2018	25,549,892	\$ 2,555	\$ 93,974,001	\$ (81,390,402)	\$ 12,586,154
Stock-based compensation	—	—	474,659	—	474,659
Issuance of common stock upon financing	702,970	70	2,228,932	—	2,229,002
Net loss	—	—	—	(8,280,916)	(8,280,916)
Balance at June 30, 2018	26,252,862	\$ 2,625	\$ 96,677,592	\$ (89,671,318)	\$ 7,008,899
Stock-based compensation	—	—	392,665	—	392,665
Issuance of common stock upon exercise of warrants	25,000	3	32,497	—	32,500
Issuance of common stock upon financing	180,800	55	1,590,612	—	1,590,667
Net loss	—	—	—	(8,281,974)	(8,281,974)
Balance at September 30, 2018	26,458,662	\$ 2,683	\$ 98,693,366	\$ (97,953,292)	\$ 742,757
Balance at December 31, 2018	30,087,213	3,009	108,485,219	(107,550,307)	937,921
Stock-based compensation	—	—	1,256,310	—	1,256,310
Issuance of common stock upon exercise of options	52,819	5	410,157	—	410,162
Issuance of warrants upon debt financing	—	—	426,000	—	426,000
Issuance of common stock upon financing	3,164,015	316	24,983,366	—	24,983,682
Net loss	—	—	—	(10,640,376)	(10,640,376)
Balance at March 31, 2019	33,304,047	\$ 3,330	\$ 135,561,052	\$ (118,190,683)	\$ 17,373,699
Stock-based compensation	—	—	888,556	—	888,556
Issuance of common stock upon exercise of options	59,720	6	205,330	—	205,336
Issuance of common stock upon exercise of warrants	24,389	2	144,868	—	144,870
Issuance of warrants upon debt financing	—	—	(39,000)	—	(39,000)
Issuance of common stock upon financing	942,285	95	19,471,603	—	19,471,698
Net loss	—	—	—	(13,762,214)	(13,762,214)
Balance at June 30, 2019	34,330,441	\$ 3,433	\$ 156,232,409	\$ (131,952,897)	\$ 24,282,945
Stock-based compensation	—	—	1,156,435	—	1,156,435
Issuance of common stock upon exercise of options	129,218	13	483,825	—	483,838
Issuance of common stock upon exercise of warrants	37,187	4	34,986	—	34,990
Net loss	—	—	—	(19,135,612)	(19,135,612)
Balance at September 30, 2019	34,496,846	\$ 3,450	\$ 157,907,655	\$ (151,088,509)	\$ 6,822,596

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

Axsome Therapeutics, Inc.
Consolidated Statements of Cash Flows
(Unaudited)

	Nine months ended September 30,	
	2019	2018
Cash flows from operating activities		
Net loss	\$ (43,538,202)	\$ (21,368,449)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation expense	3,301,301	1,401,894
Amortization of debt discount	471,742	293,580
Change in fair value of warrants	—	(2,689,000)
Depreciation	31,938	36,728
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	652,015	554,749
Other assets	(56,624)	70,596
Accounts payable	5,760,114	731,913
Accrued expenses and other current liabilities	4,569,808	708,237
Net cash used in operating activities	<u>(28,807,908)</u>	<u>(20,259,752)</u>
Cash flows from investing activities		
Purchases of equipment	(14,660)	(32,696)
Net cash used in investing activities	<u>(14,660)</u>	<u>(32,696)</u>
Cash flows from financing activities		
Proceeds from issuance of common stock upon financing, net	44,455,380	3,959,589
Proceeds from issuance of term loan	20,000,000	—
Repayment of principal on term loan	(7,238,889)	(2,500,000)
Proceeds from issuance of common stock upon exercise of options	1,099,336	—
Proceeds from issuance of common stock upon exercise of warrants	179,860	32,500
Net cash (used in) provided by financing activities	<u>58,495,687</u>	<u>1,492,089</u>
Net (decrease) increase in cash	29,673,119	(18,800,359)
Cash at beginning of period	13,968,742	34,021,123
Cash at end of period	<u>\$ 43,641,861</u>	<u>\$ 15,220,764</u>
Supplemental disclosures of cash flow information:		
Interest paid	\$ 979,167	\$ 585,025
Supplemental disclosures of non-cash financing activity:		
Issuance of warrants in connection with debt financing	\$ 387,000	\$ —

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

Axsome Therapeutics, Inc.
Notes to Consolidated Financial Statements (Unaudited)

Note 1. Nature of Business and Basis of Presentation

Axsome Therapeutics, Inc. (“Axsome” or the “Company”) is a clinical-stage biopharmaceutical company developing novel therapies for central nervous system (“CNS”) disorders for which there are limited treatment options. By focusing on this therapeutic area, the Company is addressing significant and growing markets where current treatment options are limited or inadequate. The Company’s core CNS portfolio includes four product candidates, AXS-05, AXS-07, AXS-09, and AXS-12, which are being developed for multiple indications. The Axsome Pain and Primary Care business unit (“Axsome PPC”) houses Axsome’s pain and primary care assets, including AXS-02 and AXS-06, and intellectual property which covers these and related product candidates and molecules being developed by Axsome and others. The Company aims to become a fully integrated biopharmaceutical company that develops and commercializes differentiated therapies that expand the treatment options available to caregivers and improve the lives of patients living with CNS disorders. The Company was incorporated on January 12, 2012 in the State of Delaware and now has operations in the United States and Australia.

The accompanying unaudited interim consolidated financial statements have been prepared by the Company in accordance with accounting principles generally accepted in the United States (“U.S. GAAP”) for interim information and pursuant to the rules and regulations of the Securities and Exchange Commission (the “SEC”) for reporting on Form 10-Q. Accordingly, certain information and footnote disclosures normally included in financial statements prepared in accordance with U.S. GAAP have been condensed or omitted pursuant to such rules and regulations. These unaudited interim consolidated financial statements should be read in conjunction with the audited financial statements and related notes included in the Company’s Annual Report on Form 10-K for the year ended December 31, 2018 filed with the SEC on March 15, 2019.

In the opinion of management, the unaudited interim consolidated financial statements reflect all adjustments, which are normal recurring adjustments, necessary for the fair presentation of the financial information for the interim periods. The results of operations for the three and nine months ended September 30, 2019 are not necessarily indicative of the operating results for the full fiscal year or any future period.

Liquidity and Capital Resources

The Company has incurred operating losses since its inception, and expects to continue to incur operating losses for the foreseeable future and may never become profitable. As of September 30, 2019, the Company had an accumulated deficit of \$151.1 million.

The Company’s primary sources of cash have been proceeds from the issuance and sale of its common stock in public offerings. The Company has not yet commercialized any of its product candidates and cannot be sure if it will ever be able to do so. The Company’s ability to achieve profitability depends on a number of factors, including its ability to obtain regulatory approval for its product candidates, successfully complete any post-approval regulatory obligations and successfully commercialize its product candidates alone or in partnership. The Company may continue to incur substantial operating losses even if it begins to generate revenues from its product candidates.

The Company believes its existing cash will be sufficient to fund its anticipated operating cash requirements for at least twelve months following the date of this filing. The actual amount of cash that the Company will need to operate is subject to many factors, including, but not limited to, the timing, design and conduct of clinical trials for its product candidates. The Company is dependent upon significant future financing to provide the cash necessary to execute its current operations, including the commercialization of any of its product candidates.

The Company’s common stock is listed on the Nasdaq Global Market and trades under the symbol “AXSM”.

Note 2. Summary of Significant Accounting Policies

Significant Risks and Uncertainties

The Company's operations are subject to a number of factors that can affect its operating results and financial condition. Such factors include, but are not limited to: the results of clinical testing and trial activities of the Company's product candidates; the Company's ability to obtain regulatory approval to market its products, if approved; competition from products manufactured and sold or being developed by other companies; the price of, and demand for, the Company's products, if approved; the Company's ability to negotiate favorable licensing or other manufacturing and marketing agreements for its products, if approved; and the Company's ability to raise additional financing. If the Company does not successfully commercialize any of its product candidates, it will be unable to generate recurring product revenue or achieve and maintain profitability.

Use of Estimates

Management considers many factors in developing the estimates and assumptions that are used in the preparation of these financial statements. Management must apply significant judgment in this process. In addition, other factors may affect estimates, including expected business and operational changes, sensitivity and volatility associated with the assumptions used in developing estimates, and whether historical trends are expected to be representative of future trends. The estimation process often may yield a range of potentially reasonable estimates of the ultimate future outcomes and management must select an amount that falls within that range of reasonable estimates. This process may result in actual results differing materially from those estimated amounts used in the preparation of the financial statements if these results differ from historical experience, or other assumptions do not turn out to be substantially accurate, even if such assumptions are reasonable when made. In preparing these financial statements, management used significant estimates in the following areas, among others: stock-based compensation expense; the determination of the fair value of the warrants; the accounting for research and development costs; and the recoverability of the Company's net deferred tax assets and related valuation allowance.

Foreign Currency Translation

Expenses denominated in foreign currency are translated into U.S. dollars at the exchange rate on the date the expense is incurred. Assets and liabilities of foreign operations are translated at period-end exchange rates. The effect of exchange rate fluctuations on translating foreign currency into U.S. dollars is included in the Statements of Operations and is not material to the Company's financial statements.

Segment and Geographic Information

Operating segments are defined as components of an enterprise for which separate discrete information is available for evaluation by the chief operating decision maker or decision-making group, in deciding how to allocate resources and in assessing performance. The Company views its operations and manages its business as one operating segment, which is the business of developing novel therapies for the management of CNS disorders.

Cash Equivalents

The Company considers all highly liquid investments that have maturities of three months or less when acquired to be cash equivalents. The Company's cash and cash equivalents includes holdings in checking and overnight sweep accounts. The Company's cash equivalents, which are money market funds held in a sweep account, are measured at fair value on a recurring basis. As of September 30, 2019, the balance of cash and cash equivalents was \$43.6 million, which approximates fair value and was determined based upon Level 1 inputs. The sweep account is valued using quoted market prices with no valuation adjustments applied. Accordingly, these securities are categorized as Level 1.

Concentration of Credit Risk

Financial instruments that potentially subject the Company to a concentration of credit risk consist of cash. The Company maintains its cash at financial institutions, which at times, exceed federally insured limits. At September 30, 2019, the majority of the Company's cash was held by one financial institution and the amount on deposit was in excess of Federal Deposit Insurance Corporation insurance limits. The Company has not recognized any losses from credit risks on such accounts since inception. The Company believes it is not exposed to significant credit risk on cash.

Fair Value of Financial Instruments

Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants at the measurement date. Assets and liabilities that are measured at fair value are reported using a three-level fair value hierarchy that prioritizes the inputs used to measure fair value. This hierarchy maximizes the use of observable inputs and minimizes the use of unobservable inputs. The three levels of inputs used to measure fair value are as follows:

Level 1—Quoted prices in active markets for identical assets or liabilities that the Company has the ability to access at the measurement date.

Level 2—Inputs other than quoted prices in active markets that are observable for the asset or liability, either directly or indirectly.

Level 3—Inputs that are unobservable for the asset or liability.

To the extent that 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 Company's financial instruments are cash, accounts payable, accrued liabilities, and current and long-term debt. The carrying values for cash, accounts payable and accrued liabilities reported in the accompanying consolidated financial statements approximate their respective fair values due to their short-term maturities. The carrying value of debt, the 2019 Term Loan (see Note 4 – Loan and Security Agreement), is estimated to approximate its fair value as the interest rate approximates the market rate for loans with similar terms and risk characteristics.

Debt Issuance Costs

Debt issuance costs consist of costs incurred in obtaining long-term financing. These costs are classified on the consolidated balance sheet as a direct deduction from the carrying amount of the related debt liability. These expenses are deferred and amortized as part of interest expense in the consolidated statement of operations using the effective interest rate method over the term of the debt agreement.

Equipment

Equipment consists primarily of computer equipment and is recorded at cost. Equipment is depreciated on a straight-line basis over its estimated useful life, which the Company estimates to be three years. When equipment is sold or otherwise disposed of, the cost and related accumulated depreciation are removed from the accounts and the resulting gain or loss is included in operating expenses.

Research and Development Costs

Research and development expenses primarily consist of costs incurred in performing research and development activities, including preclinical studies, clinical trials, manufacturing costs, employee salaries and benefits, stock-based compensation expense, contract services, including external research and development expenses incurred under arrangements with third parties, such as contract research organizations (“CROs”), facilities costs, overhead costs, depreciation, and other related costs.

Generally, research and development costs are expensed as incurred. Nonrefundable advance payments for goods or services that will be used or rendered for future research and development activities are deferred and amortized over the period that the goods are delivered or the related services are performed, subject to an assessment of recoverability. The Company makes estimates of costs incurred in relation to clinical site costs. The Company analyzes the progress of clinical trials, including levels of patient enrollment, invoices received and contracted costs when evaluating the adequacy of the amount expensed and the related prepaid asset and accrued liability. Significant judgments and estimates must be made and used in determining the accrued balance and expense in any accounting period. The Company reviews and accrues clinical trial study expenses based on work performed and relies upon estimates of those costs applicable to the stage of completion of a study. With respect to clinical site costs, the financial terms of these agreements are subject to negotiation and vary from contract to contract. Payments under these contracts may be uneven, and depend on factors such as the achievement of certain events, the successful recruitment of patients, the completion of portions of the clinical trial or similar conditions. The objective of the Company’s policy is to match the recording of expenses in its financial statements to the actual services received and efforts expended. As such, expense accruals related to clinical site costs are recognized based on the Company’s estimate of the degree of completion of the event or events specified in the specific clinical study or trial contract.

Income Taxes

Income taxes are accounted for under the asset and liability method. Under this method, deferred tax assets and liabilities are recognized for the future tax consequences attributable to the differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases, operating losses, and tax credit carryforwards. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect of a change in tax rates on deferred tax assets and liabilities is recognized in income in the period that includes the enactment date. 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 estimates an annual effective tax rate of 0% for the year ending December 31, 2019 and has not recorded an income tax benefit for the nine months ended September 30, 2019 and 2018 since it determined that a full valuation allowance is required against the Company’s deferred tax assets.

The Company recognizes the tax benefit from an uncertain tax position only if it is more likely than not to be sustained upon examination based on the technical merits of the position as well as consideration of the available facts and circumstances. When uncertain tax positions exist, the Company recognizes the tax benefit of tax positions to the extent that the benefit will more likely than not be realized. As of September 30, 2019, the Company does not believe any material uncertain tax positions are present. In the event the Company determines that accrual of interest or penalties are necessary in the future, the amount will be presented as a component of income tax expense.

Stock-Based Compensation

For stock options issued, the Company estimates the grant date fair value of each option using the Black-Scholes option pricing model. The Black-Scholes model takes into account the expected volatility of the Company's common stock, expected dividends of the Company's common stock, the risk-free interest rate, the estimated life of the option, the closing market price of the Company's common stock and the exercise price. The estimates utilized in the Black-Scholes calculation involve inherent uncertainties and the application of management's judgment. In addition, the Company recognizes expense for equity awards forfeitures as they occur. For awards subject to service-based vesting conditions, the Company recognizes stock-based compensation expense on a straight-line basis over the requisite service period, which is generally the vesting term. For awards subject to performance-based vesting conditions, the Company recognizes stock-based compensation expense using the accelerated attribution method when it is probable that the performance condition will be achieved. The expense related to the stock-based compensation is recorded within the same financial statement line item as the grantee's cash compensation.

The Company's policy upon exercise of stock options is that shares will be issued as new shares from the Company's 2015 Omnibus Incentive Compensation Plan available share pool.

Basic and Diluted Net Loss per Common Share

Basic net loss per share of common stock is computed by dividing net loss by the weighted average number of shares of common stock outstanding during the period. Diluted net loss per share of common stock includes the effect, if any, from the potential exercise or conversion of securities, such as warrants and stock options, which would result in the issuance of incremental shares of common stock. As the impact of these items is anti-dilutive during periods of net loss, there was no difference between basic and diluted net loss per share of common stock for the three and nine months ended September 30, 2019 and 2018.

Recent Accounting Pronouncements

In February 2016, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") No. 2016-02, *Leases (Topic 842)*, which supersedes FASB Topic 840, *Leases (Topic 840)*, requires that assets and liabilities arising under leases be recognized on the balance sheet as well as additional quantitative and qualitative disclosures that provide the amount, timing, and uncertainty of cash flows related to lease agreements. In July 2018, the FASB also issued ASU No. 2018-11, *Leases (Topic 842)*, which provides (1) optional transition method that entities can use when adopting the standard and (2) a practical expedient that permits lessors to not separate nonlease components from the associated lease component if certain conditions are met. The standard is effective for annual and interim periods beginning after December 15, 2018, with early adoption permitted upon issuance. The Company elected to use the transition method approved by the FASB in accordance with ASU No. 2018-11, *Leases*, which allows companies to apply the provisions of the new leasing standard as of January 1, 2019, without adjusting the comparative periods presented by recognizing a cumulative-effect adjustment to the opening balance of retained earnings. The Company applied a policy election to exclude short-term leases from balance sheet recognition and also elected certain practical expedients at adoption. As permitted under these expedients, the Company did not reassess whether existing contracts are or contain leases, the lease classification for any existing leases, initial direct costs for any existing lease and whether existing land easements and rights of way, that were not previously accounted for as leases, are or contain a lease. The Company has adopted this guidance effective January 1, 2019. The Company evaluated its contracts and concluded that the contracts are not leases and do not contain a lease and the adoption of this guidance did not impact its financial statements.

In August 2016, the FASB issued ASU No. 2016-15, *Statement of Cash Flows (Topic 230) – Classification of Certain Cash Receipts and Cash Payments*, which is guidance to address diversity in practice with respect to how certain cash receipts and cash payments are presented and classified in the statement of cash flows. The updated guidance addresses eight specific cash flow issues with the objective of reducing the existing diversity that occurs in practice. The guidance is effective for annual and interim periods beginning after December 15, 2017. The Company has adopted this guidance effective January 1, 2018 and the adoption of the guidance did not have a material impact on the Company's financial statements.

In May 2017, the FASB issued ASU No. 2017-09, *Compensation-Stock Compensation (Topic 718): Scope of Modification Accounting*. ASU 2017-09 provides clarity and reduces both (1) diversity in practice and (2) cost and complexity when applying the guidance in Topic 718, to a change to the terms or conditions of a share-based payment award. The amendments in ASU 2017-09 should be applied prospectively to an award modified on or after the adoption date. This ASU is effective for fiscal years beginning after December 15, 2017, including interim periods within those years. The Company has adopted this guidance effective January 1, 2018 and the adoption of the guidance did not have a material impact on the Company's financial statements.

In June 2018, the FASB issued ASU No. 2018-07, *Compensation-Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting*, to simplify the accounting for share-based payments to nonemployees by aligning it with the accounting for share-based payments to employees, with certain exceptions. The standard will be effective for annual and interim periods beginning after December 15, 2018. The Company early adopted this guidance effective October 1, 2018 and the adoption did not have a material impact on the Company's financial statements.

In July 2018, the FASB issued ASU No. 2018-09, *Codification Improvements*, which provides technical corrections, clarifications, and other improvements to several topics in the FASB Accounting Standard Codification. The transition and effective date guidance is based on the facts and circumstances of each amendment. Some of the amendments do not require transition guidance and were effective upon issuance of the ASU. Amendments that do not have transition guidance are effective for annual periods beginning after December 15, 2018. The Company has adopted this guidance effective January 1, 2019 and the adoption of the guidance did not have a material impact on the Company's financial statements.

In August 2018, the SEC adopted the final rule under SEC Release No. 33-10532, *Disclosure Update and Simplification*, amending certain disclosure requirements that were redundant, duplicative, overlapping, outdated or superseded. The changes are generally expected to reduce or eliminate certain disclosures; however, the amendments did expand interim period disclosure requirements related to changes in stockholders' equity. The final rule was effective on November 5, 2018. The Company adopted this guidance on its effective date and presented the changes in shareholders' equity in the interim financial statements in quarterly reports on Form 10-Q. See the consolidated statement of stockholders' equity.

In August 2018, the FASB issued ASU No. 2018-13, *Fair Value Measurement (Topic 820): Disclosure Framework-Changes to the Disclosure Requirements for Fair Value Measurement*, which modifies, removes and adds certain disclosure requirements on fair value measurements based on the FASB Concepts Statement, *Conceptual Framework for Financial Reporting-Chapter 8: Notes to the Financial Statements*. The amendments on changes in unrealized gains and losses, the range and weighted average of significant unobservable inputs used to develop Level 3 fair value measurements and the narrative description of measurement uncertainty should be applied prospectively for only the most recent interim or annual period presented in the initial fiscal year of adoption. All other amendments should be applied retrospectively to all periods presented upon their effective date. The ASU is effective for fiscal years beginning after December 15, 2019, including interim periods within those years. The Company is currently evaluating the potential impact of the new guidance.

Note 3. Accrued Expenses and Other Current Liabilities

At September 30, 2019 and December 31, 2018 accrued expenses and other current liabilities consisted of the following:

	September 30, 2019	December 31, 2018
Research and development	\$ 6,625,638	\$ 2,266,285
Accrued compensation	995,181	1,051,401
Other	792,288	525,613
Total	<u>\$ 8,413,107</u>	<u>\$ 3,843,299</u>

Note 4. Loan and Security Agreement

Current Term Loan

2019 Term Loan

In March 2019, the Company entered into a \$24.0 million growth capital term loan facility (the “2019 Term Loan”) with Silicon Valley Bank (“SVB”) and WestRiver Innovation Lending Fund VIII, L.P (“WestRiver”). The two-tranche loan agreement consists of an initial \$20.0 million tranche (the “Term A Loan Advance”), which was funded upon closing, with the remaining \$4.0 million (the “Term B Loan Advance”) initially available to be drawn, at the Company’s option, subject to the achievement of positive data, on or prior to August 15, 2019 (which was extended to December 31, 2019, in connection with the First Amendment to the 2019 Term Loan, as discussed below), with respect to the Company’s ongoing Phase 2 clinical trial for AXS-12 in narcolepsy, sufficient to submit a Phase 3 protocol to FDA, provided that the Company has not received any objections from the FDA within thirty days after submission of such Phase 3 protocol (the “Milestone Event”). A portion of the first tranche was used to satisfy the Company’s existing obligations under the 2016 Amended Term Loan (as defined below) with SVB, which consisted of \$5.6 million in outstanding principal balance and \$0.85 million as a final payment fee, and such obligations are considered to be fully repaid and performed.

The loan bears interest at an annual rate equal to the greater of (i) seven and one-half of one percent (7.50%) and (ii) two percent (2%) above the Prime Rate. The loan advances mature in February 2023 and initially had an interest-only payment period of 12 months (which was extended to 18 months in connection with the First Amendment to the 2019 Term Loan, as discussed below), extendable to 18 months upon the drawing of the Term B Loan Advance (which is now extendable to 24 months as a result of the First Amendment to the 2019 Term Loan). Principal payments coming due within twelve months have been classified as current liabilities in the accompanying balance sheet. In addition, the Company was initially required to pay a final payment fee of 6.0% of the principal amount extended on the date of repayment of the 2019 Term Loan (which was increased to 6.3% in connection with the First Amendment to the 2019 Term Loan, as discussed below), which is being accreted and amortized into interest expense using the effective interest rate method over the term of the loan.

The Company could initially prepay all, but not less than all, of the 2019 Term Loan, subject to a prepayment premium of 3.0% of the outstanding principal if prepaid within one year of the effective date of the loan, 2.0% of the outstanding principal if prepaid after the first anniversary of the effective date but on or prior to the second anniversary of the effective date, and 1.0% of the outstanding principal if prepaid after the second anniversary of the effective date. The 2019 Term Loan is collateralized by a security interest in all of the Company’s assets except intellectual property. The Company’s intellectual property is subject to a negative pledge.

First Amendment to the 2019 Term Loan

On July 25, 2019 (the “First Amendment Effective Date”), the Company entered into the first amendment to the 2019 Term Loan (the “First Amendment to the 2019 Term Loan”). Under the First Amendment to the 2019 Term Loan, the interest-only monthly payment period was extended to 18 months after the date of the 2019 Term Loan, which may be further extended to 24 months upon receipt by the Company of the Term B Loan Advance. The Company’s ability to draw down the Term B Loan Advance was extended to December 31, 2019, subject to the Company’s achievement of the Milestone Event prior to or on December 31, 2019. The Term B Loan Advance and the Term A Loan Advance (together, the “Loan Advances”) mature on February 1, 2023 (the “Maturity Date”).

Pursuant to the 2019 Term Loan, as amended by the First Amendment to the 2019 Term Loan, following the interest-only payment period, the Company will begin making monthly payments of principal in equal monthly installments for 30 consecutive months (provided, that, upon the occurrence of the Milestone Event, the repayment schedule will be decreased to 24 consecutive months) and monthly payments of interest, until the Maturity Date. Interest will accrue on the unpaid principal balance of the outstanding Loan Advances at a floating per annum rate equal to the greater of (i) seven and one-half of one percent (7.50%) and (ii) two percent (2.0%) above the prime rate. The First Amendment to the 2019 Term Loan increased the final payment fee, payable upon the Company's repayment of the Loan Advances from 6.0% to 6.3% of the original principal amount of the Loan Advances.

The Company may prepay all, but not less than all of the Loan Advances, subject to a prepayment fee of 3.0% of any amount prepaid prior to the first anniversary of the First Amendment Effective Date, 2.0% of the amount prepaid if the prepayment occurs after the first anniversary of the First Amendment Effective Date through and including the second anniversary of the First Amendment Effective Date, or 1.0% of the amount prepaid if the prepayment occurs after the second anniversary of the First Amendment Effective Date, but prior to the Maturity Date. These percentages are unchanged from the original 2019 Term Loan.

The Company evaluated whether the First Amendment to the 2019 Term Loan entered into in July 2019 represented a debt modification or extinguishment in accordance with ASC 470-50, *Debt – Modifications and Extinguishments*. As the present value of the cash flows under the terms of the First Amendment to the 2019 Term Loan is less than 10% different from the remaining cash flows under the terms of the 2019 Term Loan, the First Amendment to the 2019 Term Loan was accounted for as a debt modification. Therefore, the unamortized balance of debt discount costs incurred in connection with 2019 Term Loan are being amortized through maturity in February 2023 utilizing the effective interest rate method.

Previous Term Loan

Prior to the 2019 Term Loan, the Company had a \$20.0 million Term Loan Agreement with SVB which was executed in November 2016 ("2016 Original Term Loan"). The three-tranche term loan consisted of an initial \$10.0 million tranche triggered upon closing, with the remaining \$10.0 million available to be drawn in two \$5.0 million tranches, at the Company's option, subject to the achievement of certain clinical and financial milestones. The Company did not achieve the conditional criteria to access the second and third tranches before the specified dates and the \$10.0 million in additional term loan advances subsequently expired.

The 2016 Original Term Loan bore interest at an annual rate equal to 4.50% plus the prime rate, which is the greater of 3.50% or the Wall Street Journal prime rate, and was payable monthly. It was to mature in November 2020 and had an interest-only payment period until December 1, 2017, which was extendable to May 2018 upon the drawing of the second tranche. Because the Company did not achieve the conditional criteria to access the second and third term advances before the specified dates, the \$10.0 million in additional term loan advances expired and the Company began to repay principal in December 2017. Following the interest-only payment period, the Company began making monthly payments of principal and interest and such payments would continue until the maturity date. Principal payments coming due within twelve months had been classified as current liabilities in the accompanying balance sheet. In addition to principal and interest payments under the 2016 Original Term Loan, the Company was required to pay a final payment fee of 8.5% of the principal amount extended on the date of repayment of the 2016 Original Term Loan. The Company accrued the final payment fee into interest expense using the effective interest rate method until the entry into the 2019 Term Loan in March 2019, at which time the Company paid SVB \$0.85 million in satisfaction of all final payment fee liabilities due under the 2016 Original Term Loan.

The Company was permitted to prepay all, but not less than all, of the 2016 Original Term Loan subject to a prepayment premium of 3.0% of the outstanding principal if prepaid within two years of the effective date of the loan, 2.0% of the outstanding principal if prepaid during the third year of the loan, and 1.0% of the outstanding principal if prepaid after the third year. The 2016 Original Term Loan was collateralized by a security interest in all of the Company's assets except intellectual property. The Company's intellectual property was subject to a negative pledge.

In November 2018, the Company amended the 2016 Original Term Loan with SVB to provide an additional \$4.0 million growth capital loan. The additional capital was available to be drawn on the amendment effective date which was November 26, 2018 through May 31, 2019, at the Company’s option, conditioned upon the achievement of a clinical milestone, which required the Company’s receipt of positive data of the Company’s Phase 2 clinical trial of AXS-12 for the treatment of narcolepsy, sufficient to submit a Phase 3 protocol to the FDA and to proceed to a Phase 3 trial (“2016 Amended Term Loan”). The financial terms for this additional growth capital were more favorable than those of the 2016 Original Term Loan. All other terms and conditions from the 2016 Original Term Loan agreement remained in place. The additional \$4.0 million growth capital loan had to be drawn by May 31, 2019 and would bear interest at an annual rate equal to the greater of the prime rate plus 2.00%, or 7.25%, if drawn. The Company’s obligations under the 2016 Amended Term Loan, along with the ability of the Company to draw down on the additional \$4.0 million tranche, were considered performed and completed in connection with the establishment of the 2019 Term Loan.

The Company evaluated whether the 2019 Term Loan entered into in March 2019 represented a debt modification or extinguishment in accordance with ASC 470-50, *Debt – Modifications and Extinguishments*. As the present value of the cash flows under the terms of the 2019 Term Loan is less than 10% different from the remaining cash flows under the terms of the 2016 Original Term Loan and the 2016 Amended Term Loan, the 2019 Term Loan was accounted for as a debt modification. Since the borrowing capacity of the 2019 Term Loan is greater than the borrowing capacity from the 2016 Original Term Loan and the 2016 Amended Term Loan, the unamortized balance of debt discount costs incurred in connection with those loans and additional debt discount costs incurred in connection with entry into the 2019 Term Loan, are being amortized through maturity in February 2023 utilizing the effective interest rate method.

Loan Interest Expense and Amortization

The Company incurred interest expense of \$383,334 and \$979,167 for the three and nine months ended September 30, 2019, respectively, as compared to \$182,357 and \$585,025 for the three and nine months ended September 30, 2018, respectively. In addition, amortization of the final payment fee was \$120,322 and \$316,246 for the three and nine months ended September 30, 2019, respectively, as compared to \$63,636 and \$210,399 for the three and nine months ended September 30, 2018, respectively.

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

	September 30, 2019	December 31, 2018
Total Outstanding Debt	\$ 20,000,000	\$ 6,388,889
Add: accreted liability of final payment fee	284,042	663,459
Less: unamortized debt discount, long-term	(509,231)	(99,595)
Less: current portion of long-term debt	(666,667)	(3,333,333)
Loan payable, long-term	<u>\$ 19,108,144</u>	<u>\$ 3,619,420</u>
Current portion of long-term debt	\$ 666,667	\$ 3,333,333
Less: current portion of unamortized debt discount	(18,144)	(41,939)
Loan payable, current portion	<u>\$ 648,523</u>	<u>\$ 3,291,394</u>

In connection with the 2016 Original Term Loan, SVB and Life Science Loans, LLC received warrants to purchase an aggregate 65,228 shares of the Company’s common stock at an exercise price of \$7.41 per share, which are exercisable for seven years from the date of issuance. The warrants were classified as a component of stockholders’ equity. In September 2019, SVB exercised in full the 32,614 warrants it received in connection with the 2016 Original Term Loan via a cashless exercise. The Company issued SVB 24,328 shares of its common stock in connection with the warrant exercise, and did not receive any cash proceeds in connection with the warrant exercise.

Additionally, in connection with the 2016 Amended Term Loan, SVB and WestRiver Innovation Lending Fund VIII, L.P. received warrants to purchase an aggregate 15,750 shares of the Company's common stock at an exercise price of \$3.06 per share, which are exercisable for seven years from the date of issuance. Both of these warrants were classified as a component of stockholders' equity. Prior to entering into the 2019 Term Loan, the fair value of these warrants and the closing costs were recorded as debt discounts and were being amortized using the effective interest rate method over the term of the loan. In August 2019, SVB exercised in full the 7,875 warrants it received in connection with the 2016 Amended Term Loan via a cashless exercise. The Company issued SVB 6,969 shares of its common stock in connection with the warrant exercise, and did not receive any cash proceeds in connection with the warrant exercise.

Due to the debt modification upon entry of the 2019 Term Loan, the unamortized balance of the deferred debt issuance costs incurred with the 2016 Amended Term Loan will continue to be amortized through maturity in February 2023 along with the debt issuance costs of the 2019 Term Loan utilizing the effective interest rate method.

In connection with the 2019 Term Loan, SVB and WestRiver received warrants to purchase an aggregate 70,000 shares of the Company's common stock at a price per share equal to \$8.10 (the "March 2019 Warrants"). The warrants would initially be earned based upon the usage of the facility and are exercisable until March 4, 2026. The warrants were classified as a component of stockholder's equity, of which 58,332 warrants were immediately exercisable and the remaining 11,668 warrants could be earned based on usage of the second tranche of the 2019 Term Loan. The additional warrants were initially immediately exercisable if and when the Term B Loan Advance was funded (however, the March 2019 Warrants were amended in connection with the First Amendment to the 2019 Term Loan, as discussed below). The relative fair value of the warrants of approximately \$0.4 million at the time of issuance, which was determined using the Black-Scholes option-pricing model, was recorded as additional paid-in capital and reduced the carrying value of the debt. The discount on the debt is being amortized to interest expense over the term of the debt utilizing the effective interest rate method.

In connection with the First Amendment to the 2019 Term Loan, the March 2019 Warrants were amended to fix the number of shares that may be issued upon exercise of each such March 2019 Warrant at 29,167 shares of common stock, and SVB and WestRiver were issued new warrants (the "July 2019 Warrants"), which become exercisable only upon funding of the Term B Loan Advance, to purchase 5,750 shares of the Company's common stock at a price per share equal to \$25.71. The July 2019 Warrants replace the portion of the March 2019 Warrants that could originally be earned by SVB and WestRiver upon funding of the Term B Loan Advance. The July 2019 Warrants, if earned, will be exercisable until July 24, 2026 and will be exercised automatically on a net issuance basis if not exercised prior to the expiration date and if the then-current fair market value of one share of the Company's common stock is greater than the exercise price then in effect.

Amortization of the debt discount in relation to warrants issued as described above was \$56,602 and \$155,496 for the three and nine months ended September 30, 2019, respectively, as compared to \$24,940 and \$83,181 for three and nine months ended September 30, 2018, respectively.

Scheduled Principal Payments on Outstanding Debt, as of September 30, 2019, are as follows:

2020	\$ 2,666,667
2021	8,000,000
2022	8,000,000
2023	1,333,333
Total principal payments outstanding	<u>\$ 20,000,000</u>

The Company was in compliance with all covenants and requirements of its financing arrangements as of and during the nine months ended September 30, 2019.

Note 5. Net Loss per Common Share

The following table sets forth the computation of basic and diluted net loss per common share:

	<u>Three months ended September 30,</u>		<u>Nine months ended September 30,</u>	
	<u>2019</u>	<u>2018</u>	<u>2019</u>	<u>2018</u>
Basic and diluted net loss per common share:				
Net loss	\$ (19,135,612)	\$ (8,281,974)	\$ (43,538,202)	\$ (21,368,449)
Weighted average common shares outstanding— basic and diluted	34,445,489	26,325,904	33,771,671	25,875,783
Net loss per common share—basic and diluted	<u>\$ (0.56)</u>	<u>\$ (0.31)</u>	<u>\$ (1.29)</u>	<u>\$ (0.83)</u>

The following potentially dilutive securities outstanding at September 30, 2019 and 2018 have been excluded from the computation of diluted weighted average shares outstanding, as they would be anti-dilutive:

	<u>September 30,</u>	
	<u>2019</u>	<u>2018</u>
Stock options	3,184,842	2,758,499
Warrants	110,603	2,074,149
Total	<u>3,295,445</u>	<u>4,832,648</u>

Note 6. Stockholders' Equity

Capital Structure

On December 1, 2016, the Company filed a shelf registration statement (the "2016 Shelf Registration Statement") with the SEC for the issuance of common stock, preferred stock, warrants, rights, debt securities and units up to an aggregate amount of \$150.0 million. On December 16, 2016, the 2016 Shelf Registration Statement was declared effective by the SEC. The 2016 Shelf Registration Statement is currently the Company's only active shelf registration statement. There is approximately \$57.4 million of securities that remain available for future issuance under the 2016 Shelf Registration as of the date of this filing, which includes the amount remaining on the 2019 Sales Agreement with Leerink (as defined below). All of the securities issued by the Company in the transactions discussed in this note were registered under the 2016 Shelf Registration Statement.

In March 2017, the Company completed an underwritten public offering of its common stock, whereby it sold 4,304,813 shares of its common stock at a public offering price of \$3.74 per share. The Company received gross proceeds of approximately \$16.1 million, of which net proceeds were approximately \$14.8 million after deducting underwriting discounts and offering expenses.

In October 2017, the Company entered into a sales agreement (the "2017 Sales Agreement") with SVB Leerink (formerly Leerink Partners LLC) ("Leerink"), pursuant to which the Company could sell up to \$30.0 million in shares of its common stock from time to time through Leerink, acting as its sales agent, in one or more at-the-market offerings. In January 2019, the Company raised approximately \$25.8 million in gross proceeds through the sale of 3,164,015 shares under the 2017 Sales Agreement, which resulted in utilizing the full \$30.0 million facility. Upon completion of the final sale fully exhausting the \$30 million of shares allowed to be sold, the 2017 Sales Agreement was automatically terminated. Leerink received a commission of 3.0% of the gross proceeds for all shares sold under the Sales Agreement.

In December 2017, the Company completed a registered direct offering (the “2017 Registered Direct Offering”), whereby it sold an aggregate of \$9.5 million worth of units (“Units”) at a purchase price of \$5.325 per Unit with each Unit consisting of (i) one share of the Company’s common stock, and (ii) a warrant to purchase one share of the Company’s common stock at an exercise price equal to \$5.25 per share (the “Common Warrants”). The Company sold an aggregate of 1,783,587 Units for gross proceeds of approximately \$9.5 million and net proceeds of approximately \$8.8 million, after deducting placement agent fees and offering expenses. Additionally, the Company issued 107,015 warrants at an exercise price of \$6.6562 per share to certain investors affiliated with H.C. Wainwright & Co., LLC, placement agent for the 2017 Registered Direct Offering (the “Placement Agent Warrants”). The Company incurred issuance costs associated with the 2017 Registered Direct Offering of \$745,856, which included \$81,000 related to issuance of the Placement Agent Warrants, of which, \$583,768 was allocated to the common stock sold and was recorded as a reduction to equity. The remaining amount was allocated to the Common Warrants and was expensed. The Placement Agent Warrants had the same terms as the Common Warrants, except for the exercise price of \$6.6562 per share. The Common Warrants priced at \$5.25 and Placement Agent Warrants priced at \$6.6562 utilized the 2016 Shelf Registration Statement for a total of \$9.4 million and \$712,313, respectively. Both the Common Warrants and the Placement Agent Warrants were not exercised and subsequently were terminated in December 2018.

On September 27, 2018, the Company entered into a purchase agreement with certain institutional and accredited investors (collectively, the “RDO Investors”) for the sale by the Company directly to the RDO Investors of an aggregate of 2,966,667 shares of the Company’s common stock, at a purchase price of \$3.00 per share (the “2018 Registered Direct Offering”), for gross proceeds of approximately \$8.9 million. The 2018 Registered Direct Offering closed on October 1, 2018, and the Company received net proceeds of approximately \$8.8 million, after deducting transaction expenses. The 2,966,667 shares of common stock sold in the 2018 Registered Direct Offering were offered and sold by the Company directly to the RDO Investors, without a placement agent, underwriter, broker or dealer.

In May 2019, the Company entered into a new sales agreement (the “2019 Sales Agreement”) with Leerink, pursuant to which the Company may sell up to \$50.0 million in shares of its common stock from time to time through Leerink, acting as its sales agent, in one or more at-the-market offerings utilizing the 2016 Shelf Registration Statement. Leerink is entitled to receive a commission of 3.0% of the gross proceeds for any shares sold under 2019 Sales Agreement. The Company received approximately \$20.1 million in gross proceeds through the sale of 942,285 shares, of which net proceeds were approximately \$19.5 million during the nine months ended September 30, 2019.

The holders of shares of common stock are entitled to one vote for each share of common stock held at all meetings of stockholders and written actions in lieu of meetings. The holders of shares of common stock are entitled to receive dividends, if and when declared by the board of directors.

In the future, the Company may also periodically offer one or more of these securities in amounts, prices and terms to be announced when and if the securities are offered. At the time any of the securities covered by the 2016 Shelf Registration Statement are offered for sale, a prospectus supplement will be prepared and filed with the SEC containing specific information about the terms of any such offering.

Equity Incentive Plans

There were 3,668,590 shares available for the issuance of stock options or stock-based awards under the Company’s 2015 Omnibus Incentive Compensation Plan at September 30, 2019.

Stock Options

The following table sets forth the stock option activity for the nine months ended September 30, 2019:

	Number of shares	Weighted average exercise price	Weighted average contractual term	Aggregate intrinsic value
Outstanding at December 31, 2018	2,282,636	\$ 5.06		
Granted	1,197,231	15.57		
Exercised	(241,757)	4.55		
Forfeited	(53,268)	7.50		
Expired	—	—		
Outstanding at September 30, 2019	<u>3,184,842</u>	<u>\$ 9.01</u>	<u>8.0</u>	<u>\$ 36,930,345</u>
Vested and expected to vest at September 30, 2019	<u>3,168,673</u>	<u>\$ 9.05</u>	<u>8.0</u>	<u>\$ 36,632,902</u>
Exercisable at September 30, 2019	<u>1,612,322</u>	<u>\$ 6.34</u>	<u>6.6</u>	<u>\$ 22,428,613</u>

The fair value of each stock option grant is estimated on the date of grant using the Black-Scholes option pricing model. The expected term of the Company's stock options has been determined utilizing the "simplified" method as described in the SEC's Staff Accounting Bulletin No. 107 relating to stock-based compensation. The simplified method was chosen because the Company has limited historical option exercise experience due to its short operating history. The risk-free interest rate is based on the U.S. Treasury yield in effect at the time of grant for a period approximately equal to the expected term of the award. Expected dividend yield is based on the fact that the Company has never paid cash dividends and does not expect to pay any cash dividends in the foreseeable future. Expected volatility is based on historical volatilities of similar entities within the Company's industry which were commensurate with the Company's expected term assumption.

The weighted average grant date fair value of options granted was \$11.55 and \$1.98 per option for the nine months ended September 30, 2019 and 2018, respectively. As of September 30, 2019, there was \$12.9 million of total unrecognized compensation cost related to non-vested stock options which is expected to be recognized over a weighted average period of 3.3 years. These amounts do not include 20,971 options outstanding as of September 30, 2019, which are performance-based and vest upon the achievement of certain corporate milestones. The total intrinsic value of options exercised (the difference in the market price of the Company's common stock on the exercise date and the price paid by the optionee to exercise the option) was approximately \$4.3 million for the nine months ended September 30, 2019. There were no options exercised for the nine months ended September 30, 2018.

Stock-based compensation expense recognized for the three and nine months ended September 30, 2019 and 2018 was allocated as follows:

	<u>Three months ended September 30,</u>		<u>Nine months ended September 30,</u>	
	<u>2019</u>	<u>2018</u>	<u>2019</u>	<u>2018</u>
Research and development	\$ 286,234	\$ 90,891	\$ 652,666	\$ 311,753
General and administrative	870,201	301,774	2,648,635	1,090,141
Total	<u>\$ 1,156,435</u>	<u>\$ 392,665</u>	<u>\$ 3,301,301</u>	<u>\$ 1,401,894</u>

Performance-Based Awards

The Company did not issue any performance-based awards during the nine months ended September 30, 2019 and 2018. For awards granted with performance conditions, no expense will be recognized, and no measurement date can occur, until the occurrence of the event is probable. For the three and nine months ended September 30, 2019, the Company recognized expense of \$9,514 and \$29,378, respectively, and for the three and nine months ended September 30, 2018, the Company recognized expense of \$24 and income of \$247, respectively, related to performance-based awards.

Warrants

The following table summarizes warrant activity for the nine months ended September 30, 2019:

	Warrants	Weighted average exercise price
Outstanding at December 31, 2018	123,037	\$ 6.35
Issued	58,334	8.10
Exercised	(70,768)	6.30
Outstanding at September 30, 2019	<u>110,603</u>	<u>\$ 7.31</u>

Warrants associated with 2017 Registered Direct Offering

The change in the fair value of warrant liability for the nine months ended September 30, 2018 was \$2,689,000. This relates to the Company's 2017 Registered Direct Offering. As described in further detail above, the Company issued Common Warrants to certain investors to purchase an aggregate of 1,783,587 shares of its common stock. The Common Warrants were exercisable at \$5.25 per share and expired on December 11, 2018. Additionally, as part of the 2017 Registered Direct Offering, the Company issued Placement Agent Warrants to certain investors affiliated with H.C. Wainwright & Co., LLC, the placement agent in the 2017 Registered Direct Offering to purchase an aggregate of 107,015 shares of its common stock. The Placement Agent Warrants were exercisable at \$6.6562 and expired on December 11, 2018. The Common Warrants and Placement Agent Warrants were analyzed and it was determined that they required liability treatment. Under ASC 815, *Derivatives and Hedging*, registered common stock warrants that require the issuance of registered shares upon exercise and do not expressly preclude an implied right to cash settlement are accounted for as derivative liabilities. The Company classified these derivative warrant liabilities on the consolidated balance sheet as a current liability and the change in fair value of the warrant liability was reported on the statement of operations.

The fair value of the Common Warrants at September 30, 2018 and December 31, 2017 was determined to be approximately \$101,000 and \$2,683,000, respectively, as calculated using Black-Scholes with the following assumptions: (1) stock price of \$3.45 and \$5.60, respectively; (2) a risk-free rate of 2.22% and 1.76%, respectively; and (3) an expected volatility of 70% and 62%, respectively. The change in the fair value between December 31, 2017 and September 30, 2018 is reported as a change in fair value of the warrant liability on the statement of operations.

The fair value of the Placement Agent Warrants at September 30, 2018 and December 31, 2017 were determined to be approximately \$1,000 and \$108,000, respectively, as calculated using Black-Scholes with the following assumptions: (1) stock price of \$3.45 and \$5.60, respectively; (2) a risk-free rate of 2.22% and 1.76%, respectively; and (3) an expected volatility of 70% and 62%, respectively. The change in the fair value between December 31, 2017 and September 30, 2018 is reported as a change in fair value of the warrant liability on the statement of operations.

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

The following discussion and analysis contains forward-looking statements about our plans and expectations of what may happen in the future. Forward-looking statements are based on a number of assumptions and estimates that are inherently subject to significant risks and uncertainties, and our results could differ materially from the results anticipated by our forward-looking statements as a result of many known or unknown factors, including, but not limited to, those factors discussed in "Risk Factors." See also the "Cautionary Note Regarding Forward-Looking Statements" set forth at the beginning of this report.

You should read the following discussion and analysis in conjunction with the unaudited interim consolidated financial statements, and the related footnotes thereto, appearing elsewhere in this report, and in conjunction with management's discussion and analysis and the audited consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2018 which was filed with the Securities and Exchange Commission, or SEC, on March 15, 2019.

Overview

We are a clinical-stage biopharmaceutical company developing novel therapies for the management of central nervous system, or CNS, disorders for which there are limited treatment options. By focusing on this therapeutic area, we are addressing significant and growing markets where current treatment options are limited or inadequate. Our core CNS portfolio includes four CNS product candidates, AXS-05, AXS-07, AXS-09, and AXS-12, which are being developed for multiple indications. AXS-05 is currently in a Phase 3 trial in treatment resistant depression, or TRD, which we refer to as the STRIDE-1 study, a Phase 3 trial in major depressive disorder, or MDD, which we refer to as the GEMINI study, a Phase 3 open-label safety trial in patients with TRD and MDD; and a Phase 2/3 trial in agitation associated with Alzheimer's disease, or AD, which we refer to as the ADVANCE-1 study. We have completed a Phase 2 trial in MDD, which we refer to as the ASCEND study and a Phase 2 trial in smoking cessation. AXS-07 is currently in two Phase 3 trials for the acute treatment of migraine, which we refer to as the MOMENTUM and the INTERCEPT studies, and a Phase 3 open-label safety trial in patients with migraine. AXS-12 is currently in a Phase 2 trial in narcolepsy, which we refer to as the CONCERT study. The Axsome Pain and Primary Care business unit, or Axsome PPC, houses our pain and primary care assets, including AXS-02 and AXS-06, and intellectual property which covers these and related product candidates and molecules being developed by us and others. AXS-02 is being developed for the treatment of knee osteoarthritis, or OA, associated with bone marrow lesions, or BMLs. AXS-06 is being developed for the treatment of osteoarthritis and rheumatoid arthritis and for the reduction of the risk of nonsteroidal anti-inflammatory drug, or NSAID, associated gastrointestinal ulcers. Additionally, we are currently evaluating other product candidates, which we intend to develop for CNS disorders. We aim to become a fully integrated biopharmaceutical company that develops and commercializes differentiated therapies that expand the treatment options available to caregivers and improve the lives of patients living with CNS disorders.

AXS-05 is a novel, oral, investigational NMDA receptor antagonist with multimodal activity under development for the treatment of CNS disorders. AXS-05 consists of bupropion and dextromethorphan, or DM, and utilizes our metabolic inhibition technology. We are developing AXS-05 initially for the following four indications: TRD, agitation associated with AD, MDD, and as an aid to smoking cessation. The DM component of AXS-05 is a non-competitive N-methyl-D-aspartate, or NMDA, receptor antagonist, also known as a glutamate receptor modulator. The DM component of AXS-05 is also a sigma-1 receptor agonist, nicotinic acetylcholine receptor antagonist, and inhibitor of the serotonin and norepinephrine transporters. The bupropion component of AXS-05 serves to increase the bioavailability of dextromethorphan, and is a norepinephrine and dopamine reuptake inhibitor, and a nicotinic acetylcholine receptor antagonist. We intend to seek U.S. Food and Drug Administration, or FDA, approval for AXS-05 utilizing the 505(b)(2) regulatory development pathway.

AXS-07, is a novel, oral, investigational medicine with distinct dual mechanisms of action consisting of MoSEIC™, or Molecular Solubility Enhanced Inclusion Complex, meloxicam and rizatriptan. We are developing AXS-07 initially for the acute treatment of migraine. Meloxicam is a long-acting nonsteroidal anti-inflammatory drug, or NSAID, with COX-2, an enzyme involved in inflammation and pain pathways, preferential inhibition and potent pain-relieving effects. However standard meloxicam has an extended time to maximum plasma concentration, or T_{max} , which delays its onset of action. AXS-07 utilizes our proprietary MoSEIC™ technology to substantially increase the solubility and speed the absorption of meloxicam while potentially maintaining durability of action. Meloxicam is a new molecular entity for migraine enabled by our MoSEIC™ technology. Rizatriptan is a 5-HT_{1B/D} agonist that inhibits calcitonin gene-related peptide-, or CGRP-mediated vasodilation, has been shown to have central trigeminal antinociceptive activity, and may reduce the release of inflammatory mediators from trigeminal nerves. Rizatriptan is approved as a single agent for the acute treatment of migraine. We intend to seek FDA approval for AXS-07 utilizing the 505(b)(2) regulatory development pathway.

AXS-09 is a novel, oral, investigational medicine consisting of esbupropion and DM, which is being developed for the treatment of CNS disorders. AXS-09 contains esbupropion, the chirally pure *S*-enantiomer of bupropion, as compared to the company's first generation product candidate AXS-05 which contains racemic bupropion, equal amounts of the *S*- and *R*-enantiomers. We have demonstrated in a Phase 1 trial that DM plasma levels are substantially increased into a potentially therapeutic range with repeated administration of AXS-09. Results of this Phase 1 trial coupled with preclinical data also indicate the potential for enhanced absorption and therapeutic effect of the *S*-enantiomer as compared to the *R*-enantiomer.

AXS-12, reboxetine, is a novel, oral, investigational medicine in development for treatment of narcolepsy. AXS-12 is a highly selective and potent norepinephrine reuptake inhibitor. The potential utility of AXS-12 in narcolepsy is supported by positive pre-clinical and preliminary clinical results in narcolepsy, and an extensive positive clinical safety record. Reboxetine, the active agent in AXS-12, significantly and dose-dependently reduced narcoleptic episodes in hypocretin-, or orexin-deficient mice, a well-established genetic animal model of narcolepsy.

The Axsome PPC houses Axsome's pain and primary care assets, including AXS-02 and AXS-06, and intellectual property which covers these and related product candidates and molecules being developed by Axsome and others. AXS-02 is being developed for the treatment of knee osteoarthritis, or OA, associated with bone marrow lesions, or BMLs, and chronic low back pain, or CLBP, associated with Modic changes, or MCs. Lastly, AXS-06 is being developed for the treatment of osteoarthritis and rheumatoid arthritis and for the reduction of the risk of NSAID-associated gastrointestinal ulcers.

AXS-02, disodium zoledronate tetrahydrate, is a potentially first-in-class, oral, targeted, non-opioid therapeutic for chronic pain. AXS-02 is a potent inhibitor of osteoclasts, which are bone remodeling cells that break down bone tissue. We are developing AXS-02 for the treatment of pain in the following two conditions: knee OA associated with BMLs and CLBP associated with type 1 or mixed type 1 and type 2 MCs. These conditions exhibit target lesions or specific pathology that we believe may be addressed by the mechanisms of action of AXS-02, such as inhibition of osteoclast activity. These mechanisms may result in a reduction of pain in these conditions. We intend to seek FDA approval for AXS-02 utilizing the 505(b)(2) regulatory development pathway.

AXS-06, is a novel, oral, non-opioid, fixed-dose combination of MoSEIC™ meloxicam and esomeprazole. We are developing AXS-06 initially for the treatment of osteoarthritis and rheumatoid arthritis. Esomeprazole is a proton pump inhibitor which lowers stomach acidity and which has been shown to reduce the occurrence of NSAID-associated gastrointestinal ulcers. AXS-06 is designed to provide rapid, effective pain relief, and to reduce the risk of NSAID-associated gastrointestinal ulcers, with convenient once-daily dosing. We have successfully completed a Phase 1 trial of AXS-06 to characterize the pharmacokinetics of meloxicam and esomeprazole after oral administration of AXS-06. The results of our Phase 1 trial demonstrated that the median T_{max} for meloxicam, the trial's primary endpoint, was nine times faster for AXS-06 as compared to standard meloxicam. We intend to seek FDA approval for AXS-06 utilizing the 505(b)(2) regulatory development pathway.

Since our incorporation in January 2012, our operations to date have included organizing and staffing our company, business planning, raising capital, developing our compounds, and engaging in other discovery and preclinical activities. Prior to our initial public offering, or IPO, in November 2015, we financed our operations primarily through private placements of our convertible notes and subsequent to our IPO, through proceeds from sales of our common stock and warrants to purchase shares of our common stock to equity investors and debt borrowings. For a further discussion, see the section entitled “Liquidity and Capital Resources” below.

Our ability to become profitable depends on our ability to generate revenue. We do not expect to generate significant revenue unless and until we or our collaborators obtain marketing approval for and successfully commercialize one of our product candidates.

We have incurred significant operating expenses and net losses since inception. We incurred net losses of \$43.5 million and \$21.4 million for the nine months ended September 30, 2019 and 2018, respectively. Our accumulated deficit as of September 30, 2019 was \$151.1 million, and we expect to incur significant expenses and increasing operating losses for the foreseeable future. We expect our expenses to increase in connection with our ongoing activities, as we continue the development and clinical trials of, and seek regulatory approval for our current product candidates and any other product candidates that we develop or in-license and advance to clinical development. If we obtain regulatory approval for a product candidate, we expect to incur significant expenses in order to create an infrastructure to support the commercialization of the product candidate, including manufacturing, sales, marketing, and distribution functions. Further, we have incurred and will continue to incur additional costs associated with operating as a public company. Accordingly, we will need additional financing to support our continuing operations. We will seek to fund our operations through public or private equity, debt financings or other sources. Adequate additional financing may not be available to us on acceptable terms, or at all. Our failure to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategy. We will need to generate significant revenue to achieve profitability, and we may never do so.

Year to Date and Recent Developments

In January 2019, we announced that AXS-05 met the prespecified primary endpoint and significantly improved symptoms of depression in the ASCEND study.

In January 2019, we received approximately \$25.8 million in gross proceeds, of which net proceeds were approximately \$25.0 million through the sale of 3,164,015 shares under the existing at-the-market facility with SVB Leerink (formerly Leerink Partners LLC), or Leerink. Upon completion of the final sale fully exhausting the \$30 million of shares available for sale, the Sales Agreement was automatically terminated. Please see the section entitled “Liquidity and Capital Resources” below for a further discussion.

In January 2019, we initiated the CONCERT study, a Phase 2 randomized, double-blind, controlled trial to evaluate the efficacy and safety of AXS-12 in narcolepsy.

In March 2019, we initiated the MOMENTUM study, a Phase 3, randomized, double-blind, multicenter, controlled trial to assess the efficacy and safety of AXS-07 in the acute treatment of migraine.

In March 2019, we entered into a \$24.0 million growth capital term loan facility, which we refer to as the 2019 Term Loan, with Silicon Valley Bank, or SVB, and WestRiver Innovation Lending Fund VIII, L.P., or WestRiver. Further, in July 2019, the 2019 Term Loan was amended. Please see the section entitled “Liquidity and Capital Resources” below for a further discussion.

In March 2019, we received FDA Breakthrough Therapy designation for AXS-05 for the treatment of MDD.

In April 2019, we announced that AXS-05 met the prespecified primary endpoint in Phase 2 trial in smoking cessation.

In May 2019, we announced expedited development and pivotal status for AXS-05 for the treatment of MDD based on an FDA Breakthrough Therapy meeting.

In May 2019, we announced the acceleration of the timeline for reporting topline results from the MOMENTUM Phase 3 trial of AXS-07 for the acute treatment of migraine.

In May 2019, we entered into a new sales agreement with Leerink with respect to an at the market offering program, which we refer to as the 2019 Sales Agreement, under which we may, from time to time in our sole discretion, issue and sell through Leerink, acting as agent, up to \$50.0 million of shares of our common stock. We received approximately \$20.1 million in gross proceeds through the sale of 942,285 shares, of which net proceeds were approximately \$19.5 million during the nine months ended September 30, 2019.

In June 2019, we initiated the GEMINI study, a Phase 3, randomized, double-blind, multicenter, placebo-controlled trial of AXS-05 in the treatment of MDD.

In July 2019, we announced that we are enrolling two open-label studies in order to build safety databases of patients to support the filing of a New Drug Application, or NDA for (i) AXS-05 in the treatment of MDD and (ii) AXS-07 in the acute treatment of migraine.

In August 2019, we announced that David Marek has been appointed as our Chief Commercial Officer.

In September 2019, we announced positive results from a Phase 1 pharmacokinetic trial of AXS-07, a novel, oral, investigational medicine with distinct dual mechanisms of action being developed for the acute treatment of migraine.

In October 2019, we announced the completion of patient enrollment in our GEMINI and CONCERT studies.

In October 2019, we initiated the INTERCEPT study, a Phase 3, randomized, double-blind, multicenter, placebo-controlled trial evaluating the early treatment of migraine with AXS-07.

In October 2019, we announced the results of the MINDSET physician survey, which affirms the unmet need and favorable profile of AXS-07 in the acute treatment of migraine.

Financial Overview

Revenue

We have not generated any revenue since we commenced operations and we do not expect to generate any revenue in the near future. To the extent we enter into licensing or collaboration arrangements, we may have sources of revenue in the future. We expect that any revenue we generate will fluctuate from quarter to quarter as a result of the amount and timing of payments that we may recognize upon the sale of our product candidates, to the extent that any product candidates are successfully commercialized, and the amount and timing of fees, reimbursements, and milestone and other payments received under any future licensing or collaboration arrangements. If we fail to complete the development of our product candidates in a timely manner or obtain regulatory approval for them, our ability to generate future revenue, and our results of operations and financial position, would be materially and adversely affected.

Research and Development Expenses

Research and development expenses primarily include preclinical studies, clinical trials, manufacturing costs, employee salaries and benefits, stock-based compensation expense; contract services, including external research and development expenses incurred under arrangements with third parties, such as contract research organizations, or CROs, facilities costs; overhead costs, depreciation, and other related costs.

Research and development activities are central to our business model. We will incur substantial costs beyond our present and planned clinical trials in order to file an NDA, for any of our product candidates. It is difficult to determine with certainty the costs and duration of our current or future clinical trials and preclinical studies, or if, when, or to what extent we will generate revenue from the commercialization and sale of our product candidates if we obtain regulatory approval. We may never succeed in achieving regulatory approval. The duration, costs, and timing of clinical trials and development of our product candidates will depend on a variety of factors, including the uncertainties of future clinical trials and preclinical studies, uncertainties in clinical trial enrollment rate, and significant and changing government regulation. In addition, the probability of success for each product candidate will depend on numerous factors, including competition, manufacturing capability, and commercial viability. We will determine which programs to pursue and how much to fund each program in response to the scientific and clinical success of each product candidate, as well as an assessment of each product candidate's commercial potential. Management considers many factors in developing the estimates and assumptions that are used in the preparation of our unaudited interim consolidated financial statements.

Management must apply significant judgment in this process. In addition, other factors may affect estimates, including expected business and operational changes, sensitivity and volatility associated with the assumptions used in developing estimates, and whether historical trends are expected to be representative of future trends. The estimation process often may yield a range of potentially reasonable estimates of the ultimate future outcomes and management must select an amount that falls within that range of reasonable estimates. This process may result in actual results differing materially from those estimated amounts used in the preparation of our unaudited interim consolidated financial statements if these results differ from historical experience, or other assumptions do not turn out to be substantially accurate, even if such assumptions are reasonable when made.

The following table summarizes our research and development expenses for our primary programs for the three and nine months ended September 30, 2019 and 2018:

	Three months ended September 30,		Nine months ended September 30,	
	2019	2018	2019	2018
AXS-05	\$ 7,829,826	\$ 3,453,303	\$ 15,491,879	\$ 9,847,722
AXS-07	6,177,098	1,226,328	13,914,286	2,095,683
AXS-12	487,703	7,914	1,363,852	7,914
AXS-02	174,253	34,539	264,155	507,074
AXS-06	3,650	3,671	8,126	63,844
Other research and development	876,809	1,224,134	2,746,832	3,509,833
Stock-based compensation	286,234	90,891	652,666	311,753
Total research and development expenses	<u>\$15,835,573</u>	<u>\$6,040,780</u>	<u>\$34,441,796</u>	<u>\$16,343,823</u>

Other research and development expenses primarily consist of employee salaries and benefits, facilities and overhead costs. For the three and nine months ended September 30, 2019, the majority of employee salaries and benefits were allocated amongst the respective clinical development programs whereas for the three and nine months ended September 30, 2018, employee salaries and benefits were allocated to Other research and development expenses.

General and Administrative Expenses

General and administrative expenses primarily consist of salaries and related costs for personnel in executive, finance, and operational functions, including stock-based compensation and travel expenses. Other general and administrative expenses include facility-related costs, insurance expense, and professional fees for legal and accounting services and patent filing and prosecution costs. General and administrative expenses are expensed when incurred.

Interest and amortization of debt discount (expense)

Interest and amortization of debt discount (expense) primarily consists of cash interest and non-cash costs related to our term loan with SVB (see “Liquidity and Capital Resources” below for a further discussion). We record costs incurred in connection with the issuance of debt as a direct deduction from the debt liability. We amortize these costs over the term of our debt agreements in our consolidated statement of operations. For the three and nine months ended September 30, 2019, the amortization of debt discount expense related to the 2019 Term Loan, the First Amendment to the 2019 Term Loan, and the 2016 Original and Amended Term Loan, whereas for the three and nine months ended September 30, 2018, the amortization of debt discount expense related to only the 2016 Original Term Loan.

Critical Accounting Policies and Significant Judgments and Estimates

This discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with generally accepted accounting principles in the United States of America, or U.S. GAAP. The preparation of these consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities, disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of expenses during the reported period. In accordance with GAAP, we base our estimates on historical experience and on various other assumptions that we believe are reasonable under the circumstances. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are more fully described in Note 2 - Summary of Significant Accounting Policies to our unaudited interim consolidated financial statements appearing elsewhere in this report, we believe the accounting policies described in the “Financial Overview” section above are the most critical to the judgments and estimates we use in the preparation of our consolidated financial statements.

Results of Operations

The following table summarizes our results of operations for the periods indicated:

	Three months ended September 30,		Nine months ended September 30,	
	2019	2018	2019	2018
Operating expenses:				
Research and development	\$ 15,835,573	\$ 6,040,780	\$ 34,441,796	\$ 16,343,823
General and administrative	3,111,662	2,202,679	8,375,131	7,052,439
Total operating expenses	<u>18,947,235</u>	<u>8,243,459</u>	<u>42,816,927</u>	<u>23,396,262</u>
Loss from operations	(18,947,235)	(8,243,459)	(42,816,927)	(23,396,262)
Interest and amortization of debt discount (expense)	(327,825)	(270,933)	(860,723)	(878,605)
Tax credit	139,448	217,418	139,448	217,418
Change in fair value of warrant liability	—	15,000	—	2,689,000
Net loss	<u><u>\$(19,135,612)</u></u>	<u><u>\$(8,281,974)</u></u>	<u><u>\$(43,538,202)</u></u>	<u><u>\$(21,368,449)</u></u>

Comparison of the Three Months Ended September 30, 2019 and 2018

Research and Development Expenses. Our research and development expenses for the three months ended September 30, 2019 were \$15.8 million, compared to \$6.0 million for the three months ended September 30, 2018, an increase of \$9.8 million. This increase was primarily due to trials that were initiated in 2019, which include the GEMINI, MOMENTUM, INTERCEPT, and CONCERT trials, along with the AXS-05 and AXS-07 open-label safety studies.

General and Administrative Expenses. Our general and administrative expenses for the three months ended September 30, 2019 was \$3.1 million, compared to \$2.2 million for the three months ended September 30, 2018, an increase of \$0.9 million. The increase was primarily due to an increase in stock compensation expense as well as personnel costs.

Interest and Amortization of Debt Discount (Expense). Interest and amortization of debt discount (expense) for the three months ended September 30, 2019 and 2018 was \$0.3 million.

Tax Credit. Tax credit income for the three months ended September 30, 2019 was \$0.1 million, compared to \$0.2 million for the three months ended September 30, 2018, a decrease of \$0.1 million. This represents the receipt by Axxome Therapeutics Australia PTY LTD, our Australian subsidiary, of the Australia Tax Incentive Credit related to the 2018 and 2017 research and development expenses incurred for our product candidates.

Change in Fair Value of Warrant Liability. We recorded income related to the change in fair value of our warrant liability for the three months ended September 30, 2018 of less than \$0.1 million. There was no warrant liability outstanding during the three months ended September 30, 2019.

Comparison of the Nine Months Ended September 30, 2019 and 2018

Research and Development Expenses. Our research and development expenses for the nine months ended September 30, 2019 were \$34.4 million, compared to \$16.3 million for the nine months ended September 30, 2018, an increase of \$18.1 million. The increase was primarily due to the preparation for and initiation of the GEMINI, MOMENTUM, INTERCEPT, and CONCERT trials along with the AXS-05 and AXS-07 open-label safety trials; and continued progress of our STRIDE-1, and ADVANCE-1 trials, which was partially offset by the cessation of the CREATE-1 study and completion of the ASCEND trial.

General and Administrative Expenses. Our general and administrative expenses for the nine months ended September 30, 2019 were \$8.4 million, compared to \$7.1 million for the nine months ended September 30, 2018, an increase of \$1.3 million. The increase was primarily due an increase in stock compensation expense as well as personnel costs.

Interest and Amortization of Debt Discount (Expense). Interest and amortization of debt discount (expense) for the nine months ended September 30, 2019 and 2018 was \$0.9 million.

Tax Credit. Tax credit income for the nine months ended September 30, 2019 was \$0.1 million, compared to \$0.2 million for the nine months ended September 30, 2018, a decrease of \$0.1 million. This represents the receipt by Axxome Therapeutics Australia PTY LTD, our Australian subsidiary, of the Australia Tax Incentive Credit related to the 2018 and 2017 research and development expenses incurred for our product candidates.

Change in Fair Value of Warrant Liability. We recorded income related to the change in fair value of our warrant liability for the nine months ended September 30, 2018 of \$2.7 million. There was no warrant liability outstanding during the nine months ended September 30, 2019.

Liquidity and Capital Resources

We have financed our operations primarily through proceeds from equity offerings and debt borrowings. See discussion below.

In November 2016, we entered into a loan and security agreement with SVB for a term loan of up to \$20.0 million, which we refer to as the 2016 Original Term Loan. The initial tranche of \$10.0 million was funded shortly after executing the loan agreement. Because we did not achieve the conditional criteria to access the second and third tranches before the specified dates, the \$10.0 million in additional term loan advances expired. In November 2018, we amended the 2016 Original Term Loan to provide an additional \$4.0 million growth capital loan, related to our narcolepsy clinical program with AXS-12. We refer to the 2016 Original Term Loan, as amended in November 2018, as the 2016 Amended Term Loan. The additional capital under the 2016 Amended Term Loan was available to be drawn, at our option, subject to the achievement of a specified clinical milestone. Our obligations under the 2016 Amended Term Loan, along with our ability to draw down on the additional \$4.0 million tranche, were considered to be performed and completed in connection with the establishment of the 2019 Term Loan (see below).

On December 1, 2016, we filed a shelf registration statement with the SEC for the issuance of common stock, preferred stock, warrants, rights, debt securities and units up to an aggregate amount of \$150.0 million, which we refer to as the 2016 Shelf Registration Statement. On December 16, 2016, the 2016 Shelf Registration Statement was declared effective by the SEC. As discussed in greater detail below, we completed an offering of common stock in March 2017, entered into a sales agreement in October 2017 pursuant to which we sold shares of our common stock from time to time in an at-the-market offering until completion of the offering in January 2019, and completed a registered direct offering priced at the market in December 2017 and September 2018, each utilizing the 2016 Shelf Registration Statement. In the future, we may conduct additional offerings of one or more of these securities utilizing the 2016 Shelf Registration Statement in such amounts, prices and terms to be announced when and if the securities are offered. At the time any of our securities covered by the 2016 Shelf Registration Statement are offered for sale, a prospectus supplement will be prepared and filed with the SEC containing specific information about the terms of any such offering.

In March 2017, we completed an underwritten public offering, whereby we sold 4,304,813 shares of our common stock at a public offering price of \$3.74 per share. We received gross proceeds of approximately \$16.1 million and net proceeds of approximately \$14.8 million, net of underwriting discounts and offering expenses.

In October 2017, we entered into an “at-the-market” sales agreement, or the 2017 Sales Agreement, with Leerink, pursuant to which we could sell up to \$30 million in shares of our common stock from time to time through Leerink, acting as our sales agent, in one or more at-the-market offerings. We received approximately \$4.2 million in gross proceeds, of which net proceeds were approximately \$4.1 million from the sales of our common stock to Leerink under the 2017 Sales Agreement during the year ended December 31, 2018. In January 2019, we raised approximately \$25.8 million in gross proceeds through the sale of 3,164,015 shares under the 2017 Sales Agreement. Upon completion of the final sale fully exhausting the \$30 million of shares available for sale, the 2017 Sales Agreement was automatically terminated, Leerink received a commission of 3.0% of the gross proceeds for all shares sold under the 2017 Sales Agreement.

In December 2017, we completed a registered direct offering priced at the market, which we refer to as the 2017 Registered Direct Offering, whereby we sold an aggregate of \$9.5 million worth of units, or Units, at a purchase price of \$5.325 per Unit, with each Unit consisting of (i) one share of our common stock, and (ii) a warrant to purchase one share of our common stock, or Common Warrant, at an exercise price equal to \$5.25 per share. We sold an aggregate of 1,783,587 Units in the 2017 Registered Direct Offering for gross proceeds of approximately \$9.5 million and net proceeds of approximately \$8.8 million, after deducting placement agent fees and offering expenses. Additionally, we issued warrants to purchase up to 107,015 shares of our common stock at an exercise price of \$6.6562 per share to certain investors affiliated with H.C. Wainwright & Co., LLC, placement agent for the offering, which we refer to as the Placement Agent Warrants. The Placement Agent Warrants had the same terms as the Common Warrants, except for the difference in exercise price noted above. Both the Common Warrants and the Placement Agent Warrants expired on December 11, 2018.

On September 27, 2018, we entered into a purchase agreement with certain institutional and accredited investors, which we refer to as the RDO Investors, for the sale by us directly to the RDO Investors of an aggregate of 2,966,667 shares of our common stock, at a purchase price of \$3.00 per share, which we refer to as the 2018 Registered Direct Offering, for gross proceeds of approximately \$8.9 million. The 2018 Registered Direct Offering closed on October 1, 2018, and we received estimated net proceeds of approximately \$8.8 million, after deducting transaction expenses. The 2,966,667 shares of common stock sold in the 2018 Registered Direct Offering were offered and sold by us directly to the RDO Investors, without a placement agent, underwriter, broker or dealer.

In March 2019, we entered into the 2019 Term Loan with SVB and WestRiver for a term loan up to \$24.0 million, which completely replaces the 2016 Original Term Loan and the 2016 Amended Term Loan. The initial tranche of \$20.0 million, or the Term A Loan Advance, was funded shortly after executing the loan agreement. The second tranche of \$4.0 million, or the Term B Loan Advance, was initially available to be drawn, at our option, subject to the achievement of positive data, on or prior to August 15, 2019, with respect to our ongoing Phase 2 clinical trial for AXS-12 in narcolepsy, sufficient to submit a Phase 3 protocol to FDA, provided that we have not received any objections from the FDA within thirty days after submission of such Phase 3 protocol, which we refer to as the Milestone Event. A portion of the initial tranche was used to satisfy our then-existing obligations under our 2016 Amended Term Loan, and such obligations are considered to be fully repaid and completed. We refer to the Term A Loan Advance and the Term B Loan Advance as the Loan Advances.

In May 2019, we entered into the 2019 Sales Agreement with Leerink, pursuant to which we may sell up to \$50 million in shares of our common stock from time to time through Leerink, acting as our sales agent, in one or more at-the-market offerings utilizing the 2016 Shelf Registration Statement. Leerink is entitled to receive a commission of 3.0% of the gross proceeds for any shares sold under the 2019 Sales Agreement. We received approximately \$20.1 million in gross proceeds through the sale of 942,285 shares, of which net proceeds were approximately \$19.5 million during the nine months ended September 30, 2019.

In July 2019, we entered into the first amendment to the 2019 Term Loan, or the First Amendment to the 2019 Term Loan. Under the First Amendment to the 2019 Term Loan, the interest-only monthly payment period of the 2019 Term Loan was extended to 18 months after the date of the 2019 Term Loan, which may be further extended to 24 months upon receipt by us of the Term B Loan Advance. Our ability to draw down the Term B Loan Advance was extended to December 31, 2019, subject to our achievement of the Milestone Event prior to or on December 31, 2019. The Loan Advances mature on February 1, 2023. See the subsection titled “July 2019 First Amendment to Loan and Security Agreement – Silicon Valley Bank” under the “Contractual Obligations and Commitments” section below for a further description of the First Amendment to the 2019 Term Loan.

We believe our currently available cash will be sufficient to fund our anticipated operating cash requirements into the second quarter of 2021. Because the process of evaluating product candidates in clinical trials is costly and the timing of progress in these trials is uncertain, it is possible that the assumptions upon which we have based this estimate may prove to be wrong, and we could use our capital resources sooner than we currently expect.

Cash Flows

The following table summarizes our primary sources and uses of cash for the periods indicated:

	Nine months ended September 30,	
	2019	2018
Net cash (used in) provided by:		
Operating activities	\$ (28,807,908)	\$ (20,259,752)
Investing activities	(14,660)	(32,696)
Financing activities	58,495,687	1,492,089
Net increase (decrease) in cash	<u>\$ 29,673,119</u>	<u>\$ (18,800,359)</u>

Operating Activities. Cash used in operating activities for the nine months ended September 30, 2019 was \$28.8 million as compared to \$20.3 million for the nine months ended September 30, 2018. The increase of \$8.5 million in net cash used was primarily related to higher research and development spend related to multiple product candidates in clinical trials.

Investing Activities. Cash used in investing activities for the purchase of property and equipment was less than \$0.1 million for the nine months ended September 30, 2019 and 2018.

Financing Activities. Cash provided by financing activities was \$58.5 million for the nine months ended September 30, 2019, which included net proceeds from the sale of common stock through our Sales Agreement with Leerink of \$44.5 million, proceeds from the 2019 Term Loan of \$20.0 million, proceeds from issuance of common stock upon exercise of options and warrants of \$1.1 million and \$0.2 million, respectively. These proceeds were offset by the repayment on our 2016 Amended Term Loan of \$7.2 million.

Cash provided by financing activities was \$1.5 million for the nine months ended September 30, 2018, which included net proceeds from the sale of common stock through our Sales Agreement with Leerink of \$2.9 million and \$1.1 million of the \$8.9 million of cash received in connection with the Registered Direct Offering completed in October 2018, offset by the principal payments on our term loan with SVB of \$2.5 million.

Funding requirements

We have not achieved profitability since our inception and we expect to continue to incur significant losses for the foreseeable future. We expect our losses to increase as we continue the development of and seek regulatory approvals for our product candidates and begin to commercialize any approved products. We are subject to all of the risks pertinent to the development of new product candidates, and we may encounter unforeseen expenses, difficulties, complications, delays, and other unknown factors that may harm our business.

We anticipate that we will need to raise substantial additional financing in the future to fund our operations. In order to meet these additional cash requirements, we may incur debt, license certain intellectual property, and seek to sell additional equity or convertible securities that may result in dilution to our stockholders. If we raise additional funds through the issuance of equity or convertible securities, these securities could have rights or preferences senior to those of our common stock and could contain covenants that restrict our operations. There can be no assurance that we will be able to obtain additional equity or debt financing on terms acceptable to us, if at all. Our future capital requirements will depend on many factors, including:

- the scope, rate of progress, results, and cost of our clinical studies and other related activities;
- our ability to enter into collaborative agreements for the development and commercialization of our product candidates;
- the number and development requirements of any other product candidates that we pursue;

- the costs, timing, and outcome of regulatory reviews of our product candidates;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales, and distribution, for any of our product candidates for which we receive marketing approval;
- any product liability or other lawsuits related to our product candidates;
- the expenses needed to attract and retain skilled personnel;
- the general and administrative expenses related to being a public company;
- the revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval; and
- the costs involved in preparing, filing, and prosecuting patent applications, maintaining and enforcing our intellectual property rights, and defending our intellectual property-related claims.

Please see “Risk Factors” for additional risks associated with our substantial capital requirements.

Contractual Obligations and Commitments

License agreements with Antecip Bioventures

Under three exclusive license agreements with Antecip Bioventures II LLC, or Antecip, an entity owned by our Chief Executive Officer and Chairman of the Board, Herriot Tabuteau, M.D., we are obligated to make specified royalty payments ranging from 1.5% to 4.5%, subject to up to a 50% reduction depending on required payments to third parties, on net sales of licensed products. The amount, timing, and likelihood of such payments are not known.

November 2016 Loan and Security Agreement—Silicon Valley Bank

In November 2016, we entered into the 2016 Original Term Loan with SVB, for a term loan of up to \$20.0 million. The initial tranche of \$10.0 million was funded shortly after executing the loan agreement. We were scheduled to make interest only payments on the loan until December 1, 2017, which could have been extended under certain circumstances. Under the terms of the loan, we had the opportunity, but not the obligation to, draw two additional tranches of \$5.0 million each prior to November 9, 2017 and December 31, 2017, subject to the achievement of certain clinical and financial milestones. Because we did not achieve the conditional criteria to access the second and third tranches before the specified dates, the \$10.0 million in additional term loan advances expired.

The 2016 Original Term Loan accrued interest at an annual rate equal to 4.50% plus the prime rate, which was the greater of 3.50% or the Wall Street Journal prime rate, and was payable monthly. Following the interest only payment period, we began making monthly payments of principal and interest. In addition, we were required to pay a final payment fee of 8.5% of the principal amount extended to us on the date of repayment of the outstanding loan.

We were permitted to prepay all, but not less than all, of the 2016 Original Term Loan subject to a prepayment premium of 3.0% of the outstanding principal if prepaid within two years of the effective date of the loan, 2.0% of the outstanding principal if prepaid during the third year of the loan, and 1.0% of the outstanding principal if prepaid after the third year. The term loan was collateralized by a security interest in all of our assets except intellectual property. Our intellectual property was subject to a negative pledge.

In connection with the loan, SVB and Life Science Loans, LLC, received warrants to purchase an aggregate 65,228 shares of our common stock at an exercise price of \$7.41 per share, which are exercisable for seven years from the date of issuance.

We allocated the proceeds of \$10.0 million based on the relative fair values of the debt instrument and the warrant instrument. The relative fair value of the warrants of approximately \$0.3 million at the time of issuance, which was determined using the Black-Scholes option-pricing model, was recorded as additional paid-in capital and reduced the carrying value of the debt. The discount on the debt was being amortized to interest expense over the term of the debt.

In November 2018, we amended the 2016 Original Term Loan to provide an additional \$4 million growth capital loan, related to our narcolepsy clinical program with AXS-12. The additional capital was available to be drawn, at our option, subject to the achievement of a specified clinical milestone. In connection with the 2016 Amended Term Loan, SVB and WestRiver received warrants to purchase an aggregate 15,750 shares of our common stock at an exercise price of \$3.06 per share, which are exercisable for seven years from the date of issuance.

Our obligations under the 2016 Amended Term Loan, along with the ability to draw down on the additional \$4.0 million tranche, were considered to be performed and completed in connection with the establishment of the 2019 Term Loan during March 2019.

March 2019 Loan and Security Agreement—Silicon Valley Bank

In March 2019, we entered into the 2019 Term Loan with SVB and WestRiver consisting of an initial \$20.0 million tranche, which was funded shortly upon closing, with the remaining \$4.0 million available to be drawn, at our option, subject to the achievement of positive data, on or prior to August 15, 2019, with respect to our ongoing Phase 2 clinical trial for AXS-12 in narcolepsy, sufficient to submit a Phase 3 protocol to the FDA, provided that we have not received any objections from the FDA within thirty days after submission of such Phase 3 protocol. A portion of the first tranche was used to satisfy our then-existing obligations under our 2016 Amended Term Loan and such obligations are considered to be fully repaid and completed.

The 2019 Term Loan accrues interest on the unpaid principal balance of the outstanding loan advances at a floating per annum rate equal to the greater of (i) seven and one-half of one percent (7.50%) and (ii) two percent (2.0%) above the prime rate and is payable monthly. The 2019 Term Loan initially had an interest-only monthly payment period for twelve months which was extendable to 18 months upon drawing of the second tranche. Following the interest only payment period, we will begin making monthly payments of principal and interest and these payments will continue until the maturity date of February 1, 2023. In addition, we were initially required to pay a final payment fee of 6.0% of the principal amount extended to us on the date of repayment of the outstanding loan, which was increased to 6.3% in connection with the First Amendment to the 2019 Term Loan, as described below.

We were initially permitted to prepay all, but not less than all, of the 2019 Term Loan, subject to a prepayment premium of 3.0% of the outstanding principal if prepaid within one year of the effective date of the loan, 2.0% of the outstanding principal if prepaid after the first anniversary of the effective date but on prior to the second anniversary of the effective date, and 1.0% of the outstanding principal if prepaid after the second anniversary of the effective date. The term loan is collateralized by a security interest in all of our assets except intellectual property. Our intellectual property is subject to a negative pledge.

In connection with the 2019 Term Loan, SVB and WestRiver received warrants, or the March 2019 Warrants, to purchase an aggregate 70,000 shares of our common stock at an exercise price of \$8.10 per share, which are exercisable for seven years from the date of issuance. The warrants were to be earned based upon the usage of the facility and are exercisable until March 4, 2026. The warrants were classified as a component of stockholders' equity, of which 58,332 warrants were immediately exercisable and the remaining 11,668 warrants would be earned upon drawing of the second \$4.0 million tranche under the loan. In connection with the First Amendment to the 2019 Term Loan, the shares of common stock issuable under each of the March 2019 Warrants were fixed at 29,167 shares, as described further below.

We allocated the proceeds of \$20.0 million based on the relative fair values of the debt instrument and the warrant instrument. The relative fair value of the warrants of approximately \$0.4 million at the time of issuance, which was determined using the Black-Scholes option-pricing model, was recorded as additional paid-in capital and reduced the carrying value of the debt. The discount on the debt is being amortized to interest expense over the term of the debt.

July 2019 First Amendment to Loan and Security Agreement—Silicon Valley Bank

In July 2019, we entered into the First Amendment to the 2019 Term Loan. Under the First Amendment to the 2019 Term Loan, the interest-only monthly payment period of the 2019 Term Loan was extended to 18 months after the date of the 2019 Term Loan, which may be further extended to 24 months upon receipt by us of the Term B Loan Advance. Our ability to draw down the Term B Loan Advance was extended to December 31, 2019, subject to our achievement of the Milestone Event prior to or on December 31, 2019. The Loan Advances mature on February 1, 2023.

Pursuant to the 2019 Term Loan, as amended by the First Amendment to the 2019 Term Loan, following the interest-only payment period, we will begin making monthly payments of principal in equal monthly installments for 30 consecutive months (provided, that, upon the occurrence of the Milestone Event, the repayment schedule will be decreased to 24 consecutive months) and monthly payments of interest, until the Maturity Date. Interest will accrue on the unpaid principal balance of the outstanding Loan Advances at a floating per annum rate equal to the greater of (i) seven and one-half of one percent (7.50%) and (ii) two percent (2.0%) above the prime rate. The First Amendment to the 2019 Term Loan increased the final payment fee, payable upon our repayment of the Loan Advances from 6.0% to 6.30% of the original principal amount of the Loan Advances.

We may prepay all, but not less than all of the Loan Advances, subject to a prepayment fee of 3.0% of any amount prepaid prior to the first anniversary of July 25, 2019, or the First Amendment Effective Date, 2.0% of the amount prepaid if the prepayment occurs after the first anniversary of the First Amendment Effective Date through and including the second anniversary of the First Amendment Effective Date, or 1.0% of the amount prepaid if the prepayment occurs after the second anniversary of the First Amendment Effective Date, but prior to the Maturity Date. These percentages are unchanged from the original 2019 Term Loan.

In connection with the First Amendment to the 2019 Term Loan, the March 2019 Warrants were amended to fix the number of shares that may be issued upon exercise of each such March 2019 Warrant at 29,167 shares of common stock, and SVB and WestRiver were issued the July 2019 Warrants, which become exercisable only upon funding of the Term B Loan Advance, to purchase 5,750 shares of the Company's common stock at a price per share equal to \$25.71. The July 2019 Warrants replace the portion of the March 2019 Warrants that could originally be earned by SVB and WestRiver upon funding of the Term B Loan Advance. The July 2019 Warrants, if earned, will be exercisable until July 24, 2026 and will be exercised automatically on a net issuance basis if not exercised prior to the expiration date and if the then-current fair market value of one share of the Company's common stock is greater than the exercise price then in effect.

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 by applicable SEC regulations.

Recent Accounting Pronouncements

Refer to Note 2 – Summary of Significant Accounting Policies to our consolidated financial statements included in Part I, Financial Information, Item 1, Financial Statements, of this Quarterly Report on Form 10-Q for a discussion of recently issued accounting pronouncements.

ITEM 3. QUANTITATIVE AND QUALITATIVE DISCLOSURE ABOUT MARKET RISK

Interest Rate Risk

We are exposed to market risks in the ordinary course of our business and from changes in the interest rate on our debt borrowings. These market risks are principally limited to interest rate fluctuations. We had cash of \$43.6 million and \$14.0 million as of September 30, 2019 and December 31, 2018, respectively. The primary objective of our investment activities is to preserve principal and liquidity while maximizing income without significantly increasing risk. We do not enter into investments for trading or speculative purposes. Due to the short-term nature of our investment portfolio, we do not believe an immediate 10% increase in interest rates would have a material effect on the fair market value of our portfolio, and, accordingly, we do not expect our operating results or cash flows to be materially affected by a sudden change in market interest rates.

Foreign Currency Exchange Risk

We contract with vendors and third-party manufacturers in several foreign countries. Several of these contracts are denominated in Euros, British pounds, and Australian dollars. We are therefore subject to fluctuations in foreign currency rates in connection with these agreements, and recognize foreign exchange gains or losses in our statement of operations. We have not historically hedged our foreign currency exchange rate risk. To date, we have not incurred any material effects from foreign currency changes on these contracts.

We do not believe a 10% change in these currencies on September 30, 2019 would have had a material effect on our results of operations or financial condition.

Inflation Risk

Inflation generally affects us by increasing our cost of labor and pricing of contracts. We do not believe that inflation has had a material effect on our business, financial condition, or results of operations during the nine months ended September 30, 2019.

ITEM 4. CONTROLS AND PROCEDURES

Disclosure Controls and Procedures. Our management, with the participation of our principal executive officer and our principal 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. Based on that evaluation, our principal executive officer and principal financial officer concluded that our disclosure controls and procedures, as of such date, were effective in ensuring that information required to be disclosed by us in the reports that we file or submit under the Securities Exchange Act of 1934, as amended, or the Exchange Act, is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by us in the reports we file or submit under the Exchange Act is accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate to allow timely decisions regarding required disclosure.

Changes in Internal Control over Financial Reporting. There has been no change in internal controls over financial reporting that occurred during the period covered by this report that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

PART II. OTHER INFORMATION

ITEM 1. LEGAL PROCEEDINGS.

We, and our subsidiaries, are currently not a party to, and our property is not currently the subject of, any material pending legal proceedings; however, we may become involved in various claims and legal actions arising in the ordinary course of business.

ITEM 1A. RISK FACTORS.

Investing in our common stock involves a high degree of risk. You should carefully consider the risk factors set forth below as well as the other information contained in this Quarterly Report on Form 10-Q and in our other public filings in evaluating our business. Any of the following risks could materially and adversely affect our business, financial condition or results of operations. The risks described below are not the only risks facing us. Additional risks and uncertainties not currently known to us or that we currently view to be immaterial may also materially adversely affect our business, financial condition or results of operations. In these circumstances, the market price of our common stock would likely decline.

RISKS RELATED TO OUR FINANCIAL CONDITION AND CAPITAL REQUIREMENTS

We have incurred significant losses since our inception, anticipate that we will incur substantial and increasing losses for the foreseeable future, and may never achieve or maintain profitability.

We are a clinical stage biopharmaceutical company with a limited operating history. For the last several years, we have focused our efforts primarily on developing CNS product candidates, AXS-05, AXS-07, AXS-09, and AXS-12, as well as our Axsome PPC product candidates, AXS-02 and AXS-06, which we refer to herein as our product candidates, with the goal of achieving regulatory approval. Since inception, we have incurred significant operating losses. Our net losses were \$43.5 million and \$31.0 million for nine months ended September 30, 2019 and the year ended December 31, 2018, respectively. As of September 30, 2019, we had an accumulated deficit of \$151.1 million. To date, we have not received regulatory approvals for any of our product candidates or generated any revenue from the sale of products, and we do not expect to generate any revenue in the foreseeable future. We expect to continue to incur substantial and increasing expenses and operating losses over the next several years, as we continue to develop our current and future product candidates. In addition, we expect to incur significant sales, marketing, and manufacturing expenses related to the commercialization of our current and future product candidates, if they are approved by the U.S. Food and Drug Administration, or FDA. As a result, we expect to continue to incur significant losses for the foreseeable future. We anticipate that our expenses will increase substantially as we:

- conduct our Phase 3 clinical trials with AXS-05 for the treatment of depression;
- conduct our open-label safety extension trial for AXS-05;
- conduct our Phase 2/3 clinical trials with AXS-05 for the treatment of agitation associated with Alzheimer's disease, or AD agitation;
- conduct our two Phase 3 clinical trials with AXS-07 for the acute treatment of migraine;
- conduct our open-label safety extension trial for AXS-07;
- conduct our Phase 2 clinical trial with AXS-12 in narcolepsy;
- continue to evaluate, plan for, and conduct, clinical trials for AXS-05 for smoking cessation treatment and AXS-09 for the treatment of CNS disorders;

- continue to evaluate, plan for, and conduct, clinical trials for our Axsome PPC product candidates, including AXS-02 for the treatment of pain associated with knee osteoarthritis, or OA, associated with bone marrow lesions, or BMLs and AXS-06 for the treatment of osteoarthritis and rheumatoid arthritis;
- develop, in-license, or acquire additional product candidates;
- conduct late-stage clinical trials for any product candidates that successfully complete early-stage clinical trials;
- seek regulatory approval for any product candidates that successfully complete late-stage clinical trials;
- conduct additional non-clinical studies with any product candidates;
- conduct clinical studies with any additional product candidates;
- increase manufacturing batch sizes of our product candidates to satisfy FDA requirements for a marketing application submission;
- establish a sales, marketing, and distribution infrastructure, and scale up external manufacturing capabilities to commercialize any products for which we may obtain regulatory approval and that we choose not to license to a third party;
- require larger quantities of product;
- maintain, expand, and protect our intellectual property portfolio;
- hire additional clinical, quality control, and scientific personnel; and
- add operational, financial, and management information systems and personnel, including personnel to support our product candidate development and planned future commercialization efforts.

To become and remain profitable, we must succeed in developing and eventually commercializing products that generate significant revenue. We do not expect to generate significant revenue unless and until we are able to obtain marketing approval for and successfully commercialize one or more of our product candidates. This will require us to be successful in a range of challenging activities, including completing preclinical testing and clinical trials of our product candidates, discovering additional product candidates, potentially entering into collaboration and license agreements, obtaining regulatory approval for product candidates and manufacturing, marketing, and selling any products for which we may obtain regulatory approval, achieving market acceptance of our products, satisfying any post-marketing requirements, maintaining appropriate distribution, setting prices, and obtaining reimbursement for our products from private insurance or government payors. We are only in the preliminary stages of some of these activities. We may never succeed in these activities and, even if we do, may never achieve profitability.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses we may incur or when, or if, we will be able to achieve profitability. If we are required by the FDA or comparable foreign regulatory authorities to perform studies in addition to those currently expected, or if there are any delays in completing our clinical trials or the development of any of our product candidates, our expenses could increase.

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 depress the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our product offerings, or even continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

We will need additional funding to conduct our future clinical trials and to complete development and commercialization of our product candidates. If we are unable to raise capital when needed, we would be forced to delay, reduce, or eliminate our product development programs or commercialization efforts.

Conducting clinical trials, pursuing regulatory approvals, establishing outsourced manufacturing relationships, and successfully manufacturing and commercializing our product candidates is, and will be, a very time-consuming, expensive, and uncertain process that takes years to complete. We will need to raise additional capital to:

- fund our future clinical trials for our current product candidates, especially if we encounter any unforeseen delays or difficulties in our planned development activities;
- fund our operations and continue our efforts to hire additional personnel and build a commercial infrastructure to prepare for the commercialization of our current and future product candidates, if approved by the FDA or other comparable foreign regulatory authorities;
- qualify and outsource the commercial-scale manufacturing of our products under current good manufacturing practices, or cGMP;
- develop additional product candidates; and
- in-license other product candidates.

We believe our currently available cash will be sufficient to fund our anticipated operating cash requirements into the second quarter of 2021. We have based this estimate on assumptions that may prove to be wrong and we could spend our available financial resources faster than we currently expect. Further, we may not have sufficient financial resources to meet all of our objectives if any product candidate is approved, which could require us to postpone, scale back, or eliminate some, or all, of these objectives, including our potential launch activities relating to our product candidates. Our future funding requirements will depend on many factors, including, but not limited to:

- the rate of progress and costs related to the development of our product candidates;
- the costs associated with conducting additional non-clinical studies with any of our product candidates;
- the potential for delays in our efforts to seek regulatory approval for our product candidates, and any costs associated with such delays;
- the costs of establishing a commercial organization to sell, market, and distribute our product candidates;
- the rate of progress and costs of our efforts to prepare for the submission of a new drug application, or NDA, for any product candidates that we may in-license or acquire in the future, and the potential that we may need to conduct additional clinical or preclinical trials to support applications for regulatory approval;
- the costs of filing, prosecuting, defending, and enforcing any patent claims and other intellectual property rights associated with our product candidates;
- the cost and timing of manufacturing sufficient supplies of our product candidates in preparation for commercialization;
- the effect of competing technological and market developments;
- revenue, if any, received from commercial sales of our product candidates, subject to the receipt of regulatory approval;

- the terms and timing of any collaborative, licensing, co-promotion, or other arrangements that we may establish; and
- the success of the commercialization of any of our current or future product candidates.

Future capital requirements will also depend on the extent to which we acquire or invest in additional businesses, products, and technologies. Until we can generate a sufficient amount of product revenue, if ever, we expect to finance future cash needs through public or private equity offerings, debt financings, royalties, and corporate collaboration and licensing arrangements, as well as through interest income earned on cash and investment balances. We cannot be certain that additional funding will be available on acceptable terms, or at all. If adequate funds are not available, we may be required to delay, reduce the scope of, or eliminate one or more of our development programs or our commercialization efforts.

Our operating activities may be restricted as a result of covenants related to the outstanding indebtedness under our loan agreement and we may be required to repay the outstanding indebtedness in an event of default, which could have a materially adverse effect on our business.

In March 2019, we entered into a loan and security agreement with SVB and WestRiver Innovation Lending Fund VIII, L.P., or the 2019 Term Loan, consisting of an initial \$20.0 million tranche, or the Term A Loan Advance, which was funded shortly upon closing, with the remaining \$4.0 million, or the Term B Loan Advance, initially available to be drawn, at our option, subject to the achievement of positive data, on or prior to August 15, 2019, with respect to our ongoing Phase 2 clinical trial for AXS-12 in narcolepsy, sufficient to submit a Phase 3 protocol to the FDA, provided that we have not received any objections from the FDA within thirty days after submission of such Phase 3 protocol, which we refer to as the Milestone Event. A portion of the first tranche was used to satisfy our existing obligations under our original term loan facility with SVB, as amended, and such obligations are considered to be fully repaid and completed. The new term loan facility matures in February 2023 and initially had an interest-only monthly payment period for twelve months, extendable to eighteen months upon funding of the Term B Loan Advance. We refer to the Term A Loan Advance and the Term B Loan Advance together as the Loan Advances.

In July 2019, we entered into a first amendment to the loan and security agreement, or the First Amendment to the 2019 Term Loan. Under the First Amendment to the 2019 Term Loan, the interest-only monthly payment period of the 2019 Term Loan was extended to 18 months after the date of the 2019 Term Loan, which may be further extended to 24 months upon receipt by us of the Term B Loan Advance. Our ability to draw down the Term B Loan Advance was extended to December 31, 2019, subject to our achievement of the Milestone Event prior to or on December 31, 2019. The Loan Advances mature on February 1, 2023, which we refer to as the Maturity Date.

Pursuant to the 2019 Term Loan, as amended by the First Amendment to the 2019 Term Loan, following the interest-only payment period, we will begin making monthly payments of principal in equal monthly installments for 30 consecutive months (provided, that, upon the occurrence of the Milestone Event, the repayment schedule will be decreased to 24 consecutive months) and monthly payments of interest, until the Maturity Date. Interest will accrue on the unpaid principal balance of the outstanding Loan Advances at a floating per annum rate equal to the greater of (i) seven and one-half of one percent (7.50%) and (ii) two percent (2.0%) above the prime rate. The First Amendment to the 2019 Term Loan increased the final payment fee, payable upon our repayment of the Loan Advances from 6.0% to 6.30% of the original principal amount of the Loan Advances.

We may prepay all, but not less than all of the Loan Advances, subject to a prepayment fee of 3.0% of any amount prepaid prior to the first anniversary of July 25, 2019, or the First Amendment Effective Date, 2.0% of the amount prepaid if the prepayment occurs after the first anniversary of the First Amendment Effective Date through and including the second anniversary of the First Amendment Effective Date, or 1.0% of the amount prepaid if the prepayment occurs after the second anniversary of the First Amendment Effective Date, but prior to the Maturity Date. These percentages are unchanged from the original 2019 Term Loan.

The loan subjects us to various customary covenants, including requirements as to financial reporting and insurance, and restrictions on our ability to dispose of our business or property, change our line of business, liquidate or dissolve, enter into any change in control transaction, merge or consolidate with any other entity or acquire all or substantially all the capital stock or property of another entity, incur additional indebtedness, incur certain types of liens on our property, including our intellectual property, pay any dividends or other distributions on our capital stock other than dividends payable solely in capital stock or redeem our capital stock. Our business may be adversely affected by these restrictions on our ability to operate our business.

Additionally, we may be required to repay the outstanding indebtedness under the 2019 Term Loan if an event of default occurs under the 2019 Term Loan. Under the 2019 Term Loan, an event of default will occur if, among other things, we fail to make payments under the 2019 Term Loan; we breach any of our covenants under the 2019 Term Loan, subject to specified cure periods with respect to certain breaches; we or our assets become subject to certain legal proceedings, such as bankruptcy proceedings; we are unable to pay our debts as they become due; or we default on contracts with third parties which would permit SVB to accelerate the maturity of such indebtedness or that could have a material adverse effect on us. We may not have enough available cash or be able to raise additional funds through equity or debt financings to repay such indebtedness at the time any such event of default occurs. In that case, we may be required to delay, limit, reduce or terminate our product candidate development or commercialization efforts or grant to others rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. SVB could also exercise its rights as collateral agent to take possession and dispose of the collateral securing the loan for its benefit, which collateral includes all of our property other than our intellectual property. Our business, financial condition and results of operations could be materially adversely affected as a result of any of these events. Our management has broad discretion in the application of the proceeds from the 2019 Term Loan, subject to the covenants and limitations described in the 2019 Term Loan.

We have a limited operating history and no history of commercializing products, which may make it difficult to evaluate our business and prospects.

We commenced operations in 2012, and our operations to date have been limited to organizing and staffing our company, business planning, raising capital, and developing our product candidates, including undertaking preclinical studies and conducting clinical trials of our product candidates. We have not yet demonstrated an ability to obtain regulatory approval for, or successfully commercialize, a product candidate. In addition, as a relatively nascent business, we may encounter unforeseen expenses, difficulties, complications, delays, and other known and unknown difficulties. If our product candidates are approved by the FDA, we will need to expand our capabilities to support commercial activities. We may not be successful in adding such capabilities. Consequently, any predictions about our future performance may not be as accurate as they could be if we had a history of successfully developing and commercializing pharmaceutical products.

RISKS RELATED TO OUR BUSINESS AND THE DEVELOPMENT OF OUR PRODUCT CANDIDATES

We are substantially dependent on the success of our product candidates and cannot guarantee that any of our product candidates will successfully complete any planned or ongoing Phase 3 clinical trials, receive regulatory approval, or be successfully commercialized.

We currently have no products approved for commercial distribution. We have invested a significant portion of our efforts and financial resources in the development of our product candidates. Our business depends entirely on the successful development and commercialization of our product candidates, which may never occur. Our ability to generate revenues in the near term is substantially dependent on our ability to develop, obtain regulatory approval for, and then successfully commercialize our product candidates. We currently generate no revenues from sales of any products, and we may never be able to develop or commercialize a marketable product. Furthermore, given the nature of our business, the biopharmaceutical industry in general and the uncertainty and costs associated with developing our product candidates within a complicated and costly regulatory regime, our goals, plans and assumptions with respect to our product candidates may evolve or change. For example, we may not continue to emphasize, focus our research and development efforts on or direct resources to certain of our product candidates, and we may shift our focus and resources to our other current or future product candidates. Any such change in our business strategy could harm our business, cause uncertainty or confusion in the marketplace or harm the clinical prospects of our product candidates.

Our product candidates will require additional clinical and non-clinical development, regulatory approval, commercial manufacturing arrangements, establishment of a commercial organization, significant marketing efforts, and further investment before we generate any revenues from product sales. We initiated our Phase 3 clinical trial with AXS-05 for the treatment of TRD in March 2016, our Phase 2/3 trial with AXS-05 for the treatment of agitation associated with AD in July 2017, our Phase 2 with AXS-05 for the treatment of MDD in June 2018, our Phase 2 trial with AXS-12 for the treatment of narcolepsy in January 2019, our Phase 3 trial with AXS-07 for the acute treatment of migraine in March 2019, our Phase 3 trial with AXS-05 for MDD in June 2019, and our second Phase 3 trial with AXS-07 for treatment of acute migraine in October 2019. We began enrolling patients in two open-label safety studies for (i) AXS-05 in the treatment of depression and (ii) AXS-07 in the acute treatment of migraine in July 2019. As a result of one or more risks discussed in this section, we cannot assure you that we will meet projected timelines related to these trials.

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. Even if our product candidates are approved, they may be subject to limitations on the indicated uses for which they may be marketed, distribution restrictions, or to other conditions of approval, may contain significant safety warnings, including boxed warnings, contraindications, and precautions, may not be approved with label statements necessary or desirable for successful commercialization, or may contain requirements for costly post-market testing and surveillance, or other requirements, including the submission of a risk evaluation and mitigation strategy, or REMS, to monitor the safety or efficacy of the products. If we do not receive regulatory approval for, and successfully commercialize, our product candidates, we will not be able to generate revenue from these product candidates in the foreseeable future, or at all. Any significant delays in obtaining approval for and commercializing our product candidates will have a material adverse impact on our business and financial condition.

We have not previously submitted an NDA to the FDA, or similar drug approval filings to comparable foreign authorities, for any product candidate, and we cannot be certain that our current or future product candidates will be successful in clinical trials or receive regulatory approval. Moreover, we have only completed a limited number of studies with our product candidates to date. For AXS-05, we completed three Phase 1 pharmacokinetic studies and one Phase 2 trial in major depressive disorder. A Phase 2 trial of AXS-05 in smoking cessation was completed under a collaboration with Duke University. For AXS-07, we have only conducted two Phase 1 clinical trials. For AXS-09, we have only completed one Phase 1 clinical trial. Finally, for AXS-12, we have not completed a clinical trial. For AXS-02, we have only completed one Phase 1 clinical trial. Furthermore, we have only conducted one Phase 1 pharmacokinetic study for our product candidate AXS-06 and additional manufacturing work is required before we may submit an investigational new drug application, or IND, and begin late-stage clinical trials. The completion of one or more of our previously disclosed clinical trials for our product candidates is not an indication or guarantee that the final results of such trials, in and of themselves, are or will be positive, or that such results will be sufficient to support the filing of an NDA with the FDA or similar approval filings with comparable foreign authorities for our applicable product candidates.

Our product candidates are susceptible to the risks of failure inherent at any stage of product development, including the appearance of unexpected adverse events or failure to achieve its primary endpoints in subsequent clinical trials, including our initiated and planned Phase 3 clinical trials. For example, in January 2018, we conducted an interim analysis for our then-ongoing Phase 3 trial of AXS-02 for the treatment of CRPS, which we referred to as the CREATE-1 trial, and for our currently ongoing Phase 3 trial of AXS-02 for the treatment of the pain of knee OA associated with BMLs, which we refer to as the COAST-1 trial. The independent data monitoring committee recommended continuation of our COAST-1 trial and discontinuation of our CREATE-1 trial for futility. We had paused screening in the COAST-1 trial prior to the conduct of the interim analysis for that trial and currently, we are in the process of closing out the trial. We conducted one interim analysis for the ongoing Phase 3 trial of AXS-05 in TRD and one interim analysis for the Phase 2/3 trial of AXS-05 for the treatment of AD agitation. We may elect to conduct interim analyses for our other clinical trials. Interim results of a clinical trial do not necessarily predict final results, and interim results may result in early stoppage of our clinical trials for futility or modifications to our clinical trials, including the addition of additional subjects. Further, our product candidates may not receive regulatory approval even if they are successful in clinical trials.

If approved for marketing by applicable regulatory authorities, our ability to generate revenues from our product candidates depend on our ability to:

- create market demand for our product candidates through our own marketing and sales activities, and any other arrangements to promote these product candidates that we may otherwise establish;
- receive regulatory approval for claims that are necessary or desirable for successful marketing;
- hire, train, and deploy a sales force to commercialize our product candidates in the United States;
- manufacture our product candidates in sufficient quantities and at acceptable quality and manufacturing cost to meet commercial demand at launch and thereafter;
- establish and maintain agreements with wholesalers, distributors, and group purchasing organizations on commercially reasonable terms;
- create partnerships with, or offer licenses to, third parties to promote and sell our product candidates in foreign markets where we receive marketing approval;
- maintain patent and trade secret protection and regulatory exclusivity for our product candidates;
- launch commercial sales of our product candidates, whether alone or in collaboration with others;
- achieve market acceptance of our product candidates by patients, the medical community, and government and private third-party payors;

- achieve appropriate reimbursement for our product candidates;
- effectively compete with other therapies; and
- maintain a continued acceptable safety profile of our product candidates following launch.

Potential conflicts of interest exist with respect to the intellectual property rights that we license from an entity owned by our Chief Executive Officer and Chairman of the Board, and it is possible that our interests and their interests may diverge.

In 2012, we entered into three exclusive license agreements with Antecip Bioventures II LLC, or Antecip, an entity owned by our Chief Executive Officer and Chairman of the Board, Herriot Tabuteau, M.D., in which we were granted exclusive licenses to develop, manufacture, and commercialize Antecip's patents and applications related to the development of our current product candidates. Although Dr. Tabuteau dedicates all of his working time to us because Antecip is an inactive intellectual property holding company, he may face potential conflicts of interest regarding these licensing transactions as a result of his ownership of Antecip. The license agreements provide that, subject to the reasonable consent of Antecip, we have the right to control the prosecution or defense, as the case may require, of a patent infringement claim involving the licensed intellectual property. Our interests with respect to pleadings and settlements in such cases may be at odds with those of Antecip. If there is a dispute between us and Antecip, Dr. Tabuteau will have a conflict of interest because he may, at the time of a prospective dispute, simultaneously have a financial interest in and owe a fiduciary duty to Antecip and simultaneously have a financial interest in and owe a fiduciary duty to us. For example, if a contractual dispute arises between us and Antecip under any of the license agreements we have with Antecip, Dr. Tabuteau may be in a position where he would benefit if Antecip prevails, to the detriment of our business or our investors, even though he is an officer and director of our company, because he is the sole owner of Antecip. Similarly, if we have a claim of any kind against Antecip, Dr. Tabuteau may be, even as our Chief Executive Officer and Chairman of the Board, reluctant to assert a claim by us against Antecip because of his financial interest in Antecip. We cannot assure you that any conflicts will be resolved in our favor, and as a result, our business could be impeded or materially harmed.

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

Because we have limited financial and managerial resources, we focus on developing product candidates for specific indications that we identify as most likely to succeed, in terms of both its regulatory approval and commercialization. As such, we are currently primarily focused on the development of, AXS-05 for the treatment of depression, agitation associated with AD, and smoking cessation, AXS-07 for the acute treatment of migraine, and AXS-12 for the treatment of narcolepsy. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that may prove to have greater commercial potential. Additionally, as more fully described in "Business—Material License Agreements," we are required to pay to an entity owned by our Chief Executive Officer and Chairman of the Board certain royalty payments related to the development of AXS-02 and AXS-05, as well as AXS-04, a product candidate that is currently in early-stage development, but not with respect to the development of other product candidates, which may influence management's decision concerning which product candidates or indications to pursue. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing, or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

Our future growth may depend on our ability to identify and develop product candidates and if we do not successfully identify and develop product candidates or integrate them into our operations, we may have limited growth opportunities.

A component of our business strategy is to continue to develop a pipeline of product candidates by developing products that we believe are a strategic fit with our focus on central nervous system, or CNS, therapeutics. However, these business activities may entail numerous operational and financial risks, including:

- difficulty or inability to secure financing to fund business activities for such development;
- disruption of our business and diversion of our management’s time and attention;
- higher than expected development costs;
- exposure to unknown liabilities;
- difficulty in managing multiple product development programs; and
- inability to successfully develop new products or clinical failure.

For instance, our prior efforts have resulted in our decision not to further develop certain product candidates that, at one time, appeared to be promising. We have limited resources to identify and execute the developments of products. Moreover, we may devote resources to potential development that are never completed, or we may fail to realize the anticipated benefits of such efforts. If we do not successfully develop and commercialize product candidates, we may not be able to obtain product revenues in future periods.

If safety and efficacy data for our product candidates, a reference listed drug, or published literature does not satisfactorily demonstrate safety and efficacy to the FDA, or if the FDA and other regulators do not permit us to rely on the data of a reference listed drug or published literature, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.

We are not permitted to commercialize, market, promote, or sell any product candidate in the United States without obtaining marketing approval from the FDA. Comparable foreign regulatory authorities, such as the European Medicines Agency, or EMA, impose similar restrictions.

In the United States, we currently plan to at least initially seek approval of our product candidates using the 505(b)(2) pathway. The FDA interprets Section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, or FDCA, for purposes of approving an NDA, to permit the applicant to rely, in part, upon published literature or the FDA’s previous findings of safety and efficacy for an approved product. The FDA, though, requires companies to perform additional clinical trials or preclinical studies to support any deviation from the previously approved product and to support reliance on the FDA’s prior findings of safety and efficacy or published literature.

Under the 505(b)(2) pathway, the FDA may approve our product candidates for all or some of the label indications for which the referenced product has been approved, as well as for any new indication sought pursuant to the Section 505(b)(2) process. The label, however, may require all or some of the limitations, contraindications, warnings, or precautions included in the reference product’s label, including a box warning (commonly referred to as a “black box warning”), or may require additional limitations, contraindications, warnings, or precautions, including class-wide warnings. For instance, antidepressants, including bupropion, include a class-wide black box warning regarding the increased risk of suicidal thoughts and behavior.

Based on the side effects disclosed in FDA product labels for marketed drugs that contain the same active molecule as our product candidate, AXS-02 may result in nausea, fatigue, anemia, bone pain, constipation, fever, vomiting, dyspnea, hypersensitivity reactions, osteonecrosis of the jaw, renal toxicity, musculoskeletal pain, atypical fractures, hypocalcemia, bronchoconstriction, or other adverse events or potential adverse events reported or discussed in the product labels for zoledronic acid-containing products including Zometa, Reclast, and Aclasta.

Based on the side effects disclosed in FDA product labels for marketed drugs that contain the same active molecules as our product candidate, AXS-05 may result in dry mouth, nausea, insomnia, dizziness, pharyngitis, abdominal pain, agitation, anxiety, tremor, seizure, increase in blood pressure and heart rate, hepatotoxicity, hypoglycemia, thrombocytopenia or other hypersensitivity reactions, QRS prolongation, left ventricular hypertrophy or left ventricular dysfunction, palpitation, sweating, tinnitus, myalgia, anorexia, urinary frequency, rash, seizure, hypertension, activation of mania or hypomania, psychosis and other neuropsychiatric reactions, suicidal ideation, suicide attempt, completed suicide, angle closure glaucoma, allergic or anaphylactoid or anaphylactic reactions, diarrhea, cough, vomiting, asthenia, peripheral edema, urinary tract infection, influenza, increased gamma-glutamyltransferase, flatulence, or other adverse events or potential adverse events reported or discussed in the product labels for bupropion-containing products or dextromethorphan-containing products including Wellbutrin, Wellbutrin SR, Wellbutrin XL, Zyban, Contrave, and Nuedexta.

Based on the side effects disclosed in FDA product labels for marketed drugs that contain the same active molecules as our product candidate, AXS-07 may result in fatigue, confusion, dry mouth, diarrhea, nausea, insomnia, anemia, increased appetite, anxiety, sweating, dizziness, palpitations, arrhythmia, tachycardia, abnormal vision, syncope, seizure, tremor, tinnitus, dizziness, somnolence, paresthesia, dysgeusia, dyspepsia, constipation, weight increase or decrease, gastritis, hematuria, flatulence, esophagitis, gastric ulcers, gastroesophageal reflux, gastrointestinal hemorrhages, colitis, rash, pain or tightness in the chest, neck, throat or jaw, upper respiratory tract infections, influenza-like symptoms, or other adverse events or potential adverse events reported or discussed in the product labels for meloxicam containing or rizatriptan-containing products including Vivlodex, Mobic, and Maxalt.

Based on the side effects disclosed in EMA product label for marketed drugs that contain the same active molecule as our product candidate, AXS-12 may result in decreased appetite, insomnia, agitation, anxiety, dizziness, headache, paraesthesia, akathisia, dysgeusia, accommodation disorder, mydriasis, glaucoma, vertigo, tachycardia, palpitations, vasodilation, hypotension, hypertension, dry mouth, vomiting, hyperhidrosis, rash, sensation of incomplete bladder emptying, urinary tract infection, dysuria, urinary retention, erectile dysfunction, ejaculatory pain, ejaculatory delay, chills, or other adverse events or potential adverse events reported or discussed in the product labels for reboxetine containing products including Edronax.

In addition, because we plan to file our product candidates under an NDA submitted pursuant to 505(b)(2), we will rely, at least in part, upon a reference listed drug and published literature. For example, we intend to rely on data collected in certain investigator-initiated Phase 2 clinical trials and other third-party studies in the published literature as well as FDA findings of safety and efficacy for approved drug products containing the same active molecules in AXS-05 and AXS-07. If the FDA disagrees with our conclusions regarding the appropriateness of our reliance on a reference listed drug or published literature, we could be required to conduct additional clinical trials or other studies to support our NDA, which could lead to unanticipated costs and delays or to the termination of our development program. If we are unable to obtain approval for our pharmaceutical formulations through the 505(b)(2) NDA process, we may be required to pursue the more expensive and time-consuming 505(b)(1) approval process, which consists of full reports of investigations of safety and effectiveness conducted by or for the applicant. In addition, because we plan to submit NDAs for AXS-05 and AXS-07 pursuant to the 505(b)(2) process, we have not conducted certain additional clinical trials for these product candidates and, as such, we will have less experience with actual testing of the product candidate.

There may also be circumstances under which the FDA would not allow us to pursue a 505(b)(2) application. For instance, should the FDA approve a pharmaceutically equivalent product to our product candidates before we obtain approval, we would no longer be able to use the 505(b)(2) pathway. In that case, it is the FDA's policy that the appropriate submission would be an Abbreviated New Drug Application, or ANDA, for a generic version of the approved product. We may, however, not be able to immediately submit an ANDA or have an ANDA approval made effective, as we could be blocked by others' periods of patent and regulatory exclusivity protection.

Notwithstanding the approval of a number of products by the FDA under 505(b)(2) over the last few years, pharmaceutical companies and others have objected to the FDA's interpretation of Section 505(b)(2). If the FDA's interpretation of Section 505(b)(2) is successfully challenged, the FDA may change its policies and practices with respect to Section 505(b)(2) regulatory approvals, which could delay or even prevent the FDA from approving any NDA that we submit pursuant to the 505(b)(2) process. Moreover, our inability to pursue a 505(b)(2) application could result in new competitive products reaching the market more quickly than our product candidates, which could hurt our competitive position and our business prospects.

We may never receive approval for any of our product candidates, and even if our product candidates are approved under 505(b)(2), the approval may be subject to limitations on the indicated uses for which the products may be marketed, distribution restrictions, or to other conditions of approval; may contain significant safety warnings, including boxed warnings, contraindications, and precautions; may not be approved with label statements necessary or desirable for successful commercialization; or may contain requirements for costly post-market testing and surveillance or other requirements, including REMS, to monitor the safety or efficacy of the products. Moreover, any future actions or inquiries by the FDA with respect to the reference listed drug may require that we make changes to our labeling, discontinue development, or, possibly, withdraw the product from the market.

An NDA submitted under Section 505(b)(2) subjects us to the risk that we may be subject to a patent infringement lawsuit or regulatory actions that would delay or prevent the review or approval of our product candidate.

Applicants submitting NDAs under Section 505(b)(2) of the FDCA must provide a patent certification with the application for all reference listed drugs and for all brand name products identified in published literature upon which the 505(b)(2) application relies. One such certification is known as a paragraph IV certification, which certifies that any patents listed in the FDA's publication, the *Approved Drug Products with Therapeutic Equivalence Evaluations*, commonly known as the Orange Book, are invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of the product that is the subject of the 505(b)(2) NDA.

Under the Hatch-Waxman Act, the holder of patents or NDAs that the 505(b)(2) application references may file a patent infringement lawsuit after receiving notice of the paragraph IV certification. Filing of a patent infringement lawsuit against the filer of the 505(b)(2) applicant within 45 days of the patent or NDA owner's receipt of notice triggers a one-time, automatic, 30-month stay of the FDA's ability to make the 505(b)(2) NDA approval effective. In such a case, the FDA may not make the 505(b)(2) NDA approval effective until the earlier of 30 months from the receipt of the notice of the paragraph IV certification, the expiration of the patent, when the infringement case concerning each such patent was favorably decided in the applicant's favor or settled, or such shorter or longer period as may be ordered by a court. Accordingly, we may invest a significant amount of time and expense in the development of one or more product candidates only to be subject to significant delay and patent litigation before such product candidates may be commercialized, if at all. In addition, a 505(b)(2) application approval will not be made effective until any existing non-patent exclusivity, such as exclusivity for obtaining approval of a new chemical entity, or NCE, or exclusivities for changes to NCEs listed in the Orange Book for the referenced product have expired or, if possible, are carved out from the label.

Companies that produce branded reference listed drugs routinely bring litigation against applicants that seek regulatory approval to manufacture and market generic and reformulated forms of their branded products. These companies often allege patent infringement or other violations of intellectual property rights as the basis for filing suit. Likewise, patent holders may bring patent infringement suits against companies that are currently marketing and selling their approved generic or reformulated products. Litigation to enforce or defend intellectual property rights is often complex and often involves significant expense and can delay or prevent introduction or sale of our product candidates. If patents are held to be valid and infringed by our product candidates in a particular jurisdiction, we may be required to cease selling, relinquish or destroy existing stock, or pay monetary damages in that jurisdiction unless we can obtain a license from the patent holder. There may also be situations where we use our business judgment and decide to market and sell our approved products, notwithstanding the fact that allegations of patent infringement(s) have not been finally resolved by the courts, which is known as an “at-risk launch.” The risk involved in doing so can be substantial because the remedies available to the owner of a patent for infringement may include, among other things, damages measured by the profits lost by the patent owner which may be greater than the profits earned by the infringer. In the case of willful infringement, such damages may be increased up to three times. An adverse decision in patent litigation could have a material adverse effect on our business, financial position, and results of operations and could cause the market value of our common stock to decline. Should we need to file a paragraph IV certification in the future for our product candidates, we may risk patent litigation and substantial delays.

The regulatory approval processes of the FDA and comparable foreign authorities are lengthy, time consuming, and inherently unpredictable. If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize our product candidates as expected, and our ability to generate revenue will be materially impaired.

The time required to obtain approval by the FDA and comparable foreign authorities is unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. 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, and may require us to amend our clinical trial protocols or conduct additional studies that require regulatory or institutional review board, or IRB, approval, or otherwise cause delays in the approval or rejection of an application. We have not 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. Any delay in obtaining or failure to obtain required approvals could materially adversely affect our ability or that of any of our collaborators to generate revenue from the particular product candidate, which likely would result in significant harm to our financial position and adversely impact our stock price.

Our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale, and distribution, are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States, and by the EMA and similar regulatory authorities outside the United States and Europe. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate. We have no experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third-party contract research organizations, or CROs, and consultants to assist us in this process. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate’s safety and efficacy for that indication and the submission of information about the product manufacturing process to, and inspection of manufacturing facilities and clinical trial sites by, the regulatory authorities.

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 trial process. The results of preclinical studies; our product candidates' mechanism of action; studies conducted by third parties in different patient populations, using different products, or using different study designs; and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through preclinical studies and initial clinical trials. Preclinical studies may also reveal unfavorable product candidate characteristics, including safety concerns. A number of companies in the pharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials. Our future clinical trial results may not be successful. Moreover, should there be a flaw in a clinical trial, it may not become apparent until the clinical trial is well advanced.

We may also experience numerous unforeseen events during, or as a result of, clinical trials and in the course of our preparation, submission, and review of NDA filings that could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including:

- regulators or IRBs may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site or amend trial protocols;
- we may experience delays in reaching, or fail to reach, agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites and our CROs;
- clinical trials of our product candidates may produce negative or inconclusive results, or our studies may fail to reach the necessary level of statistical or clinical significance, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- interim analyses may result in our clinical trials being discontinued for safety or futility reasons or may result in modifications to our clinical trials that prolong the trials or make them difficult and more expensive to complete, such as increases in the number of subjects;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate, or participants may drop out of these clinical trials at a higher rate than we anticipate;
- our third-party contractors may fail to comply with regulatory requirements or the clinical trial protocol, or meet their contractual obligations to us in a timely manner, or at all, or we may be required to engage in additional clinical trial site monitoring;
- we, the regulators, or IRBs may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks, undesirable side effects, or other unexpected characteristics of the product candidate, or due to findings of undesirable effects caused by a chemically or mechanistically similar drug or drug candidate. We may also discontinue clinical research and programs due to changing business priorities;
- changes in marketing approval policies during the development period rendering our data insufficient to obtain marketing approval;
- changes in or the enactment of additional statutes or regulations;
- changes in regulatory review for each submitted product application;

- the cost of clinical trials of our product candidates may be greater than we anticipate or we may have insufficient funds for a clinical trial or to pay the substantial user fees required by the FDA upon the filing of an NDA;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate;
- we may decide, or regulators may require us, to conduct additional clinical trials, analyses, reports, data, or preclinical/nonclinical studies than we currently plan, or we may abandon product development programs. For instance, with respect to AXS-05, we may need to conduct additional clinical and preclinical studies in addition to our Phase 3 and Phase 2/3 trials in order to file an NDA for this product candidate. Additionally, although we believe that we may be able to rely on the completed Phase 2 ASCEND trial and either the Phase 3 STRIDE-1 trial or the Phase 3 placebo-controlled GEMINI trial in MDD to support an NDA for AXS-05 for the treatment of MDD and on the MOMENTUM study, which is being conducted pursuant to a Special Protocol Assessment, or SPA, to support an NDA for AXS-07 for the acute treatment of migraine, the FDA may ultimately require us to conduct additional one or more clinical studies to support the filing of an NDA for either of these product candidates. Finally, for AXS-12, we will need to conduct additional clinical studies in addition to our newly initiated Phase 2 trial in order to file an NDA for this product candidate. The outcome of our studies may further necessitate additional clinical or preclinical work;
- we may fail to reach an agreement with regulators regarding the scope or design of our clinical trials;
- we may have delays in adding new investigators or clinical trial sites, or we may experience a withdrawal of clinical trial sites;
- patients that enroll in our studies may misrepresent their eligibility or may otherwise not comply with the clinical trial protocol, resulting in the need to drop the patients from the study or clinical trial, increase the needed enrollment size for the study or clinical trial, or extend the study's or clinical trial's duration;
- there may be regulatory questions regarding interpretations of data and results, or new information may emerge regarding our product candidates;
- the FDA or comparable foreign regulatory authorities may disagree with our study design or our interpretation of data from preclinical studies and clinical trials or find that a product candidate's benefits do not outweigh its safety risks. For instance, in our communications with the FDA, the FDA has raised questions and had comments regarding our preclinical studies and clinical trials, such as comments on the acceptability of the proposed trial designs for our product candidates, the number of patients planned for our studies, our data analysis plans, the applicability of the serum biomarkers studied in our Phase 1 study of AXS-02, the species and doses used in our preclinical studies, and the results of our preclinical studies;
- the FDA or comparable foreign regulatory authorities may disagree with our belief that certain product attributes are advantageous or may require further study of product attributes that are different than our reference listed drugs. For instance, while we believe that certain of the pharmacokinetic results for AXS-06 are favorable, the FDA may disagree, refuse labeling claims based upon these results, or determine that additional studies are necessary to substantiate the benefits. Pharmacokinetic differences between our product candidates and the reference listed drugs, may also make bridging studies more difficult or may prevent us from using the 505(b)(2) pathway. If we are prevented from using the 505(b)(2) pathway, we will need to use the more time consuming and expensive NDA pathway to receive product approval;
- the FDA or comparable foreign regulatory authorities may not accept data from studies with clinical trial sites in foreign countries;
- the FDA or comparable foreign regulatory authorities may disagree with our intended indications;

- the FDA or comparable foreign regulatory authorities may fail to approve or subsequently find fault with the manufacturing processes or our manufacturing facilities for clinical and future commercial supplies;
- in connection with the chemistry, manufacturing, and controls (CMC) data necessary for our NDA filings, we will need to conduct stability studies and provide stability data to establish appropriate retest or expiration dating period;
- applicable to all future drug substance and drug product batches manufactured, packaged, and stored under similar circumstances, to establish the long-term storage conditions, and to provide evidence of the effect of various environmental conditions on the quality of the drug substance and drug product. Our product candidates may not demonstrate sufficient long-term stability to support an NDA filing or obtain approval, or the product shelf life may be limited by stability results;
- the FDA or comparable foreign regulatory authorities may take longer than we anticipate to make a decision on our product candidates; and
- we may not be able to demonstrate that a product candidate provides an advantage over current standards of care or current or future competitive therapies in development.

Moreover, if we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials or other testing of our product candidates, if the results of these trials or tests are not positive, or are only modestly positive or if there are safety concerns, we may:

- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired or are not covered by our intellectual property;
- obtain approval with labeling that includes significant use or distribution restrictions, including restrictions on the intended patient population, or safety warnings, including boxed warnings, contraindications, and precautions, or may not include label statements necessary or desirable for successful commercialization;
- be subject to additional post-marketing testing and surveillance requirements, including REMS; or
- have the product removed from the market after obtaining marketing approval.

Our product candidate development costs will also increase if we experience delays in testing or approvals and we may not have sufficient funding to complete the testing and approval process for any of our product candidates. We may be required to obtain additional funds to complete clinical trials and prepare for possible commercialization of our product candidates. We do not know whether any additional preclinical tests or clinical trials will be required, will begin as planned, will need to be restructured, or will be completed on schedule, or at all. Significant delays relating to any preclinical studies or clinical trials also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors, or the competitors of our collaborators, to bring products to market before we do and impair our ability to successfully commercialize our product candidates and may harm our business and results of operations. In addition, many of the factors that cause, or lead to, such delays may ultimately lead to the denial of marketing approval of any of our product candidates. If any of this occurs, our business, financial condition, results of operations, and prospects will be materially harmed.

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 studies, clinical trials, or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit, or prevent marketing approval of a product candidate. During the course of review, the FDA may also request or require additional CMC, or other data and information, and the development and provision of these data and information may be time consuming and expensive. Furthermore, there is the possibility that the FDA or comparable foreign regulatory authorities have not previously reviewed product candidates for the indications we are pursuing, such as bisphosphonates for the treatment of pain. As a result, we may experience delays in regulatory approval due to uncertainties in the approval process.

Finally, even if we were to obtain approval, regulatory authorities may approve any of our product candidates for fewer or more limited indications or uses than we request, may contain significant safety warnings, including black box warnings, contraindications, and precautions, may grant approval contingent on the performance of costly post-marketing clinical trials, surveillance, or other requirements, including REMS to monitor the safety or efficacy of the product, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. Any of these scenarios could compromise the commercial prospects for our product candidates.

If we experience delays in obtaining approval, if we fail to obtain approval of a product candidate or if the label for a product candidate does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate, the commercial prospects for such product candidate may be harmed and our ability to generate revenues from that product candidate will be materially impaired.

If we cannot demonstrate an acceptable safety and toxicity profile for our product candidates, we will not be able to continue our clinical trials of or obtain approval for those product candidates.

In order to obtain approval of a product candidate we must demonstrate safety in various nonclinical tests (including, for example, carcinogenicity studies, drug-drug interaction studies, and toxicity studies), in addition to human clinical trials. At the time of initiating human clinical trials, we may not have conducted or may not conduct all the types of nonclinical testing ultimately required by regulatory authorities, or future nonclinical tests may indicate safety concerns regarding our product candidates. Nonclinical testing and clinical testing are both expensive and time-consuming and have uncertain outcomes. Even if initial tests appear favorable, later testing may have unfavorable results. We may experience numerous unforeseen events during, or as a result of, the testing process, which could delay or prevent our ability to develop or commercialize our product candidates, including:

- our preclinical or nonclinical testing may produce inconclusive or negative safety results, which may require us to conduct additional nonclinical testing or to abandon product candidates;
- our product candidates may have unfavorable pharmacology or toxicity characteristics or suggest possible drug-drug interaction;
- our product candidates may cause undesirable side effects; and
- the FDA or other regulatory authorities may determine that additional safety testing is required.

Any such events would increase our costs and could delay or prevent our ability to commercialize our product candidates, which could adversely impact our business, financial condition and results of operation.

The FDA may determine that any of our current or future product candidates have undesirable side effects that could delay or prevent their regulatory approval or commercialization.

Undesirable side effects caused by our product candidates could cause us, IRBs, and other reviewing entities or regulatory authorities to interrupt, delay, or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign authorities. For example, if concerns are raised regarding the safety of a new drug as a result of undesirable side effects identified during clinical or preclinical testing, the FDA may order us to cease further development, decline to approve the drug, or issue a letter requesting additional data or information prior to making a final decision regarding whether or not to approve the drug.

The number of requests for additional data or information issued by the FDA in recent years has increased, and resulted in substantial delays in the approval of several new drugs. Undesirable side effects caused by any of our current or future product candidates could also result in denial of regulatory approval by the FDA or other comparable foreign authorities for any or all targeted indications or the inclusion of unfavorable information in our product labeling, such as limitations on the indicated uses for which the products may be marketed or distributed, a label with significant safety warnings, including boxed warnings, contraindications, and precautions, a label without statements necessary or desirable for successful commercialization, or may result in requirements for costly post-marketing testing and surveillance, or other requirements, including REMS, to monitor the safety or efficacy of the products, and in turn prevent us from commercializing and generating revenues from the sale of any of our current or future product candidates.

To date, the most commonly reported adverse events observed in the completed clinical trial of AXS-02 include headache, fever, musculoskeletal pain, diarrhea, abdominal pain, nausea, myalgia, and chills. Some reported adverse events led to discontinuation from our trial of AXS-02. These adverse events included abdominal pain.

To date, the most commonly reported adverse events observed in a completed clinical trial with zoledronic acid, the active molecule in AXS-02, for the treatment of the pain of knee OA associated with BMLs include acute phase reactions, primarily cold or flu-like symptoms and headaches.

To date, the most commonly reported adverse events observed in a completed clinical trial with zoledronic acid, the active molecule in AXS-02, for the treatment of CLBP associated with MCs include fever, headache, myalgia, arthralgia, pain, nausea, and flu-like symptoms. Sinusitis requiring temporary hospitalization following zoledronic acid infusion was reported in one patient and was therefore classified as a serious adverse event.

To date, the most commonly reported adverse events observed in the completed clinical trials of the combination of DM, one of the active molecules in AXS-05, and quinidine for the treatment of pseudobulbar affect and agitation in patients with probable AD include falls, dizziness, headache, nausea, diarrhea, and urinary tract infection.

To date, the most commonly reported adverse events observed in the completed clinical trials of AXS-05 include headache, nausea, dizziness, insomnia, dry mouth, fatigue, hypoesthesia, disturbance in attention, hyperhidrosis, increased heart rate, palpitation, constipation, diarrhea, increased blood pressure, and tremor. Some reported adverse events resulted in discontinuations from our trials of AXS-05. These adverse events included chest pain, headache, abdominal pain, diarrhea, signs of potential allergic reactions, atrial tachycardia, disturbance in attention, metamorphosis, tremor, feeling hot, dizziness, dyspnea, and increased respiratory rate. AXS-05 consists of DM and bupropion, and this combination may exacerbate any known adverse events for each individual component, or may result in new toxicities as compared to those of the individual components.

If any of our other product candidates is associated with serious adverse events or undesirable side effects or have properties that are unexpected, we may need to abandon development or limit development of that product candidate to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe, or more acceptable from a risk-benefit perspective. The drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may significantly harm our business, financial condition, results of operations, and prospects.

If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

We may not be able to initiate or continue conducting clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside the United States. Some of our competitors have ongoing clinical trials for product candidates that treat the same indications as our product candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates. Patient enrollment is affected by other factors including:

- the size and nature of the patient population;
- the severity of the disease under investigation;
- the eligibility criteria for, and design of, the clinical trial in question, including factors such as frequency of required assessments, length of the study, and ongoing monitoring requirements;
- the perceived risks and benefits of the product candidate under study, including the potential advantages or disadvantages of the product candidate being studied in relation to other available therapies;
- competition in recruiting and enrolling patients in clinical trials;
- the efforts to facilitate timely enrollment in clinical trials;
- the patient referral practices of physicians;
- effectiveness of publicity created by clinical trial sites regarding the trial;
- patients' ability to comply with the specific instructions related to the trial protocol, proper documentation, and use of the drug product;
- inability to obtain or maintain patient informed consents;
- risk that enrolled patients will drop out before completion;
- the ability to monitor patients adequately during and after treatment; and
- the proximity and availability of clinical trial sites for prospective patients.

Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays which would cause us to miss our projected timelines and could require us to abandon one or more clinical trials altogether. For instance, because we are seeking regulatory approval for certain indications that may have a narrow or small patient population, it may be difficult to find patients eligible to participate in our clinical studies at a sufficient rate or in a sufficient quantity. For clinical trials with AXS-02 for the treatment of the pain of knee OA associated with BMLs and clinical trials in CLBP associated with type 1 or mixed type 1 and type 2 MCs, enrollment will require the existence of radiographic biomarkers, we may require patients to discontinue use of their existing medication before participating in our clinical trials, and we may exclude patients with advanced disease. In addition, for any Phase 3 clinical trial with AXS-02 in CLBP associated with type 1 or mixed type 1 and type 2 MCs, we will exclude women of childbearing potential from our potential patient population. We may also exclude patients who have been treated with opioids or other classes of medications. For our Phase 3 clinical trial with AXS-05 for the treatment of TRD, we are requiring patients to have previously failed one or two antidepressant treatments, which further limits our potential patient population. For our Phase 2/3 clinical trial with AXS-05 for the treatment of agitation associated with AD, we exclude patients who have been treated with certain classes of medications. For our Phase 3 MOMENTUM clinical trial with AXS-07 for the acute treatment of migraine, only patients with a history of inadequate response to prior migraine treatments will be enrolled. These and other entry criteria may make it difficult for us to enroll patients in any of our clinical trials. We may be required by the FDA to modify the entry criteria for our ongoing or planned Phase 3 clinical trials and these changes may make it more difficult to enroll patients in our clinical trials. Moreover, patients in our clinical trials, especially patients in our control groups, may be at risk for dropping out of our studies if they are not experiencing relief of their symptoms. A significant number of withdrawn patients would compromise the quality of our data.

Enrollment delays or slower periods of enrollment in our clinical trials may result in increased development costs for our product candidates, or the inability to complete development of our product candidates, which would cause the value of our company to decline, limit our ability to obtain additional financing, and materially impair our ability to generate revenues.

Currently approved products containing bupropion are subject to restrictive marketing and distribution regulations, which if applied to our product candidates would restrict their use and harm our ability to generate profits.

Some of the currently approved products containing the same active ingredients as our product candidates require medication guides. Medication guides can be required independently or as part of REMS programs. REMS programs, in addition to medication guides, may require special communication plans to healthcare professionals, or elements to assure safe use, such as restricted distribution methods, distribution only to certain medical professionals, training for medical professionals prescribing our product candidates, patient registries, or other risk minimization tools. The FDA may determine that our product candidates will require a REMS program or medication guide. We cannot predict whether either will be required as part of the FDA's approval of our product candidates and, if required, what those requirements might be. Any limitations on approval or marketing could restrict the commercial promotion, distribution, prescription, or dispensing of our product candidates, if approved. If a REMS program is required, depending on the extent of the REMS requirements, the program might significantly increase our costs to commercialize these product candidates or could place a substantial burden on medical professionals, discouraging their use of our product candidates, if approved. Furthermore, risks of our product candidates that are not adequately addressed through proposed REMS or medication guides for such product candidates may also prevent or delay their approval for commercialization.

Development of combination product candidates may present more or different challenges than development of a single agent product candidate.

Certain of our product candidates, including AXS-05, AXS-06, AXS-07, and AXS-09 are combination therapies. A combination therapy is a single drug product that consists of two or more active ingredients, with each component making a contribution to the claimed effect of the drug. The development of combination drugs may be more complex than the development of single agent products and generally requires that sponsors demonstrate the contribution of each component to the claimed effect and the safety and efficacy of the product as a whole. This requirement may make the design and conduct of clinical trials more complex, requiring more clinical trial subjects. We also may not be able to meet the FDA's approval standards required for combination products. The FDA's requirements concerning combination products may change in the future. Moreover, the applicable requirements for approval may differ from country to country.

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

As product candidates are developed through preclinical studies to late-stage clinical trials towards approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods and formulation, are altered along the way in an effort to optimize processes and results. For instance, two of our initial studies of AXS-05 were completed with two separate tablets containing DM and bupropion. Our Phase 3 studies, however, are being conducted using a single tablet containing both active ingredients. Such changes carry the risk that they will not achieve these intended objectives. Any of these changes could cause our product candidates to perform differently and affect the results of planned clinical trials or other future clinical trials conducted with the altered materials. Such changes may also require additional testing, FDA notification, or FDA approval. This could delay completion of clinical trials; require the conduct of bridging clinical trials or studies, or the repetition of one or more clinical trials; increase clinical trial costs; delay approval of our product candidates; and jeopardize our ability to commence product sales and generate revenue.

Failure to obtain marketing approval in international jurisdictions would prevent our product candidates from being marketed abroad.

In order to market and sell our products in the European Union, or EU, and many other jurisdictions, we or our third-party collaborators must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We or these third parties may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. However, the failure to obtain approval in one jurisdiction may compromise our ability to obtain approval elsewhere. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any market.

A Fast Track product designation or other designation to facilitate product candidate development may not lead to faster development or regulatory review or approval process, and it does not increase the likelihood that our product candidates will receive marketing approval.

We have received a Fast Track product designation for AXS-02 for the treatment of the pain of knee OA associated with BMLs, and for AXS-05 for both the treatment of TRD as well as for the treatment of agitation associated with AD, and we may seek Fast Track designation for other of our current or future product candidates. Receipt of a designation to facilitate product candidate development is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for a designation, the FDA may disagree. In any event, the receipt of such a designation for a product candidate may not result in a faster development process, review, or approval compared to drugs considered for approval under conventional FDA procedures and does not assure ultimate marketing approval by the FDA. In addition, the FDA may later decide that the products no longer meet the designation conditions.

Although the breakthrough therapy process is designed to expedite the review and development of drugs, Breakthrough Therapy designation by the FDA for AXS-05 for the treatment of MDD may not ultimately lead to a faster development or regulatory review or approval process, and it will not increase the likelihood that the product candidate will receive marketing approval.

We received Breakthrough Therapy designation for AXS-05 for the treatment of MDD. A breakthrough therapy is defined as a product candidate that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the product candidate may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For product candidates that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Product candidates designated as breakthrough therapies by the FDA are also eligible for priority review if supported by clinical data at the time of the submission of the NDA.

Designation as a breakthrough therapy is within the discretion of the FDA. The receipt of a Breakthrough Therapy designation for a product candidate may not ultimately result in a faster development process or review, and it does not in any way assure approval of product candidates by the FDA. In addition, the FDA may later decide to rescind the Breakthrough Therapy designation if our product candidate no longer meets the conditions for qualification of this program.

Regulatory approval is limited by the FDA or comparable foreign regulatory authorities to those specific indications and conditions for which clinical safety and efficacy have been demonstrated, and we may be subject to fines, penalties, injunctions, or other enforcement actions if we are determined to be promoting the use of our products for unapproved or “off-label” uses, resulting in damage to our reputation and business.

We, and any of our collaborators, must comply with requirements concerning advertising and promotion for any of our product candidates for which we or they obtain marketing approval. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and continuing review by the FDA, Department of Justice, Department of Health and Human Services’ Office of Inspector General, state attorneys general, members of Congress, and the public. When the FDA or comparable foreign regulatory authorities issue regulatory approval for a product candidate, the regulatory approval is limited to those specific uses and indications for which a product is approved. If we are not able to obtain FDA approval for any desired uses or indications for our products and product candidates, we may not market or promote our products for those indications and uses, referred to as off-label uses, and our business may be adversely affected. We further must be able to sufficiently substantiate any claims that we make for our products including claims comparing our products to other companies’ products.

While physicians may choose to prescribe drugs for uses that are not described in the product’s labeling and for uses that differ from those tested in clinical studies and approved by the regulatory authorities, we are prohibited from marketing and promoting the products for indications and uses that are not specifically approved by the FDA or comparable foreign regulatory authorities. These off-label uses are common across medical specialties and may constitute an appropriate treatment for some patients in varied circumstances. Regulatory authorities in the United States and in many other major markets do not generally restrict or regulate the behavior of physicians in their choice of treatment within the practice of medicine. Regulatory authorities do, however, restrict communications by pharmaceutical companies concerning off-label use.

If we are found to have impermissibly promoted any of our product candidates, we may become subject to significant liability and government fines. The FDA and other agencies actively enforce the laws and regulations regarding product promotion, particularly those prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted a product may be subject to significant sanctions. 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 of permanent injunctions under which specified promotional conduct is changed or curtailed. Thus, we and any of our collaborators will not be able to promote any products we develop for indications or uses for which they are not approved.

In the United States, engaging in the impermissible promotion of our products, following approval, for off-label uses can also subject us to false claims and other litigation under federal and state statutes, including fraud and abuse and consumer protection laws, which can lead to civil and criminal penalties and fines, agreements with governmental authorities that materially restrict the manner in which we promote or distribute drug products and do business through, for example, corporate integrity agreements, suspension or exclusion from participation in federal and state healthcare programs, and debarment from government contracts and refusal of future orders under existing contracts. Recent court decisions have impacted the FDA's enforcement activity regarding off-label promotion in light of First Amendment considerations; however, there are still significant risks in this area in part due to the potential False Claims Act exposure. The False Claims Act allows any individual to bring a lawsuit against a pharmaceutical company on behalf of the federal government alleging submission of false or fraudulent claims, or causing others to present such false or fraudulent claims, for payment by a federal program such as Medicare or Medicaid. If the government decides to intervene and prevails in the qui tam lawsuit, the individual will share in the proceeds from any fines or settlement funds. If the government declines to intervene, the individual may pursue the case alone. Under the False Claims Act, a penalty may be imposed for each false claim, for example, a claim for payment for each prescription for the product, and, when aggregated, these penalties often total millions of dollars and incentivize qui tam lawsuits. These False Claims Act lawsuits against pharmaceutical companies have increased significantly in volume and breadth, leading to several substantial civil and criminal settlements, up to \$3.0 billion, pertaining to certain sales practices and promoting off-label drug uses. This growth in litigation has increased the risk that a pharmaceutical company will have to defend a false claim action; pay settlement fines or restitution, as well as criminal and civil penalties; agree to comply with burdensome reporting and compliance obligations; and be excluded from Medicare, Medicaid, or other federal and state healthcare programs. If we or our collaborators do not lawfully promote our approved products, if any, we may become subject to such litigation and, if we do not successfully defend against such actions, those actions may have a material adverse effect on our business, financial condition, results of operations, and prospects.

In the United States, the distribution of product samples to physicians must further comply with the requirements of the U.S. Prescription Drug Marketing Act. If the FDA determines that our promotional materials or activities violate its regulations and policies pertaining to product promotion, it could request that we modify our promotional materials or activities or subject us to regulatory or other enforcement actions, including issuance of warning letters or untitled letters, suspension or withdrawal of an approved product from the market, requests for recalls, payment of civil fines, disgorgement of money, imposition of operating restrictions, injunctions, or criminal prosecution. These regulatory and enforcement actions could significantly harm our business, financial condition, results of operations, and prospects.

We are, and if any of our product candidates receive regulatory approval, will continue to be subject to ongoing obligations and continued regulatory review, which may result in significant additional expense. Additionally, any of our product candidates, if approved, could be subject to labeling and other restrictions and market withdrawal and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our products.

Any product candidate for which we obtain marketing approval will be subject to extensive and ongoing requirements of and review by the FDA and other regulatory authorities, including requirements related to the manufacturing processes, post-approval clinical data, labeling, packaging, distribution, adverse event reporting, storage, recordkeeping, export, import, advertising, marketing, and promotional activities for such product. These requirements further include submissions of safety and other post-marketing information, including manufacturing deviations and reports; registration and listing requirements; the payment of annual program fees for our product candidates, if approved; continued compliance with cGMP requirements relating to manufacturing, quality control, quality assurance, and corresponding maintenance of records and documents; requirements regarding the distribution of samples to physicians and recordkeeping; and good clinical practices, or GCPs, for any clinical trials that we conduct post-approval. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses and populations for which the product may be marketed or to the conditions of approval, including significant safety warnings, including boxed warnings, contraindications, and precautions that are not desirable for successful commercialization and any requirement to implement a REMS that render the approved product not commercially viable or other post-market requirements or restrictions. Any such restrictions could limit sales of the product.

We and any of our collaborators, including our contract manufacturers, could be subject to periodic unannounced inspections by the FDA to monitor and ensure compliance with cGMPs. Application holders must further notify the FDA, and depending on the nature of the change, obtain FDA pre-approval for product and manufacturing changes. Application fees may apply to certain changes.

In addition, later discovery of previously unknown adverse events or that the drug is less effective than previously thought or other problems with our products, manufacturers, or manufacturing processes, or failure to comply with regulatory requirements both before and after approval, may yield various results, including:

- restrictions on manufacturing or distribution, or marketing of such products;
- restrictions on the labeling, including required additional warnings, such as black box warnings, contraindications, precautions, and restrictions on the approved indication or use;
- modifications to promotional pieces;
- requirements to conduct post-marketing studies or clinical trials; clinical holds or termination of clinical trials;
- requirements to establish or modify a REMS or a comparable foreign authority may require that we establish or modify a similar strategy, that may, for instance, require us to create a Medication Guide outlining the risks of the previously unidentified side effects for distribution to patients, or restrict distribution of the product, if and when approved, and impose burdensome implementation requirements on us:
- changes to the way the drug is administered;
- liability for harm caused to patients or subjects;
- reputational harm;
- the drug becoming less competitive;
- warning; or untitled letters;

- suspension of marketing or withdrawal of the products from the market;
- regulatory authority issuance of safety alerts, Dear Healthcare Provider letters, press releases, or other communications containing warnings or other safety information about the drug;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, damages, restitution, or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of our products;
- product seizure or detention;
- FDA debarment, debarment from government contracts, and refusal of future orders under existing contracts, exclusion from federal healthcare programs, consent decrees, or corporate integrity agreements; or
- injunctions or the imposition of civil or criminal penalties, including imprisonment.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, or could substantially increase the costs and expenses of commercializing such product, which in turn could delay or prevent us from generating significant revenues from its sale. Any of these events could further have other material and adverse effects on our operations and business and could adversely impact our stock price and could significantly harm our business, financial condition, results of operations, and prospects.

The FDA's policies may change and additional government regulations may be enacted that could prevent, limit, or delay regulatory approval of our product candidates or that could impose additional regulatory obligations on us if our product candidates are approved. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and be subject to regulatory enforcement action.

Should any of the above actions take place, they could adversely affect our ability to achieve or sustain profitability. Further, the cost of compliance with post-approval regulations may have a negative effect on our operating results and financial condition.

If we obtain approval to commercialize our product candidates outside of the United States, a variety of risks associated with international operations could materially adversely affect our business.

If any of our product candidates are approved for commercialization, we may enter into agreements with third parties to market them on a worldwide basis or in more limited geographical regions. We expect that we will be subject to additional risks related to entering into international business relationships, including:

- different regulatory requirements for approval of drugs in foreign countries;
- the potential for so-called parallel importing, particularly within Europe, which is what happens when a local seller, faced with high or higher local prices, opts to import goods from a foreign market (with low or lower prices) rather than buying them locally with EU laws supporting such "free movement of goods" within the EU;

- stricter harmonized EU rules on data privacy particularly in relation to health data than is the case in the United States which are being further toughened with the EU General Data Protection Regulation, or the GDPR, which became enforceable beginning May 25, 2018;
- challenges enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the United States;
- unexpected changes in tariffs, trade barriers, and regulatory requirements and in the health care policies of foreign jurisdictions;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration, and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- difficulties staffing and managing foreign operations;
- workforce uncertainty in countries where labor unrest is more common than in the United States and worker rights tend to be stronger;
- costs of compliance with U.S. laws and regulations for foreign operations, including the Foreign Corrupt Practices Act or comparable foreign regulations, and the risks and costs of noncompliance;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters including earthquakes, typhoons, floods, and fires.

These and other risks associated with our international operations may materially adversely affect our ability to attain or maintain profitable operations.

We will need to obtain FDA approval (and that of comparable foreign regulatory authorities) of any proposed product names, and any failure or delay associated with such approval may adversely affect our business.

Any name we intend to use for our product candidates will require approval from the FDA regardless of whether we have secured a formal trademark registration from the U.S. Patent and Trademark Office, or USPTO. The FDA typically conducts a review of proposed product names, including an evaluation of the potential for confusion with other product names. The FDA may also object to a product name if it believes the name inappropriately implies medical claims or contributes to an overstatement of efficacy. If the FDA objects to any of our proposed product names, we may be required to adopt alternative names for our product candidates. If we adopt alternative names, we would lose the benefit of any existing trademark applications for such product candidate and may be required to expend significant additional resources in an effort to identify a suitable product name that would qualify under applicable trademark laws, not infringe the existing rights of third parties, and be acceptable to the FDA. We may be unable to build a successful brand identity for a new trademark in a timely manner or at all, which would limit our ability to commercialize our product candidates.

RISKS RELATED TO THE COMMERCIALIZATION OF OUR PRODUCT CANDIDATES

We face significant competition from other pharmaceutical and biotechnology companies, academic institutions, government agencies, and other research organizations. Our operating results will suffer if we fail to compete effectively.

The development and commercialization of new drug products is highly competitive. We face competition with respect to our current product candidates, and will face competition with respect to any product candidates that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies, and biotechnology companies worldwide. There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of pain and CNS disorders. 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.

Specifically, there are a large number of companies developing or marketing therapies for CNS disorders, including many major pharmaceutical and biotechnology companies. Among the companies that currently market or are developing therapies that, if approved, our product candidates would potentially compete with include: Acadia Pharmaceuticals, Inc.; Alder Biopharmaceuticals, Inc.; Alkermes plc; Allergan plc; Amgen Inc.; Biohaven Pharmaceutical Holding Company Ltd.; Carbylan Therapeutics, Inc.; Eli Lilly and Company; Flexion Therapeutics, Inc.; Grunenthal GmbH; Intra-Cellular Therapies, Inc.; Janssen Research & Development, LLC; Jazz Pharmaceuticals plc; Levolta Pharmaceuticals, Inc.; Otsuka Pharmaceutical Co. Ltd.; and OPKO Health, Inc.

Our commercial opportunities could be reduced or eliminated if our competitors develop and commercialize products that are safer, are more effective, have fewer or less severe side effects, are more convenient, or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic products or therapeutically similar lower cost brands. If our product candidates achieve marketing approval, we expect that they will be priced at a significant premium over competitive generic products, which would further impact our commercialization efforts.

Generic forms of the active ingredients of our product candidates, including zoledronic acid, DM, bupropion, meloxicam, rizatripan, reboxetine, and esomeprazole, are available and could be used off-label. Any such off-label use could adversely affect our profitability and have a negative effect on our operating results and financial condition. For example, even though zoledronic acid is not currently approved for the treatment of pain, we would not be able to prevent a physician from prescribing zoledronic acid in intravenous form for such treatment. Nor could we prevent a payor from offering favorable coverage for such product and disadvantaging our product candidates, even if the generics would be used off-label.

Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals, and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with, or acquisition by large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

If the FDA or comparable foreign regulatory authorities approve generic or similar versions of any of our products that receive marketing approval, or such authorities do not grant our products appropriate periods of data exclusivity before approving generic or similar versions of our products, the sales of our products could be adversely affected.

Once an NDA is approved, the covered product becomes a “reference listed drug” in the FDA’s Orange Book. Manufacturers may seek approval of generic versions of reference listed drugs through submission of ANDAs in the United States. In support of an ANDA, a generic manufacturer need not conduct full clinical studies. Rather, the applicant generally must show that its product has the same active ingredient(s), dosage form, strength, route of administration, and conditions of use or labeling, among other commonalities, as the reference listed drug and that the generic version is bioequivalent to the reference listed drug, meaning it is absorbed in the body at the same rate and to the same extent. Recently, the FDA and Congress have also taken steps to encourage increased generic drug competition in the market. Generic products may be significantly less costly to bring to market than the reference listed drug and companies that produce generic products are generally able to offer them at lower prices, and are generally preferred by third-party payors. Thus, following the introduction of a generic drug, a significant percentage of the sales of any branded product or reference listed drug is typically lost to the generic product.

Moreover, in addition to generic competition, we could face competition from other companies seeking approval of drug products that are similar to ours using the 505(b)(2) pathway. Such applicants may be able to rely on our product candidates, if approved, or other approved drug products or published literature to develop drug products that are similar to ours. The introduction of a drug product similar to our product candidates could expose us to increased competition.

Further, if we do not file a patent infringement lawsuit against a generic manufacturer within 45 days of receiving notice of its paragraph IV certification, the ANDA or 505(b)(2) applicant would not be subject to a 30-month stay. Litigation or other proceedings to enforce or defend intellectual property rights are often very complex in nature, may be expensive and time consuming, may divert our management’s attention from our core business, and may result in unfavorable results that could adversely impact our ability to prevent third parties from competing with our products. Accordingly, upon approval of our product candidates we may be subject to generic competition or competition from similar products, or may need to commence patent infringement proceedings, which would divert our resources.

We currently anticipate that we may be eligible for three years of non-patent marketing exclusivity in the United States for our product candidates if they are approved. These three years, however, would only protect our modifications in formulation or approved uses in comparison to the reference listed drug and would not prevent other companies from submitting full NDAs, and would not prevent physicians from prescribing other products off-label or third party payors from reimbursing for them. Moreover, a 505(b)(2) applicant could rely on a reference listed drug that is not one of our product candidates, or published literature, in which case any periods of patent or non-patent protection may not prevent FDA making an approval effective.

Competition that our products may face from generic or similar versions of our products could materially and adversely impact our future revenue, profitability, and cash flows and substantially limit our ability to obtain a return on the investments we have made in those product candidates.

AXS-12 received Orphan Drug Designation from the FDA. However, there is no guarantee that we will receive this designation for any of our other product candidates, or receive or maintain any corresponding benefits for any of our other product candidates that may receive Orphan Drug Designation in the future, including periods of exclusivity.

AXS-12 received Orphan Drug Designation from FDA for the treatment of narcolepsy. We may also seek Orphan Drug Designation for our other product candidates, as appropriate.

Orphan Drug Designation, however, may be lost if the indications for which we develop any of our future product candidates do not meet the orphan drug criteria. Moreover, following product approval, orphan drug exclusivity may be lost if the FDA determines, among other reasons, that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of patients with the rare disease or condition. Even if we obtain orphan drug exclusivity for any of our current or future product candidates, that exclusivity may not effectively protect the product from competition because different products can be approved for the same condition. Even after an orphan product is approved, the FDA can subsequently approve a product containing the same principal molecular features for the same condition if the FDA concludes that the later product is clinically superior in that it is shown to be safer or more effective or makes a major contribution to patient care.

The FDA or the EMA may grant orphan exclusivity to two different sponsors for the same compound or active molecule and for the same indication. For example, subsequent to our Orphan Drug Designation, the FDA granted Orphan Drug Designation to Thar Pharmaceuticals, Inc. for a zoledronic acid-containing product for the treatment of CRPS. Thar Pharmaceuticals was subsequently acquired by Grunenthal GmbH. Although we are no longer pursuing CRPS, if Grunenthal GmbH or another sponsor had received FDA approval for a zoledronic acid-containing product for the treatment of CRPS before we had obtained FDA approval for AXS-02 for the treatment of pain associated with CRPS, we would have been prevented from launching our product in the United States for this indication for a period of at least 7 years. If another sponsor had received EMA approval for a zoledronic acid-containing product for the treatment of CRPS before we had obtained EMA approval for AXS-02 for the treatment of pain associated with CRPS, we would have been prevented from launching our product in the EU for this indication for a period of at least 10 to 12 years.

In response to a recent court decision regarding the plain meaning of the exclusivity provision of the Orphan Drug Act, the FDA may undertake a reevaluation of aspects of its orphan drug regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business, financial condition, results of operations, and prospects could be harmed.

If we are unable to establish effective marketing and sales capabilities or enter into agreements with third parties to market and sell our product candidates, if they are approved, we may be unable to generate product revenues.

We currently do not have a commercial infrastructure for the marketing, sale, and distribution of pharmaceutical products. If approved, in order to commercialize our products, we must build our marketing, sales, and distribution capabilities or make arrangements with third parties to perform these services. We may not be successful in doing so. If one of our product candidates is approved by the FDA, we plan to build a commercial infrastructure, including the creation of a specialty sales force to launch that product candidate throughout the United States. In the future, we may seek to further penetrate the U.S. market by expanding our sales force or through collaborations with other pharmaceutical or biotechnology companies or third-party manufacturing and sales organizations. If approved for marketing outside the United States, we intend to commercialize our product candidates outside the United States with a marketing and sales collaborator or collaborators, rather than with our own sales force.

We have no prior experience in the marketing, sale, and distribution of pharmaceutical products, and there are significant risks involved in the building and managing of a commercial infrastructure. The establishment and development of our own sales force and related compliance plans to market any products we may develop will be expensive and time consuming and could delay any product launch, and we may not be able to successfully develop this capability. We, or our future collaborators, will have to compete with other pharmaceutical and biotechnology companies to recruit, hire, train, manage, and retain marketing and sales personnel. In the event we are unable to develop a marketing and sales infrastructure, we may not be able to commercialize any of our current or future product candidates, which would limit our ability to generate product revenues. Factors that may inhibit our efforts to commercialize any of our current or future product candidates on our own include:

- our inability to recruit, train, manage, and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any of our current or future product candidates;

- our inability to effectively oversee a geographically dispersed sales and marketing team;
- the costs associated with training sales and marketing personnel on legal and regulatory compliance matters and monitoring their actions;
- an inability to secure adequate coverage and reimbursement by government and private health plans;
- the clinical indications and labeled claims for which the product is approved;
- limitations or warnings, including distribution or use restrictions, contained in the product's approved labeling;
- any distribution and use restrictions imposed by the FDA or to which we agree as part of a mandatory REMS or voluntary risk management plan;
- liability for sales or marketing personnel who fail to comply with the applicable legal and regulatory requirements;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization or engaging a contract sales organization.

Although our current plan is to hire most of our sales and marketing personnel only if a product candidate is approved by the FDA, we will incur expenses prior to product launch in recruiting this sales force and developing a marketing and sales infrastructure. If a commercial launch is delayed as a result of FDA requirements or other reasons, we would incur these expenses prior to being able to realize any revenue from sales of our product candidates. Even if we are able to effectively hire a sales force and develop a marketing and sales infrastructure, our sales force and marketing teams may not be successful in commercializing any of our current or future product candidates.

In the event we are unable to collaborate with a third-party marketing and sales organization to commercialize any approved product candidates outside the United States, our ability to generate product revenues may be limited. To the extent we rely on third parties to commercialize any products for which we obtain regulatory approval, we may receive less revenues than if we commercialized these products ourselves. In addition, we would have less control over the sales efforts of any other third parties involved in our commercialization efforts, and could be held liable if they failed to comply with applicable legal or regulatory requirements.

If any of our current or future product candidates do not achieve broad market acceptance, the revenues that we generate from their sales will be limited.

We have never commercialized a product candidate for any indication. Even if any of our current or future product candidates are approved by the appropriate regulatory authorities for marketing and sale, it may not gain acceptance among physicians, patients, third-party payors, and others in the medical community. If any product candidates for which we obtain regulatory approval do not gain an adequate level of market acceptance, we may not generate significant product revenues or become profitable. Market acceptance of any of our current or future product candidates by the medical community, patients, and third-party payors will depend on a number of factors, some of which are beyond our control. For example, physicians are often reluctant to switch their patients from existing therapies even when new and potentially more effective or convenient treatments enter the market. Further, patients often acclimate to the therapy that they are currently taking and do not want to switch unless their physicians recommend switching products or they are required to switch therapies due to lack of reimbursement for existing therapies. Even if physicians prescribe our products, third party payors may not consider them cost effective without a significant price concession, which could negatively impact our revenue.

Efforts to educate the medical community and third-party payors on the benefits of our product candidates may require significant resources and may not be successful. If any of our product candidates is approved but does not achieve an adequate level of market acceptance, we may not generate significant revenues and we may not become profitable. The degree of market acceptance of any of our product candidates will depend on a number of factors, including:

- the efficacy of our product candidates;
- the prevalence and severity of adverse events associated with such product candidate;
- the clinical indications for which the product is approved and the approved claims that we may make for the product;
- limitations or warnings contained in the product's FDA-approved labeling, including potential limitations or warnings for such product candidate, that may be more restrictive than other competitive products;
- changes in the standard of care for the targeted indications for such product candidate, which could reduce the marketing impact of any claims that we could make following FDA approval, if obtained;
- the relative convenience and ease of administration of such product candidate;
- cost of treatment versus economic and clinical benefit in relation to alternative treatments or therapies;
- the availability of adequate coverage or reimbursement by third parties, such as insurance companies and other healthcare payors, and by government healthcare programs, including Medicare and Medicaid;
- the willingness of third party payors to prefer similar but less expensive products even if not approved for our product's indication;
- the extent and strength of our marketing and distribution of such product candidate;
- the safety, efficacy, and other potential advantages over, and availability of, alternative treatments already used or that may later be approved for any of our intended indications;
- distribution and use restrictions imposed by the FDA with respect to such product candidate or to which we agree as part of a mandatory risk evaluation and mitigation strategy or voluntary risk management plan;

- the timing of market introduction of such product candidate, as well as competitive products;
- our ability to offer such product candidate for sale at competitive prices, including prices that are competitive with generic products;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the clinical indications for which such product candidate is approved;
- the extent and strength of our third-party manufacturer and supplier support;
- the approval of other new products for the same indications;
- adverse publicity about the product or favorable publicity about competitive products; and
- potential product liability claims.

Our efforts to educate the medical community and third-party payors on the benefits of our product candidates may require significant resources and may never be successful. Even if the medical community accepts that one of our product candidates is safe and effective for its approved indications, physicians and patients may not immediately be receptive to such product candidate and may be slow to adopt it as an accepted treatment of the approved indication. It is unlikely that any labeling approved by the FDA will contain claims that one of our product candidates is safer or more effective than competitive products or will permit us to promote such product candidate as being superior to competing products. Further, the availability of inexpensive generic forms of pain management products for acute pain may also limit acceptance of certain of our product candidates among physicians, patients, and third-party payors. If any of our current or future product candidates is approved but does not achieve an adequate level of acceptance among physicians, patients, and third-party payors, we may not generate meaningful revenues from our product candidates, and we may not become profitable.

The ability of patients to purchase certain of the active ingredients of our product candidates in generic form could put us at a competitive disadvantage. For example, in some foreign jurisdictions, generic oral forms of DM and bupropion are currently available individually for consumer purchase. In addition, physicians may prescribe generic zoledronic acid for the treatment of pain off-label. Any use of these generic forms of the active molecules of our product candidates could adversely affect our business and our results of operations.

The potential market opportunities for our product candidates are difficult to precisely estimate. Our estimates of the potential market opportunities are predicated on many assumptions including industry knowledge and publications, third-party research reports, and other surveys. While we believe that our internal assumptions are reasonable, these assumptions involve the exercise of significant judgment on the part of our management and are inherently uncertain, and the reasonableness of these assumptions has not been assessed by an independent source. If any of the assumptions proves to be inaccurate, the actual markets for our product candidates could be smaller than our estimates of the potential market opportunities.

We face potential product liability exposure, and if successful claims are brought against us, we may incur substantial liability for any of our current or future product candidates and may have to limit their commercialization.

The use of any of our current or future product candidates in clinical trials, and the sale of any of our product candidates for which we obtain regulatory approval, exposes us to the risk of product liability claims. We face inherent risk of product liability related to the testing of our product candidates in human clinical trials and will face an even greater risk if we commercially sell any product candidates that we may develop. For example, we may be sued if any product candidate we develop allegedly causes injury or is found to be otherwise unsuitable during clinical testing, manufacturing, marketing, or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. Product liability claims might be brought against us by consumers, healthcare providers, or others using, administering, or selling our products. If we cannot successfully defend ourselves against these claims, we will incur substantial liabilities or be required to limit commercialization of our product candidates. Even successful defense would require significant financial and management resources. Regardless of merit or eventual outcome, liability claims may result in:

- loss of revenue from decreased demand for our products and/or product candidates;
- impairment of our business reputation or financial stability;
- costs of related litigation;
- substantial monetary awards to patients or other claimants;
- diversion of management attention;
- loss of revenues;
- withdrawal of clinical trial participants and potential termination of clinical trial sites or entire clinical programs;
- the inability to commercialize our product candidates;
- significant negative media attention;
- decrease in our stock price;
- initiation of investigations and enforcement actions by regulators; and
- product recalls, withdrawals, or labeling, marketing, or promotional restrictions.

We have obtained limited product liability insurance coverage for our products and our clinical trials with a \$8 million annual aggregate coverage limit. We have also obtained local policies in those foreign jurisdictions where it was appropriate. However, our insurance coverage may not reimburse us or may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive, and, 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 due to liability. We intend to expand our insurance coverage to include the sale of commercial products if we obtain FDA approval for our product candidates in development, but we may be unable to obtain commercially reasonable product liability insurance for any products approved for marketing, or at all. On occasion, large judgments have been awarded in class action lawsuits based on drugs that had unanticipated side effects. A successful product liability claim or series of claims brought against us could cause our stock price to fall and, if judgments exceed our insurance coverage, could decrease our cash and adversely affect our business and our prospects.

RISKS RELATED TO OUR DEPENDENCE ON THIRD PARTIES

We rely, and expect to continue to rely, on third parties to conduct, supervise, and monitor our preclinical studies and clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials or failing to comply with regulatory requirements.

We rely on third-party CROs to conduct, supervise, and monitor our preclinical studies and certain clinical trials for our product candidates and do not currently plan to independently conduct preclinical studies or clinical trials of any other potential product candidates. We expect to continue to rely on third parties, such as CROs, clinical data management organizations, medical institutions, and clinical investigators, to conduct our preclinical studies and clinical trials. While we have agreements governing their activities, we have limited influence over their actual performance and control only certain aspects of their activities. The failure of these third parties to successfully carry out their contractual duties or meet expected deadlines could substantially harm our business because we may not obtain marketing approval for or commercialize our product candidates in a timely manner or at all. Moreover, these agreements might terminate for a variety of reasons, including a failure to perform by the third parties. If we need to enter into alternative arrangements, that would delay our product development activities and adversely affect our business.

Our reliance on these third parties for development activities will reduce our control over these activities. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory, and scientific standards and our reliance on the CROs does not relieve us of our regulatory responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial and for ensuring that our preclinical trials are conducted in accordance with good laboratory practice, or GLP, as appropriate. Moreover, the FDA and comparable foreign regulatory authorities require us to comply with standards, commonly referred to as good clinical practices, or GCPs, for conducting, recording, and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity, and confidentiality of trial participants are protected. As a clinical trial sponsor, we also have regulatory requirements that directly apply to us. Regulatory authorities enforce these requirements through periodic inspections of trial sponsors, clinical investigators, and trial sites. If we or any of our CROs fail to comply with applicable GCPs, we or our CROs may be subject to enforcement or other legal actions, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials.

In addition, once we have an approved product, we will be required to report certain financial interests of our third-party investigators if these relationships exceed certain financial thresholds or meet other criteria. The FDA and comparable foreign regulatory authorities may question the integrity of the data from those clinical trials conducted by investigators who previously served or currently serve as scientific advisors or consultants to us from time to time and receive cash compensation in connection with such services or otherwise receive compensation from us that could be deemed to impact study outcome, proprietary interests in a product candidate, certain company equity interests, or significant payments of other sorts.

We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials complies with GCP regulations. In addition, our clinical trials must be conducted with product candidates that were produced under cGMP regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process. We also are required to register certain clinical trials and post the results of certain completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within specified timeframes. Failure to do so can result in enforcement actions and adverse publicity.

Our CROs may also have relationships with other entities, some of which may be our competitors, for whom they may also be conducting clinical trials or other drug development activities that could harm our competitive position. In addition, our CROs are not our employees, and except for remedies available to us under our agreements with such CROs, we cannot control whether or not they devote sufficient time and resources to our ongoing clinical, non-clinical, and preclinical programs. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our preclinical studies or clinical trials in accordance with regulatory requirements or our stated protocols, 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 or regulatory requirements or for other reasons, our clinical trials may be extended, delayed, or terminated and we may not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates, or we or they may be subject to regulatory enforcement actions. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed. To the extent we are unable to successfully identify and manage the performance of third-party service providers in the future, our business may be materially and adversely affected.

If any of our relationships with these third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs or to do so on commercially reasonable terms. Switching or adding additional CROs involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays could occur, which could compromise our ability to meet our desired development timelines. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects, and results of operations.

If the manufacturers upon whom we rely fail to produce our product candidates in the volumes that we require on a timely basis, or to comply with stringent regulations applicable to pharmaceutical drug manufacturers, we may face delays in the development and commercialization of, or be unable to meet demand for, our products and may lose potential revenues.

We do not manufacture any of our product candidates, and we do not currently plan to develop any capacity to do so. We currently outsource all manufacturing of our product candidates to third parties typically without any guarantee that there will be sufficient supplies to fulfill our requirements or that we may obtain such supplies on acceptable terms. Any delays in obtaining adequate supplies with respect to our product candidates may delay the development or commercialization of our product candidates. Moreover, we do not yet have agreements established regarding commercial supply of our product candidates, and we may not be able to establish or maintain commercial manufacturing arrangements on commercially reasonable terms for any of our current or future product candidates for which we obtain approval in the future.

We may not succeed in our efforts to establish manufacturing relationships or other alternative arrangements for any of our existing or future product candidates and programs. Our product candidates may compete with other products and product candidates for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that are both capable of manufacturing for us and willing to do so. If our existing third-party manufacturers, or the third parties that we engage in the future to manufacture a product for commercial sale or for our clinical trials, should cease to continue to do so for any reason, we likely would experience delays in obtaining sufficient quantities of our product candidates for us to meet commercial demand or to advance our clinical trials while we identify and qualify replacement suppliers. If for any reason we are unable to obtain adequate supplies of our product candidates or the drug substances used to manufacture them, it will be more difficult for us to develop our product candidates and compete effectively. Further, even if we do establish such collaborations or arrangements, our third-party manufacturers may breach, terminate, or not renew these agreements.

Any problems or delays we experience in preparing for commercial-scale manufacturing of a product candidate may result in a delay in FDA approval of the product candidate or may impair our ability to manufacture commercial quantities or such quantities at an acceptable cost, which could result in the delay, prevention, or impairment of clinical development and commercialization of our product candidates and could adversely affect our business. For example, our manufacturers will need to produce specific batches of our product candidates to demonstrate acceptable stability under various conditions and for commercially viable lengths of time. We and our contract manufacturers will need to demonstrate to the FDA and other regulatory authorities that this is acceptable stability data for our product candidates, as well as validate methods and manufacturing processes, in order to receive regulatory approval to commercialize any of our current or future product candidates. Furthermore, if our commercial manufacturers fail to deliver the required commercial quantities of bulk drug substance or finished product on a timely basis and at commercially reasonable prices, we would likely be unable to meet demand for our products and we would lose potential revenues.

We have a limited number of contract manufacturers for our products. At times we may have only one manufacturer for a product. In addition, we do not have any long-term commitments from our suppliers of clinical trial material or guaranteed prices for our product candidates. The manufacture of pharmaceutical products requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of pharmaceutical products often encounter difficulties in production, particularly in scaling up initial production. These problems include difficulties with production costs and yields; quality control, including stability of the product candidate and quality assurance testing; shortages of qualified personnel; and compliance with strictly enforced federal, state, and foreign regulations. Our manufacturers may not perform as agreed. If our manufacturers were to encounter any of these difficulties, our ability to provide product candidates to patients in our clinical trials and for commercial use, if approved, would be jeopardized.

In addition, all manufacturers of our product candidates must comply with cGMP requirements enforced by the FDA and comparable foreign regulatory authorities that are applicable to both finished drug products and active pharmaceutical ingredients used both for clinical and commercial supply, through its facilities inspection program. Our manufacturers must be approved by the FDA and comparable foreign regulatory authorities pursuant to inspections that will be conducted after we submit our marketing applications to the agency and comparable foreign regulatory authorities. The cGMP requirements include quality control, quality assurance, and the maintenance of records and documentation. Manufacturers of our product candidates may be unable to comply with our specifications, these cGMP requirements and with other FDA, state, and foreign regulatory requirements. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or other regulatory authorities, they will not be able to secure or maintain regulatory approval for their manufacturing facilities. While we are ultimately responsible for the manufacture of our product candidates, other than through our contractual arrangements, we have little control over our manufacturers' compliance with these regulations and standards. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for, or market our product candidates, if approved. A failure to comply with these requirements may result in regulatory enforcement actions against our manufacturers or us, including fines and civil and criminal penalties, including imprisonment; suspension or restrictions of production; suspension, delay, or denial of product approval or supplements to approved products; clinical holds or termination of clinical studies; warning or untitled letters; regulatory authority communications warning the public about safety issues with the drug; refusal to permit the import or export of the products; product seizure, detention, or recall; suits under the civil False Claims Act; corporate integrity agreements; consent decrees; or withdrawal of product approval. If the safety of any quantities supplied is compromised due to our manufacturers' failure to adhere to applicable laws or for other reasons, we may not be able to obtain regulatory approval for or successfully commercialize our product candidates.

Any failure or refusal to supply our product candidates or components for our current or future product candidates that we may develop could delay, prevent, or impair our clinical development or commercialization efforts. Any change in our manufacturers could be costly because the commercial terms of any new arrangement could be less favorable and because the expenses relating to the transfer of necessary technology and processes could be significant.

We may rely on third parties to perform many essential services for any products that we commercialize, including services related to warehousing and inventory control, distribution, government price reporting, customer service, accounts receivable management, cash collection, and adverse event reporting. If these third parties fail to perform as expected or to comply with legal and regulatory requirements, our ability to commercialize any of our current or future product candidates will be significantly impacted and we may be subject to regulatory sanctions.

We may retain third-party service providers to perform a variety of functions related to the sale and distribution of any of our current or future product candidates, key aspects of which will be out of our direct control. These service providers may provide key services related to warehousing and inventory control, distribution, government price reporting, customer service, accounts receivable management, and cash collection, and, as a result, most of our inventory may be stored at a single warehouse maintained by one such service provider. If we retain a service provider, we would substantially rely on it as well as other third-party providers that perform services for us, including entrusting our inventories of products to their care and handling. If these third-party service providers fail to comply with applicable laws and regulations, fail to meet expected deadlines, or otherwise do not carry out their contractual duties to us, or encounter physical or natural damage at their facilities, our ability to deliver product to meet commercial demand would be significantly impaired and we may be subject to regulatory enforcement action.

In addition, we may engage third parties to perform various other services for us relating to adverse event reporting, safety database management, fulfillment of requests for medical information regarding our product candidates and related services. If the quality or accuracy of the data maintained by these service providers is insufficient, or these third parties otherwise fail to comply with regulatory requirements related to adverse event reporting, we could be subject to regulatory sanctions.

Additionally, if a third party errs in calculating government pricing information from transactional data in our financial records, it could impact our discount and rebate liability and potentially cause government programs to overpay providers for our products.

Any collaboration arrangements that we are a party to or may enter into in the future may not be successful, which could adversely affect our ability to develop and commercialize our product candidates.

Our business model is to commercialize our product candidates in the United States and generally to seek future collaboration arrangements with pharmaceutical or biotechnology companies, or academic institutions, for the development or commercialization of our product candidates in the rest of the world. For example, in December 2017, we entered into a research collaboration agreement with Duke University for the conduct of a Phase 2 clinical trial of AXS-05 for smoking cessation treatment, which was completed in April 2019. We currently have not entered into any sub-license agreements. Our current and future collaboration arrangements may not be successful, and the success of them 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 collaboration arrangements. For clinical trials of our product candidates being conducted by our collaborators, for example, the Phase 2 clinical trial of AXS-05 for smoking cessation in collaboration with Duke University, we rely on timeline estimates provided by our collaborators for these trials. Such timeline estimates may differ materially from actual trial completion dates. 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.

We may license the right to market and sell our product candidates under our collaborators' labeler codes. Alternatively, we may enter into agreements with collaborators to market and sell our product candidates under our own labeler code, in which case errors and omissions by collaborators in capturing and transmitting transactional data may impact the accuracy of our government price reporting.

Collaborations with pharmaceutical 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. Any future collaborations we might enter into may pose a number of risks, including the following:

- collaborators may not perform their obligations as expected;
- collaborators may not pursue development and commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials, or require a new formulation of a product candidate for clinical testing;
- collaborators could fail to make timely regulatory submissions for a product candidate;
- collaborators may not comply with all applicable regulatory requirements or may fail to report safety data in accordance with all applicable regulatory requirements;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates 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;
- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;
- a collaborator with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of such product candidate or product;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation, or the preferred course of development, might cause delays or termination of the research, development, or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time consuming and expensive;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation; and
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability.

If any collaborations we might enter into in the future do not result in the successful development and commercialization of products or if one of our collaborators subsequently terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under the collaboration. If we do not receive the funding we expect under the agreements, our development of our product candidates could be delayed and we may need additional resources to develop our product candidates and our product platform.

Additionally, if any future collaborator of ours is involved in a business combination, the collaborator might deemphasize or terminate development or commercialization of any product candidate licensed to it by us. If one of our collaborators terminates its agreement with us, we may find it more difficult to attract new collaborators and our reputation in the business and financial communities could be adversely affected.

We may in the future determine to collaborate with additional pharmaceutical and biotechnology companies and academic institutions for the development and potential commercialization of any of our current or future product candidates. We face significant competition in seeking appropriate collaborators. Our ability to reach a definitive agreement for collaboration will depend upon, among other things, 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. If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms, or at all, we may have to curtail the development of a product candidate, 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 fund and undertake development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms, or at all. If we fail to enter into collaborations and do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our product candidates or bring them to market or continue to develop our product platform and our business may be materially and adversely affected.

We are dependent on third parties to decide to utilize our product candidates to make them readily available at the point of care throughout their networks of pharmacies.

In addition to extensive internal efforts, the successful commercialization of our product candidates will require many third parties, over whom we have no control, to decide to utilize our product candidates, and to make them readily available at the point of care throughout their networks of pharmacies. These third parties include HMOs, long term care facilities, and pharmacy benefit managers, or PBMs, which use pharmacy and therapeutics committees, commonly referred to as P&T committees, to make purchasing and reimbursement decisions. Generally, before an HMO or long-term care facility will acquire any of our product candidate for its own pharmacies, or a PBM will pay retail network pharmacies on behalf of its health plans, any such product candidates must be approved for addition to that organization's list of approved drugs, or formulary list, by the organization's P&T committee. An institutional P&T committee typically governs all matters pertaining to the use of medications within the institution, including review of medication formulary data and recommendations for the appropriate use of drugs within the institution to the medical staff. PBM P&T committees develop the criteria for plan beneficiaries to access prescription medication, including such cost control measures as step therapy and prior authorization. The frequency of P&T committee meetings varies considerably, and P&T committees often require additional information to aid in their decision-making process, so we may experience substantial delays in obtaining formulary approvals. Additionally, P&T committees may be concerned that the cost of acquiring any of our product candidates for use in their institutions or reimbursing retail pharmacies outweighs clinical benefits and will resist efforts to add any such product candidate to the formulary, or implement restrictions on the usage of the drug in order to control costs. Third party payors often have tiered formularies in which the non-preferred drugs have significantly higher co-pays, causing prescription rejections, and define therapeutic class broadly to increase competition for preferred status. We cannot guarantee that we will be successful in getting the approvals we need from enough P&T committees quickly enough to maintain and grow sales of any of our product candidates.

We are dependent upon our license agreements with an entity owned by our Chief Executive Officer and Chairman of the Board related to the development of our current product candidates, and if the agreements are terminated for any reason our business will be materially harmed.

In 2012, we entered into three exclusive license agreements with Antecip Bioventures II LLC, or Antecip, an entity owned by our Chief Executive Officer and Chairman of the Board, Herriot Tabuteau, M.D., in which we were granted exclusive licenses to develop, manufacture, and commercialize Antecip's patents and applications related to the development of AXS-02 and AXS-05, as well as AXS-04, a product candidate that is currently in early stage development, anywhere in the world for veterinary and human therapeutic and diagnostic use. The agreements were amended in August 2015 to update the schedule of patents and applications subject to the license agreements. Pursuant to the agreements, we are required to use commercially reasonable efforts to develop, obtain regulatory approval for, and commercialize AXS-02, AXS-05, and AXS-04. Under the terms of the agreements, we are required to pay to Antecip a royalty equal to 4.5% for AXS-02, 3.0% for AXS-05, and 1.5% for AXS-04, of net sales of products containing the licensed technology by us, our affiliates, or permitted sublicensees. These royalty payments are subject to reduction by an amount up to 50.0% of any required payments to third parties. Unless earlier terminated by a party for cause or by us for convenience, the agreements remain in effect on a product-by-product and country-by-country basis until the later to occur of (1) the applicable product is no longer covered by a valid claim in that country or (2) 10 years from the first commercial sale of the applicable product in that country. Upon expiration of the agreements with respect to a product in a country, our license grant for that product in that country will become a fully paid-up, royalty-free, perpetual non-exclusive license. If Antecip terminates any of the agreements for cause, or if we exercise our right to terminate any of the agreements for convenience, the rights granted to us under such terminated agreement will revert to Antecip. To date, we have not been required to make any payments to Antecip under any of the license agreements. If any of the license agreements with Antecip are terminated for any reason, our business, financial condition, results of operations, and prospects will be materially harmed.

RISKS RELATED TO INTELLECTUAL PROPERTY

It is difficult and costly to protect our proprietary rights and as a result we may not be able to ensure their protection. In addition, patents have a limited lifespan and will eventually expire.

Market exclusivity awarded by the FDA upon the approval of an NDA is limited in scope and duration. Our commercial success will depend in part on obtaining, maintaining, enforcing, and defending against third-party challenges, our patent and trade secret protection for any of our current and future product candidates that we may develop, license, or acquire, and the related manufacturing methods. We will only be able to fully protect our technologies from unauthorized use by third parties to the extent that valid and enforceable patents or trade secrets cover them.

The patent prosecution process is expensive and time consuming, and 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 before it is too late to obtain patent protection. Moreover, should we enter into additional collaborations we may be required to consult with or cede control to collaborators regarding the prosecution, maintenance, and enforcement of our patents. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. The patent positions of pharmaceutical and biotechnology companies can be highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved. No consistent policy regarding the breadth of claims allowed in pharmaceutical or biotechnology patents has emerged to date in the United States. The patent situation outside the United States is even more uncertain. Changes in either the patent laws or in interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property. Accordingly, we cannot predict the breadth of claims that may be allowed or enforced in our patents or in third-party patents. The degree of future protection for our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. Moreover, the patent application process is also subject to numerous risks and uncertainties, and there can be no assurance that we or any of our future development partners will be successful in protecting any of our current or future product candidates that we may develop, license, or acquire by obtaining and defending patents. For example:

- we may not have been the first to make the inventions covered by each of our pending patent applications and issued patents;
- we may not have been the first to file patent applications for these inventions;
- others may independently develop similar or alternative technologies or duplicate any of our product candidates or technologies;
- it is possible that none of the pending patent applications will result in issued patents;
- the issued patents may not cover commercially viable active products, may not provide us with any competitive advantages, or may be successfully challenged by third parties;
- we may not develop additional proprietary technologies that are patentable;
- patents of others may have an adverse effect on our business;
- noncompliance with governmental patent agencies requirements can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction, potentially allowing competitors to enter the market earlier than would otherwise have been the case;
- our competitors, many of whom have substantially greater resources than we do and many of whom have made significant investments in competing technologies, may seek or may have already obtained patents that will limit, interfere with, or eliminate our ability to make, use, and sell our potential product candidates; or
- there may be significant pressure on the U.S. government and international governmental bodies to limit the scope of available patent protection both inside and outside the United States for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns.

Patents have a limited lifespan. In most countries, including the United States, the expiration of a patent is typically 20 years from the date that the application for the patent is filed. Various extensions of patent term may be available in particular countries; however, in all circumstances the life of a patent, and the protection it affords, has a limited term. If we encounter delays in obtaining regulatory approvals, the period of time during which we could market a product under patent protection could be reduced. We expect to seek extensions of patent terms where these are available in any countries where we are prosecuting patents. Such possible extensions include those permitted under the Drug Price Competition and Patent Term Restoration Act of 1984 in the United States, which permits a patent term extension of up to five years to cover an FDA-approved product. The actual length of the extension will depend on the amount of patent term lost while the product was in clinical trials. However, the applicable authorities, including the USPTO and the FDA in the United States, and any equivalent regulatory authority in other countries, may not agree with our assessment of whether such extensions are available, and may refuse to grant extensions to our patents, or may grant more limited extensions than we request. If this occurs, our competitors may be able to take advantage of our investment in development and clinical trials by referencing our clinical and preclinical data, and then may be able to launch their product earlier than might otherwise be the case.

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

On September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. In particular, under the Leahy-Smith Act, the United States transitioned in March 2013 to a "first to file" system in which the first inventor to file a patent application will be entitled to the patent. Third parties are allowed to submit prior art before the issuance of a patent by the USPTO, and may become involved in post-grant proceedings including reexamination, post-grant review, inter-partes review, or derivation or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope or enforceability of, or invalidate, our patent rights, which could adversely affect our competitive position.

The USPTO has developed regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first to file provisions, did not become effective until March 16, 2013. However, the full impact of the Leahy-Smith Act and the courts' review of any appeals to related proceedings, is in its early stages. Accordingly, the full impact that the Leahy-Smith Act will have on the operation of our business is not clear. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, as well as our ability to bring about timely favorable resolution of any disputes involving our patents and the patents of others. Patent applications in the United States are maintained in confidence for at least 18 months after their earliest effective filing date. Consequently, we cannot be certain we were the first to invent or the first to file patent applications of our current or future product candidates that we may develop, license, or acquire. In the event that a third party has also filed a U.S. patent application relating to our product candidates or a similar invention, we may have to participate in interference proceedings declared by the USPTO to determine priority of invention in the United States. The costs of these proceedings could be substantial and it is possible that our efforts would be unsuccessful, resulting in a material adverse effect on our U.S. patent position. The results of these types of proceedings may reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop, or commercialize current or future product candidates. Such results could have a material adverse effect on our business, financial condition, results of operations, and prospects.

In addition, the patentability of claims in pending patent applications covering AXS-02, AXS-05, or any other of our current or future product candidates can be challenged by third parties during prosecution in the USPTO, for example by third-party observations and derivation proceedings, and the validity of claims in issued patents can be challenged by third parties in various post-grant proceedings such as post-grant review, reexamination, and inter-partes review proceedings. For example, in December 2016, a petition for post-grant review of U.S. Patent No. 9,283,239, which we refer to as the '239 patent, was filed at the USPTO by Grunenthal GmbH, or Grunenthal, and the post-grant review was instituted on July 7, 2017. In addition, in May 2017, a petition for post-grant review of U.S. Patent No. 9,408,862, which we refer to as the '862 patent, was filed at the USPTO by Grunenthal; in October 2017, a petition for post-grant review of U.S. Patent No. 9,539,268, which we refer to as the '268 patent, was filed at the USPTO by Grunenthal; in April 2018, a petition for post-grant review of U.S. Patent No. 9,707,245, which we refer to as the '245 patent, was filed at the USPTO by Grunenthal; in August 2018, a petition for post-grant review of U.S. Patent No. 9,820,999, which we refer to as the '999 patent, was filed at the USPTO by Grunenthal; in October 2018, a petition for post-grant review of U.S. Patent No. 9,867,839, which we refer to as the '839 patent, and on January 3, 2018, petitions for post-grant reviews of U.S. Patents No. 9,931,352, which we refer to as the '352 patent, 10,039,774, which refer to as the '774 patent, and 10,052,338, which we refer to as the '338 patent, were filed at the USPTO by Grunenthal.

The '239 patent contains claims directed to the use of orally administered zoledronic acid, the active moiety in AXS-02, for the treatment of CRPS, and is one of several issued patents containing claims covering the use of AXS-02 for the treatment of CRPS. The '862 and '268 patents contain claims directed to certain dosage forms containing zoledronic acid, the active moiety in AXS-02. The '862 patent also contains claims directed to certain oral dosage forms containing zoledronic acid, including AXS-02, and use of certain oral dosage forms containing zoledronic acid, including AXS-02, for the treatment of knee pain and arthritis, respectively. The '862 and '268 patents are two of several issued patents containing claims covering dosage forms of zoledronic acid such as AXS-02, and the use of certain oral dosage forms containing zoledronic acid, including AXS-02, in the treatment of knee pain and arthritis. The '245, '999, '352, '774, and '338 patents contain claims directed to the use of neridronic acid for the treatment of CRPS, and are some of several issued patents containing claims covering the use of neridronic acid for the treatment of CRPS. The '839 patent contains claims directed to the use of neridronic acid and oral zoledronic acid for the treatment of joint pain. The petitions request that the Patent Trial and Appeal Board, or PTAB, institute proceedings to review the validity of the '239, the '862, the '268, the '245, the '999, the '839, the '352, the '774, and the '338 patents.

In April 2017, we responded to and opposed Grunenthal's petition for post-grant review of the '239 patent. In July 2017, the PTAB issued a decision in which it refused to institute a post-grant-review of the '239 patent on the grounds of novelty, obviousness, or enablement. The PTAB ruled that Grunenthal had not established that it is more likely than not that the stated prior art would have rendered the claims of the '239 patent obvious or not novel, and that Grunenthal had failed to demonstrate that it is more likely than not that the claims are unpatentable for lack of enablement. However, a post-grant review was instituted on the ground of written description. The PTAB further ordered that the post-grant review for the '239 patent be limited to written description and that no other grounds of unpatentability are authorized for post-grant review. In October 2017, we responded to the PTAB decision to institute a post-grant review. On June 22, 2018, the Patent Trial and Appeal Board, or PTAB, entered a final written decision holding that the claims were invalid for lack of written description.

In August 2017, we responded to and opposed the petition for the '862 patent. In November 2017, the PTAB rendered a decision to institute a post-grant review for that patent. In February 2018, we responded to the PTAB decision to institute a post-grant review. On November 14, 2018, the Patent Trial and Appeal Board, or PTAB, entered a final written decision holding that the claims were invalid for lack of enablement, and for some claims, lack of novelty and/or obviousness. On January 16, 2019, we appealed the decision of the PTAB to the United States Court of Appeals for the Federal Circuit, or Federal Circuit, but recently decided not to further pursue the appeal.

In February 2018, we responded to and opposed the petition for the '268 patent. In May 2018, the PTAB rendered a decision to institute a post-grant review for the patent. In August 2018, we responded to the PTAB decision to institute a post-grant review. In April 2019, the PTAB entered a final written decision holding that the claims were invalid for lack of enablement, but left several of the grounds raised in the Petition unaddressed. In June, we filed a request for rehearing with the PTAB.

In October 2018, the PTAB rendered a decision to institute a post grant review for the '245 patent. In January 2019, we responded to the petition to institute a post-grant review. In October 2019, the PTAB entered a final written decision holding that the claims were invalid for lacking novelty and for obviousness. We are currently exploring whether we should request a rehearing or appeal the decision to the United States Court of Appeals for the Federal Circuit.

In February 2019, the PTAB rendered a decision to institute a post-grant review for the '999 patent. In May 2019, we responded to the petition to institute a post-grant review.

In May 2019, the PTAB rendered a decision to institute a post-grant review for the '839 patent. In October 2019, we responded to the petition to institute a post-grant review.

In July 2019, the PTAB rendered a decision to institute a post-grant review for the '352 patent. In October 2019, we responded to the petition to institute a post-grant review.

In July 2019, the PTAB rendered a decision to institute a post-grant review for the '774 patent. In October 2019, we responded to the petition to institute a post-grant review.

In August 2019, the PTAB rendered a decision to institute a post-grant review for the '338 patent. In October 2019, we responded to the petition to institute a post-grant review.

Any patent claim the PTAB determines to be unpatentable as a result of these proceedings would be stricken from the challenged patents or modified. Additionally, we cannot be sure that the validity of the claims in other issued patents covering any of our current or future product candidates will not also be challenged, or that Grunenthal will not file any additional petitions for post-grant review with respect to any of our current or future product candidates. We may incur increased expenses related to the growth of our intellectual property portfolio and to its defense.

Furthermore, we may not have identified all United States and foreign patents or published applications that affect our business either by blocking our ability to commercialize our drugs or by covering similar technologies that affect our drug market. In addition, some countries, including many in Europe, do not grant patent claims directed to methods of treating humans, and in these countries patent protection may not be available at all to protect our product candidates. Even if patents issue, we cannot guarantee that the claims of those patents will be valid and enforceable or provide us with any significant protection against competitive products, or otherwise be commercially valuable to us.

We also rely on trade secrets to protect our technology, particularly where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. While we use reasonable efforts to protect our trade secrets, our licensors, employees, consultants, contractors, outside scientific collaborators, and other advisors may unintentionally or willfully disclose our information to competitors. Enforcing a claim that a third party illegally obtained and is using our trade secrets is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States are sometimes less willing to protect trade secrets. Moreover, our competitors may independently develop equivalent knowledge, methods, and know how.

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

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

If we or any future collaboration partner are sued for infringing intellectual property rights of third parties, it will be costly and time consuming, and an unfavorable outcome in any litigation would harm our business.

Our ability to develop, manufacture, market, and sell any of our current and future product candidates depends upon our ability to avoid infringing the proprietary rights of third parties, and our commercial success depends upon our ability, and the ability of our collaborators, to develop, manufacture, market, and sell our product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. There is considerable intellectual property litigation in the biotechnology and pharmaceutical industries. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the general field of treatment and management of pain and other CNS disorders and cover the use of numerous compounds and formulations in our targeted markets. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future. Because of the uncertainty inherent in any patent or other litigation involving proprietary rights, we and our licensors may not be successful in defending intellectual property claims by third parties, which could have a material adverse effect on our business, financial condition, results of operations, and prospects. Regardless of the outcome of any litigation, defending the litigation may be expensive, time consuming, and distracting to management. In addition, because patent applications can take many years to issue, there may be currently pending applications, unknown to us, which may later result in issued patents that any of our current or future product candidates may infringe. There could also be existing patents of which we are not aware that any of our current or future product candidates may inadvertently infringe.

If a third party claims that we infringe on their products or technology, we could face a number of issues, including:

- infringement and other intellectual property claims which, whether meritorious or not, can be expensive and time consuming to litigate and can divert management's attention from our core business;
- substantial damages for past infringement which we may have to pay if a court decides that our product infringes on a competitor's patent;
- a court prohibiting us from selling or licensing our product unless the patent holder licenses the patent to us, which it would not be required to do;
- if a license is available from a patent holder, we may have to pay substantial royalties or grant cross licenses to our patents; and
- redesigning our product candidates and processes so they do not infringe, which may not be possible or could require substantial funds and time.

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 products and technology. However, we may not be able to obtain any required license on commercially reasonable terms, or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. We could be forced, including by court order, to cease commercializing the infringing technology or product. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business, financial condition, results of operations, and prospects.

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

Competitors may infringe our issued patents, our in-licensed patents, or other intellectual property that we own or in-license. Under the terms of our license agreements with Antecip, if we believe a third party is infringing on the patents subject to the licenses, we are obligated, at our own expense, to initiate suit against those third parties. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents. In addition, in a patent infringement proceeding, a court may decide that a patent of ours is invalid or unenforceable, in whole or in part; construe the patent's claims narrowly; or 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. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly. 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.

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

We may need to license certain intellectual property from third parties, and such licenses may not be available or may not be available on commercially reasonable terms.

A third party may hold intellectual property, including patent rights that are important or necessary to the development or commercialization of our products. It may be necessary for us to use the patented or proprietary technology of third parties to commercialize our products, in which case we would be required to obtain a license from these third parties. Such a license may not be available on commercially reasonable terms, or at all, which could materially harm our business, financial condition, results of operations, and prospects.

We may be subject to claims that our employees, independent contractors, or consultants have wrongfully used or disclosed alleged trade secrets of their former employers or other third parties.

As is common in the biotechnology and pharmaceutical industry, we employ individuals who were previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although no claims against us are currently pending, we may be subject to claims that these individuals or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. 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.

We may be unable to adequately prevent disclosure of trade secrets and other proprietary information.

We rely on trade secrets to protect our proprietary technological advances and know-how, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. We rely in part on confidentiality agreements with our employees, consultants, contractors, outside scientific collaborators, sponsored researchers, and other advisors, including the third parties we rely on to manufacture our product candidates, to protect our trade secrets and other proprietary information. However, any party with whom we have executed such an agreement may breach that agreement and disclose our proprietary information, including our trade secrets. Accordingly, these agreements may not effectively prevent disclosure of confidential information and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights. In addition, others may independently discover our trade secrets and proprietary information. Further, the FDA, as part of its Transparency Initiative, a proposal to increase disclosure and make data more accessible to the public, is currently considering whether to make additional information publicly available on a routine basis, including information that we may consider to be trade secrets or other proprietary information, and it is not clear at the present time how the FDA's disclosure policies may change in the future, if at all. Failure to obtain or maintain trade secret protection could enable competitors to use our proprietary information to develop products that compete with our products or cause additional, material adverse effects upon our competitive business position and financial results.

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

Filing, prosecuting, and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those 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. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement rights are not as strong as those in the United States. These products may compete with our product candidates and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

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

RISKS RELATED TO LEGAL AND COMPLIANCE MATTERS

If we fail to comply with federal state, and foreign healthcare laws, including fraud and abuse and health and other information privacy and security laws, we could face substantial penalties and our business, financial condition, results of operations, and prospects could be adversely affected.

As a pharmaceutical company, we are subject to many federal and state healthcare laws, including those described in the “Business—Government Regulation and Product Approval” section of our Annual Report on Form 10-K, filed with the Securities and Exchange Commission, or SEC, on March 15, 2019, such as the federal Anti-Kickback Statute, the federal civil and criminal False Claims Act, the civil monetary penalties statute, the Medicaid Drug Rebate statute and other price reporting requirements, the Veterans Health Care Act of 1992, the federal Health Insurance Portability and Accountability Act of 1996 (as amended by the Health Information Technology for Economics and Clinical Health Act), the Foreign Corrupt Practices Act of 1977, the Patient Protection and Affordable Care Act of 2010, and similar state and foreign laws. Even though we do not and will not control referrals of healthcare services or bill directly to Medicare, Medicaid, or other third-party payors, certain federal and state healthcare laws and regulations pertaining to fraud and abuse and patients’ rights are and will be applicable to our business. We would be subject to healthcare fraud and abuse by both the federal government and the states in which we conduct our business.

If we or our operations are found to be in violation of any federal or state healthcare law, or any other governmental regulations that apply to us, we may be subject to penalties, including civil, criminal, and administrative penalties, damages, fines, disgorgement, debarment from government contracts, refusal of orders under existing contracts, exclusion from participation in U.S. federal or state health care programs, corporate integrity agreements, and the curtailment or restructuring of our operations, any of which could materially adversely affect our ability to operate our business and our financial results. If any of the physicians or other healthcare providers or entities with whom we expect to do business, including our collaborators, is found not to be in compliance with applicable laws, it may be subject to criminal, civil, or administrative sanctions, including but not limited to, exclusions from participation in government healthcare programs, which could also materially affect our business.

Although an effective compliance program can mitigate the risk of investigation and prosecution for violations of these laws, the risks cannot be entirely eliminated. Moreover, achieving and sustaining compliance with applicable federal and state fraud laws may prove costly. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management’s attention from the operation of our business.

If the government or third-party payors fail to provide adequate coverage and payment rates for any of our current or future product candidates, or if HMOs or long-term care facilities choose to use therapies that are less expensive, our revenue and prospects for profitability will be limited.

In both domestic and foreign markets, sales of our future products will depend in part upon the availability of coverage and reimbursement from third-party payors. Such third-party payors include government health programs such as Medicare and Medicaid, managed care providers, private health insurers, and other organizations. Coverage decisions may depend upon clinical and economic standards that disfavor new drug products when more established or lower cost therapeutic alternatives are already available or subsequently become available. If reimbursement is not available, or is available only to limited levels, our product candidates may be competitively disadvantaged, and we, or our collaborators, may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us, or our collaborators, to establish or maintain a market share sufficient to realize a sufficient return on our or their investments. Alternatively, securing favorable reimbursement terms may require us to compromise pricing and prevent us from realizing an adequate margin over cost.

There is significant uncertainty related to third-party payor coverage and reimbursement of newly approved drugs. Marketing approvals, pricing, and reimbursement for new drug products vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay commercial launch of the product, possibly for lengthy time periods, which may negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability or the ability of our collaborators to recoup our or their investment in one or more product candidates, even if our product candidates obtain marketing approval. Our ability, and the ability of our collaborators, to commercialize our product candidates will depend in part on the extent to which coverage and reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers, and other organizations. Regulatory authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will cover and establish reimbursement levels. The healthcare industry is acutely focused on cost containment, both in the United States and elsewhere. Several third-party payors are requiring that drug companies provide them with predetermined discounts from list prices, are using preferred drug lists to leverage greater discounts in competitive classes, are disregarding therapeutic differentiators within classes, and are challenging the prices charged for drugs. Brand drugs without generic equivalents are often included in therapeutic classes with other brands that have generic versions and may be similarly disadvantaged by the availability of low cost alternatives within the class, particularly if a generic version of the same agent is available in another form.

Third-party payors, whether foreign or domestic, or governmental or commercial, are developing increasingly sophisticated methods of controlling healthcare costs. In addition, in the United States, no uniform policy of coverage and reimbursement for drug products exists among third-party payors. Therefore, coverage and reimbursement for drug products can differ significantly from payor to payor. Further, we believe that future coverage and reimbursement will likely be subject to increased restrictions both in the United States and in international markets. Third-party coverage and reimbursement for our products or product candidates for which we receive regulatory approval may not be available or adequate in either the United States or international markets, which could have a negative effect on our business, financial condition, results of operations, and prospects.

Assuming coverage is approved, the resulting reimbursement payment rates might not be adequate. If payors subject our product candidates to maximum payment amounts, or impose limitations that make it difficult to obtain reimbursement, providers may choose to use therapies which are less expensive when compared to our product candidates. Additionally, if payors require high copayments, beneficiaries may decline prescriptions and seek alternative therapies. We may need to conduct post-marketing studies in order to demonstrate the cost-effectiveness of any future products to the satisfaction of hospitals and other target customers and their third-party payors. Such studies might require us to commit a significant amount of management time and financial and other resources. Our future products might not ultimately be considered cost-effective. Adequate third-party coverage and reimbursement might not be available to enable us to maintain price levels sufficient to realize an appropriate return on investment in product development.

In addition, federal programs impose penalties on manufacturers of drugs marketed under an NDA, including 505(b)(2) drugs, in the form of mandatory additional rebates and/or discounts if commercial prices increase at a rate greater than the Consumer Price Index-Urban, and these rebates and/or discounts, which can be substantial, may impact our ability to raise commercial prices. Regulatory authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications, which could affect our ability or that of our collaborators to sell our product candidates profitably. These payors may not view our products, if any, as cost-effective, and coverage and reimbursement may not be available to our customers, or those of our collaborators, or may not be sufficient to allow our products, if any, to be marketed on a competitive basis. Cost-control initiatives could cause us, or our collaborators, to decrease, discount, or rebate a portion of the price we, or they, might establish for products, which could result in lower than anticipated product revenues. If the realized prices for our products, if any, decrease or if governmental and other third-party payors do not provide adequate coverage or reimbursement, our prospects for revenue and profitability will suffer.

There may also be delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the indications for which the drug is approved by the FDA or comparable foreign regulatory authorities. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale, and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may only be temporary. Reimbursement rates may vary, by way of example, according to the use of the drug and the clinical setting in which it is used. Reimbursement rates may also be based on reimbursement levels already set for lower cost drugs or may be incorporated into existing payments for other services.

Prices paid for a drug also vary depending on the class of trade. Prices charged to government customers are subject to price controls, including ceilings, and private institutions obtain discounts through group purchasing organizations. Net prices for drugs may be further reduced by mandatory discounts or rebates required by government healthcare programs and demanded by private payors. Drugs approved under NDAs, including 505(b)(2) drugs, are subject to greater discounts and reporting obligations under federal programs than drugs approved under ANDAs, and the inflation penalty applicable to these products can equal the selling price. It is also not uncommon for market conditions to warrant multiple discounts to different customers on the same unit, such as purchase discounts to institutional care providers and rebates to the health plans that pay them, which reduces the net realization on the original sale.

In addition, increasingly, third-party payors are requiring higher levels of evidence of the benefits and clinical outcomes of new technologies and are challenging the prices charged. We, and our collaborators, cannot be sure that coverage will be available for any product candidate that we, or they, commercialize and, if available, that the reimbursement rates will be adequate. Further, the net reimbursement for drug products may be subject to additional reductions if there are changes to laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. An inability to promptly obtain coverage and adequate payment rates from both government-funded and private payors for any our product candidates for which we obtain marketing approval could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products, and our overall financial condition.

We are subject to new legislation, regulatory proposals, and healthcare payor initiatives that may increase our costs of compliance, and adversely affect our ability to market our products, obtain collaborators, and raise capital.

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 marketing approval of our product candidates, restrict or regulate post-approval activities, and affect our ability, or the ability of our collaborators, to profitably sell any products for which we obtain marketing approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we, or our collaborators, may receive for any approved products.

For example, legislative changes have been proposed and adopted since enactment of the Affordable Care Act, or ACA, in 2010. These changes include, among other things, aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which became effective on April 1, 2013, and significant reductions to Medicare payment to certain safety net hospitals for outpatient drugs purchased under the “340B” drug discount program, effective January 1, 2018. These laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on customers for our drugs, if approved, and, accordingly, on our results of operations.

On January 20, 2017, the current administration signed an Executive Order directing 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. Further, in December 2017, the current administration signed into law legislation that repealed the individual mandate in the ACA and increased manufacturer liability for payment on behalf of Medicare Part D beneficiaries during the coverage gap. Congress also could consider additional legislation to repeal and replace elements of the ACA. The United States District Court for the Northern District of Texas struck down the ACA, deeming it unconstitutional given that Congress repealed the individual mandate in 2017. While this decision has been stayed pending outcome of an appeal to the Fifth Circuit Court of Appeals, so the ruling does not have immediate effect, it is unclear how this decision, subsequent appeals, and other efforts to repeal and replace the ACA will impact the ACA. It is also unclear how regulatory and subregulatory policy, which fluctuate continually, may affect interpretation and implementation of the ACA and its practical effects on our business.

While the full effect that the ACA may have on our business continues to evolve, we expect that the ACA, as well as other federal and state healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria, increased regulatory burdens and operating costs, decreased net revenue from our pharmaceutical products, decreased potential returns from our development efforts, and additional downward pressure on the price that we receive for any approved drug. There is increasing focus on the price of drugs, and states such as California have begun enacting transparency laws aimed at curbing drug price increases. Any reduction in reimbursement from Medicare or other government healthcare programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our drugs.

Legislative and regulatory proposals may also be made to expand post-approval requirements and restrict sales and promotional activities 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 product labeling and post-marketing testing and other requirements.

In addition, there have been a number of other legislative and regulatory proposals aimed at changing the pharmaceutical industry. For instance, the enacted Drug Supply Chain Security Act, or DSCSA imposes obligations on manufacturers of prescription drug products for commercial distribution, regulating the distribution of the products at the federal level, and sets certain standards for federal or state registration and compliance of entities in the supply chain (manufacturers and repackagers, wholesale distributors, third-party logistics providers, and dispensers). The DSCSA preempts previously enacted state pedigree laws and the pedigree requirements of the Prescription Drug Marketing Act, or PDMA. Trading partners within the drug supply chain must now ensure certain product tracing requirements are met that they are doing business with other authorized trading partners; and they are required to exchange transaction information, transaction history, and transaction statements. Further, the DSCSA limits the distribution of prescription pharmaceutical products and imposes requirements to ensure overall accountability and security in the drug supply chain. As of November 27, 2018 product identifier information (an aspect of the product tracing scheme) is required.

Compliance with the federal track and trace requirements may increase our operational expenses and impose significant administrative burdens. As a result of these and other new proposals, we may determine to change our current manner of operation, provide additional benefits, or change our contract arrangements, any of which could have a material adverse effect on our business, financial condition, and results of operations.

Governments outside the United States tend to impose strict price controls, which may adversely affect our revenues, if any.

In international markets, reimbursement and health care payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. In some countries, particularly the countries of the EU, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain coverage and reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. There can be no assurance that our products will be considered cost-effective by third-party payors, that an adequate level of reimbursement will be available, or that the third-party payors' reimbursement policies will not adversely affect our ability to sell our products profitably. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially.

Our employees, independent contractors, consultants, commercial partners, principal investigators, or CROs may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have a material adverse effect on our business.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees, independent contractors, consultants, commercial partners, principal investigators, or CROs could include intentional, reckless, negligent, or unintentional failures to comply with FDA regulations, comply with applicable fraud and abuse laws, provide accurate information to the FDA, report financial information or data accurately, or disclose unauthorized activities to us. This misconduct could also involve the improper use or misrepresentation of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter this type of misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, financial condition, and results of operations, including the imposition of significant fines or other sanctions.

Our third-party manufacturers may use hazardous materials in the production of our product candidates and if so, they must comply with environmental laws and regulations, which can be expensive and restrict how we or they do business.

Manufacturing activities for the production of our product candidates involve the controlled storage, use, and disposal of hazardous materials, including the components of our product candidates, and other hazardous compounds. Our third-party manufacturers and we are subject to federal, state, and local laws and regulations governing the use, manufacture, storage, handling, release, and disposal of, and exposure to, these hazardous materials. Violation of these laws and regulations could lead to substantial fines and penalties. Although we believe that our safety procedures, and those of our third-party manufacturers, for handling and disposing of these materials comply with the standards prescribed by these laws and regulations, we cannot eliminate the risk of accidental contamination or injury from these materials. In the event of an accident, state or federal authorities may curtail our use of these materials and interrupt our business operations. In addition, we could become subject to potentially material liabilities relating to the investigation and cleanup of any contamination, whether currently unknown or caused by future releases.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous, or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health, and safety laws and regulations. These current or future laws and regulations may impair our research, development, or production efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties, or other sanctions.

RISKS RELATED TO OUR BUSINESS OPERATIONS

We will need to significantly increase the size of our organization, and we may experience difficulties in managing growth.

As of November 1, 2019, we had only 41 full-time employees. We will need to substantially expand our managerial, commercial, financial, manufacturing, and other personnel resources in order to manage our operations and prepare for the commercialization of our product candidates, if approved. Our management, personnel, systems, and facilities currently in place may not be adequate to support this future growth. In addition, we may not be able to recruit and retain qualified personnel in the future, particularly for sales and marketing positions, due to competition for personnel among pharmaceutical businesses, and the failure to do so could have a significant negative impact on our future product revenues and business results. Our need to effectively manage our operations, growth and various projects requires that we:

- continue the hiring and training of personnel for an effective commercial organization in anticipation of the potential approval of our product candidates, and establish appropriate systems, policies and infrastructure to support that organization;
- ensure that our consultants and other service providers successfully carry out their contractual obligations, provide high quality results, and meet expected deadlines;
- continue to carry out our own contractual obligations to our licensors and other third parties; and
- continue to improve our operational, financial, and management controls, reporting systems, and procedures.

We may be unable to successfully implement these tasks on a larger scale and, accordingly, may not achieve our development and commercialization goals.

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

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 assure you that, following any such acquisition, we will achieve the expected synergies to justify the transaction.

We may not be able to manage our business effectively if we are unable to attract and retain key personnel.

We may not be able to attract or retain qualified management and commercial, scientific, and clinical personnel due to the intense competition for qualified personnel among biotechnology, pharmaceutical, and other businesses. If we are not able to attract and retain necessary personnel to accomplish our business objectives, we may experience constraints that will significantly impede the achievement of our development objectives, our ability to raise additional capital and our ability to implement our business strategy.

Our industry has experienced a high rate of turnover of management personnel in recent years. We are highly dependent on the skills and leadership of our management team, including Dr. Herriot Tabuteau, our Chief Executive Officer and Chairman of the Board. We do not have formal employment agreements with any of our management team. However, we typically enter into offer letters with our executive officers and key personnel. Our senior management may terminate their employment with us at any time. If we lose one or more members of our senior management team, our ability to successfully implement our business strategy could be seriously harmed. Replacing these employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to develop, gain regulatory approval of, and commercialize products successfully. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain, or motivate additional key personnel. We do not maintain “key person” insurance for any of our executives or other employees.

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

As a public company, we continue to incur significant legal, accounting and other expenses that we did not incur as a private company. In addition, the Sarbanes-Oxley Act, as well as rules subsequently implemented by the SEC and the Nasdaq Global Market, impose various requirements on public companies, including requiring establishment and maintenance of effective disclosure controls and internal control over financial reporting and changes in corporate governance practices. Our management and other personnel devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased our legal and financial compliance costs and have made some activities more time-consuming and costly.

Section 404(a) of the Sarbanes-Oxley Act requires annual management assessments of the effectiveness of our internal control over financial reporting. However, for as long as we remain an “emerging growth company” as defined in the Jumpstart Our Business Startups Act of 2012, or JOBS Act, 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(b) of the Sarbanes-Oxley Act. We may take advantage of these reporting exemptions until we are no longer an “emerging growth company.” We will remain an “emerging growth company” until the earliest of (i) the last day of the fiscal year in which we have total annual gross revenues of \$1.07 billion or more; (ii) December 31, 2020; (iii) the date on which we have issued more than \$1.0 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a “large accelerated filer” under the rules of the SEC.

Our testing, or the subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal control over financial reporting that are deemed to be material weaknesses. We will incur substantial accounting expense and expend significant management efforts to comply with internal control over financial reporting requirements. We currently do not have an internal audit group, and we may need to hire additional accounting and financial staff with appropriate public company experience and technical accounting knowledge. Moreover, if we are not able to comply with these requirements in a timely manner or if we or our independent registered public accounting firm identifies deficiencies in our internal control over financial reporting that are deemed to be material weaknesses, the market price of our stock could decline, and we could be subject to sanctions or investigations by the Nasdaq Global Market, the SEC or other regulatory authorities, which would require additional financial and management resources.

If we fail to maintain an effective system of internal control over financial reporting in the future, we may not be able to accurately report our financial condition, results of operations or cash flows, which may adversely affect investor confidence in us and, as a result, the value of our common stock.

Effective internal controls over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation, could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with Section 404 of the Sarbanes-Oxley Act, or the subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. If we are unable to conclude that our internal control over financial reporting is effective, or if our independent registered public accounting firm determines we have a material weakness or significant deficiency in our internal control over financial reporting once that firm begins its Section 404 reviews, we could lose investor confidence in the accuracy and completeness of our financial reports, the market price of our common stock could decline, and we could be subject to sanctions or investigations by the Nasdaq Global Market, the SEC or other regulatory authorities. Failure to remedy any material weakness in our internal control over financial reporting, or to implement or maintain other effective control systems required of public companies, could also restrict our future access to the capital markets.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

We are subject to the periodic reporting requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act. Our disclosure controls and procedures are designed to reasonably assure that information required to be disclosed by us in reports we file or submit under the Exchange Act is accumulated and communicated to management, recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met.

These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements or insufficient disclosures due to error or fraud may occur and not be detected.

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

Despite our implementation of security measures, our internal computer systems and those of our CROs and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war, telecommunication and electrical failures, cyber-attacks or cyber-intrusions over the Internet, attachments to emails, persons inside our organization, or persons with access to systems inside our organization. The risk of a security breach or disruption, particularly through cyber-attacks or cyber intrusion, including by computer hackers, foreign governments, and cyber terrorists, has generally increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our product candidate development programs. For example, the loss of clinical trial data from completed, ongoing, or planned clinical trials 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 were to result in a loss of or damage to our data or applications, or inappropriate disclosure of personal, confidential, or proprietary information, we could incur liability and the further development of any of our product candidates could be delayed.

Our failure to comply with international data protection laws and regulations could lead to government enforcement actions and significant penalties against us, and adversely impact our operating results.

EU member states and other foreign jurisdictions, including Switzerland, have adopted data protection laws and regulations which impose significant compliance obligations. Moreover, the collection and use of personal health data in the EU, which was formerly governed by the provisions of the EU Data Protection Directive, was replaced with the EU General Data Protection Regulation, or the GDPR, in May 2018. The GDPR, which is wide-ranging in scope, imposes several requirements relating to the consent of the individuals to whom the personal data relates, the information provided to the individuals, the security and confidentiality of the personal data, data breach notification and the use of third party processors in connection with the processing of personal data. The GDPR also imposes strict rules on the transfer of personal data out of the EU to the U.S., provides an enforcement authority and imposes large penalties for noncompliance, including the potential for fines of up to €20 million or 4% of the annual global revenues of the noncompliant company, whichever is greater. The GDPR requirements apply not only to third-party transactions, but also to transfers of information between us and our subsidiaries, including employee information. The recent implementation of the GDPR has increased our responsibility and liability in relation to personal data that we process, including in clinical trials, and we may in the future be required to put in place additional mechanisms to ensure compliance with the GDPR, which could divert management's attention and increase our cost of doing business. In addition, new regulation or legislative actions regarding data privacy and security (together with applicable industry standards) may increase our costs of doing business. In this regard, we expect that there will continue to be new proposed laws, regulations and industry standards relating to privacy and data protection in the United States, the EU and other jurisdictions, and we cannot determine the impact such future laws, regulations and standards may have on our business.

Our failure to comply with state and/or national data protection laws and regulations could lead to government enforcement actions and significant penalties against us, and adversely impact our operating results.

There are numerous other laws and legislative and regulatory initiatives at the federal and state levels addressing privacy and security concerns, and some state privacy laws apply more broadly than the Health Insurance Portability and Accountability Act (HIPAA) and associated regulations. For example, California recently enacted legislation – the California Consumer Privacy Act, or CCPA – which goes into effect January 1, 2020. The CCPA, among other things, creates new data privacy obligations for covered companies and provides new privacy rights to California residents, including the right to opt out of certain disclosures of their information. The CCPA also creates a private right of action with statutory damages for certain data breaches, thereby potentially increasing risks associated with a data breach. Legislators have stated that they intend to propose amendments to the CCPA before it goes into effect, and the California Attorney General will issue clarifying regulations. Although the law includes limited exceptions, including for certain information collected as part of clinical trials as specified in the law, it may regulate or impact our processing of personal information depending on the context. It remains unclear what, if any, modifications will be made to this legislation or how it will be interpreted.

RISKS RELATED TO OWNERSHIP OF OUR COMMON STOCK

An active trading market for our common stock may not be sustained.

In November 2015, we closed our initial public offering. Prior to our initial public offering, there was no public market for shares of our common stock. Although we have completed our initial public offering and shares of our common stock are listed and trading on The Nasdaq Global Market, an active trading market for our shares may not 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.

The market price of our common stock may be highly volatile.

The trading price of our common stock is likely to be volatile. As a result of this volatility, investors may not be able to sell their common stock at or above the price paid for the shares. The market price for our common stock may be influenced by many factors, including:

- delays in the commencement, enrollment, and ultimate completion, of our planned and ongoing Phase 3 clinical trials for our product candidates;
- any delay or refusal on the part of the FDA in approving an NDA for any of our current and future product candidates;
- the commercial success of any of our current and future product candidates, if approved by the FDA;
- results of clinical trials of any of our current and future product candidates or those of our competitors;
- actual or anticipated variations in quarterly or annual operating results;
- failure to meet or exceed financial projections we provide to the public, if any;
- failure to meet or exceed the estimates and projections of the investment community, including securities analysts;
- introduction of competitive products or technologies;
- changes or developments in laws or regulations applicable to our product candidates;
- the perception of the pharmaceutical industry by the public, legislatures, regulators, and the investment community;
- general economic and market conditions and overall fluctuations in U.S. equity markets;
- data or security breaches;
- developments concerning our sources of manufacturing supply, warehousing, and inventory control;
- disputes or other developments relating to patents or other proprietary rights;
- additions or departures of key scientific or management personnel;
- announcements of investigations or regulatory scrutiny of our operations or lawsuits filed against us;
- capital commitments;
- investors' general perception of our company and our business;
- announcements and expectations of additional financing efforts, including the issuance of debt, equity or convertible securities;
- sales of our common stock, including sales by our directors and officers or significant stockholders;
- changes in the market valuations of companies similar to us;

- announcements by us or our competitors of significant acquisitions, strategic partnerships, or divestitures;
- general conditions or trends in our industry; and
- the other factors described in this “Risk Factors” section.

In addition, the stock market in general, and the market for small pharmaceutical and biotechnology companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance.

Further, in the past, stockholders have initiated class action lawsuits against pharmaceutical and biotechnology companies following periods of volatility in the market prices of these companies’ stocks. Such litigation, if instituted against us, could cause us to incur substantial costs and divert management’s attention and resources from our business.

If equity research analysts do not publish research or reports, or publish unfavorable research or reports, about us, our business, or our market, our stock price and trading volume could decline.

The trading market for our common stock is influenced by the research and reports that equity research analysts publish about us and our business. We do not have any control over the equity research analysts that provide research coverage of our common stock or the content and opinions included in their reports. The price of our stock could decline if one or more equity research analysts downgrades our stock or issue other unfavorable commentary or research. If one or more equity research analysts ceases coverage of our company or fails to publish reports on us regularly, demand for our stock could decrease, which in turn could cause our stock price or trading volume to decline.

Our quarterly operating results may fluctuate significantly.

We expect our operating results to be subject to quarterly fluctuations. Our net loss and other operating results will be affected by numerous factors, including:

- whether the FDA requires us to complete additional, unanticipated studies, tests, or other activities prior to approving any of our current and future product candidates, which would likely further delay any such approval;
- if any of our current or future product candidates is approved, our ability to establish the necessary commercial infrastructure to launch this product candidate without substantial delays, including hiring sales and marketing personnel and contracting with third parties for warehousing, distribution, cash collection, and related commercial activities;
- our ability to identify and enter into third-party manufacturing arrangements capable of manufacturing any of our current or future product candidates in commercial quantities;
- our execution of other collaborative, licensing, or similar arrangements and the timing of payments we may make or receive under these arrangements;
- variations in the level of expenses related to our future development programs;
- any product liability or intellectual property infringement lawsuit in which we may become involved;

- regulatory developments affecting our current and future product candidates, or the product candidates of our competitors; and
- if any of our current or future product candidates receive regulatory approval, the level of underlying demand for such product candidate and wholesaler buying patterns.

If our quarterly or annual operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially. Furthermore, any quarterly or annual fluctuations in our operating results may, in turn, cause the price of our stock to fluctuate substantially. We believe that quarterly comparisons of our financial results are not necessarily meaningful and should not be relied upon as an indication of our future performance.

Raising additional funds by issuing securities may cause dilution to existing stockholders and raising funds through lending and licensing arrangements may restrict our operations or require us to relinquish proprietary rights.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, grants, and license and development agreements in connection with any collaborations. We do not have any committed external source of funds. To the extent that we raise additional capital by issuing equity securities, our existing stockholders' ownership will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures, or declaring dividends.

If we raise additional funds through collaborations, strategic alliances, or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs, or product candidates or grant licenses on terms that may not be favorable to us. Any debt financing we enter into may involve covenants that restrict our operations. These restrictive covenants may include limitations on additional borrowing and specific restrictions on the use of our assets as well as prohibitions on our ability to create liens, pay dividends, redeem our stock, or make investments. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce, or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval.

As of November 1, 2019, our executive officers, directors, and 5% stockholders and their affiliates beneficially owned an aggregate of approximately 24% of our outstanding common stock. As a result, these stockholders have significant influence and may be able to determine all matters requiring stockholder approval. For example, these stockholders may be able to control elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This concentration of ownership could delay or prevent any acquisition of our company on terms that other stockholders may desire, and may adversely affect the market price of our common stock.

Some of these persons or entities may have interests different than yours. For example, these stockholders, if they acted together, could significantly influence all matters requiring approval by our stockholders, including the election of directors and the approval of mergers or other business combination transactions. These stockholders may be able to determine all matters requiring stockholder approval. The interests of these stockholders may not always coincide with our interests or the interests of other stockholders. This may also prevent or discourage unsolicited acquisition proposals or offers for our common stock that other stockholders may feel are in their best interest and our large stockholders may act in a manner that advances their best interests and not necessarily those of other stockholders, including seeking a premium value for their common stock, and might affect the prevailing market price for our common stock.

Sales of a substantial number of shares of our common stock in the public market by our existing stockholders could cause our stock price to fall.

Sales of a substantial number of shares of our common stock in the public market or the perception that these sales might occur, could depress the market price of our common stock and could impair our ability to raise adequate capital through the sale of additional equity securities. We are unable to predict the effect that sales may have on the prevailing market price of our common stock.

As of November 1, 2019, we have outstanding 34,508,626 shares of common stock and 3,517,227 shares of common stock equivalents that would increase the number of common stock outstanding if these instruments were exercised or converted, including stock options to purchase common stock based on vesting requirements and warrants to purchase common stock. Of our currently outstanding shares of common stock, 26,331,915 are freely tradable. The remainder of the outstanding shares of common stock are held by our affiliates and may be considered “control securities” for purposes of Rule 144 under the Securities Act.

In addition, we have filed one or more registration statements on Form S-8 registering the issuance of an aggregate of 7,481,050 shares of common stock subject to options or other equity awards issued or reserved for future issuance under our 2015 Omnibus Incentive Compensation Plan, or the Plan. Shares registered under registration statements on Form S-8 will be available for sale in the public market subject to vesting arrangements and exercise of options, the lock-up agreements described above and the restrictions of Rule 144 in the case of our affiliates.

Our management will have broad discretion in the use of the net proceeds from our capital raises, including our December 2017 registered direct offering, our October 2018 registered direct offering, and the proceeds from sales pursuant to our previous and current Sales Agreements, and may not use them effectively.

Our management will have broad discretion in the application of the net proceeds from our capital raises, which we refer to as our Capital Raises, including our December 2017 registered direct offering, our October 2018 registered direct offering, and the proceeds from sales pursuant to our October 2017 (which was fully utilized in January 2019), and May 2019 “at-the-market” sales agreements with SVB Leerink (formerly Leerink Partners LLC), which provided and currently provide for the sale of up to \$30.0 and \$50.0 million, respectively, of our common stock from time to time, and our stockholders will not have the opportunity as part of their investment decision to assess whether the net proceeds from our Capital Raises are being used appropriately. You may not agree with our decisions, and our use of the proceeds may not yield any return on your investment. Because of the number and variability of factors that will determine our use of the net proceeds from our Capital Raises, their ultimate use may vary substantially from their currently intended use. Our failure to apply the net proceeds of our Capital Raises effectively could compromise our ability to pursue our growth strategy and we might not be able to yield a significant return, if any, on our investment of those net proceeds. You will not have the opportunity to influence our decisions on how to use our net proceeds from our Capital Raises. Pending their use, we may invest the net proceeds from our Capital Raises in short-term, investment-grade, interest-bearing instruments and U.S. government securities. These temporary investments are not likely to yield a significant return.

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 Jumpstart Our Business Startups Act of 2012, or JOBS Act, and we intend to take advantage of some of the exemptions from reporting requirements that are applicable to other public companies that are not emerging growth companies, including 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. We may take advantage of these reporting exemptions until we are no longer an emerging growth company. 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 will remain an emerging growth company until the earlier of (1) December 31, 2020, (2) the last day of the fiscal year (a) in which we have total annual gross revenue of at least \$1.07 billion, or (b) in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds \$700 million as of the prior June 30th, and (3) the date on which we have issued more than \$1.0 billion in non-convertible debt during the prior three-year period. To the extent we are no longer eligible to use exemptions from various reporting requirements under the JOBS Act, we may be unable to realize our anticipated cost savings from these exemptions, which could have a material adverse impact on our operating results.

The use of our net operating loss carryforwards and research tax credits may be limited.

Our net operating loss carryforwards and any future research and development tax credits may expire and not be used. Net operating loss carry forwards amounting to \$60 million generated before the 2018 tax year will start expiring beginning 2033, if we have not used them prior to that time, and the net operating losses of approximately \$27 million generated in 2018 have an indefinite carryforward period. Net operating loss carry forwards arising in taxable years ending after December 31, 2018 are no longer subject to expiration under the Internal Revenue Code of 1986, as amended, or the Code. Additionally, our ability to use any net operating loss and credit carryforwards to offset taxable income or tax, respectively, in the future will be limited under Sections 382 and 383 of the Code, respectively, if we have a cumulative change in ownership of more than 50% within a three-year period. The completion of our initial public offering, together with our March 2017 public offering, our December 2017 registered direct offering, our October 2018 registered direct offering, private placements and other transactions that have occurred, may trigger, or may have already triggered, such an ownership change. In addition, since we will need to raise substantial additional funding to finance our operations, we may undergo further ownership changes in the future. We have never completed an analysis as to whether such a change of ownership has occurred, but in such an event, we will be limited regarding the amount of net operating loss carryforwards and research tax credits that could be utilized annually in the future to offset taxable income or tax, respectively. Any such annual limitation may significantly reduce the utilization of the net operating loss carryforwards and research tax credits before they expire. In addition, certain states have suspended use of net operating loss carryforwards for certain taxable years, and other states are considering similar measures. As a result, we may incur higher state income tax expense in the future. Depending on our future tax position, continued suspension of our ability to use net operating loss carryforwards in states in which we are subject to income tax could have an adverse impact on our results of operations and financial condition.

Because we do not intend to pay dividends on our common stock, your returns will be limited to any increase in the value of our stock.

We have never declared or paid any cash dividends on our capital stock. We currently intend to retain all available funds and any future earnings to support our operations and finance the growth and development of our business and do not anticipate declaring or paying any cash dividends on our common stock for the foreseeable future. Any return to stockholders will therefore be limited to the appreciation of their stock, if any. Investors seeking cash dividends should not purchase our common stock.

Provisions in our corporate charter documents and under Delaware law may prevent or frustrate attempts by our stockholders to change our management and hinder efforts to acquire a controlling interest in us, and the market price of our common stock may be lower as a result.

There are provisions in our amended and restated certificate of incorporation and amended and restated bylaws that may make it difficult for a third party to acquire, or attempt to acquire, control of our company, even if a change in control was considered favorable by you and other stockholders. For example, our board of directors will have the authority to issue up to 10,000,000 shares of preferred stock and to fix the price, rights, preferences, privileges, and restrictions of the preferred stock without any further vote or action by our stockholders. The issuance of shares of preferred stock may delay or prevent a change in control transaction. As a result, the market price of our common stock and the voting and other rights of our stockholders may be adversely affected. An issuance of shares of preferred stock may result in the loss of voting control to other stockholders.

In addition, we are subject to the anti-takeover provisions of Section 203 of the Delaware General Corporation Law, or DGCL, which regulates corporate acquisitions by prohibiting Delaware corporations from engaging in specified business combinations with particular stockholders of those companies. These provisions could discourage potential acquisition proposals and could delay or prevent a change in control transaction. They could also have the effect of discouraging others from making tender offers for our common stock, including transactions that may be in your best interests. These provisions may also prevent changes in our management or limit the price that investors are willing to pay for our stock.

Our amended and restated certificate of incorporation designates the Court of Chancery of the State of Delaware as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated certificate of incorporation provides that, unless we consent in writing to the selection of an alternate form, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, employees or agents to us or our stockholders, (3) any action asserting a claim arising pursuant to the DGCL, or (4) any other action asserting a claim against us that is governed by the internal affairs doctrine, in each such case subject to such Court of Chancery having personal jurisdiction over the indispensable parties named as defendants therein.

Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock shall be deemed to have notice of and to have consented to the provisions of our amended and restated certificate of incorporation described above. This choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers, or other employees or agents, which may discourage such lawsuits against us and our directors, officers, employees, and agents. Further, this choice of forum provision does not preclude or contract the scope of exclusive federal or concurrent jurisdiction for any actions brought under the Securities Act or the Exchange Act. Section 27 of the Exchange Act creates exclusive federal jurisdiction over all suits brought to enforce any duty or liability created by the Exchange Act or the rules and regulations thereunder. As a result, the exclusive forum provision will not apply to suits brought to enforce any duty or liability created by the Exchange Act or any other claim for which the federal courts have exclusive jurisdiction. In addition, Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all suits brought to enforce any duty or liability created by the Securities Act or the rules and regulations thereunder. As a result, the exclusive forum provision will not apply to suits brought to enforce any duty or liability created by the Securities Act or any other claim for which the federal and state courts have concurrent jurisdiction. Accordingly, our exclusive forum provision will not relieve us of our duties to comply with the federal securities laws and the rules and regulations thereunder, and our stockholders will not be deemed to have waived our compliance with these laws, rules and regulations.

If a court were to find these provisions of our amended and restated certificate of incorporation 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 adversely affect our business, financial condition, and results of operations. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management and other employees.

Item 6. Exhibits.

The exhibits filed as part of this Quarterly Report on Form 10-Q are set forth on the Exhibit Index, which is incorporated herein by reference.

INDEX OF EXHIBITS

<u>Exhibit Number</u>	<u>Description</u>
31.1	Certification of Principal Executive Officer pursuant to Rule 13a-14(a)/15d-14(a), as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2	Certification of Principal Financial Officer pursuant to Rule 13a-14(a)/15d-14(a), as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1	Certification of Principal Executive Officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 (furnished herewith).
32.2	Certification of Principal Financial Officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 (furnished herewith).
101	Interactive data files pursuant to Rule 405 of Regulation S-T: (i) Consolidated Balance Sheets, (ii) Consolidated Statements of Operations, (iii) Consolidated Statements of Cash Flows, and (iv) the Notes to Consolidated Financial Statements.

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.

AXSOME THERAPEUTICS, INC.

Date: November 7, 2019

By /s/ Herriot Tabuteau, M.D.
Herriot Tabuteau, M.D.
President and Chief Executive Officer
(Principal Executive Officer)

Date: November 7, 2019

By /s/ Nick Pizzie
Nick Pizzie
Chief Financial Officer
(Principal Financial and Accounting Officer)

**CERTIFICATION OF PERIODIC REPORT
PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002**

I, Herriot Tabuteau, M.D., certify that:

1. I have reviewed this quarterly report on Form 10-Q of Axsome Therapeutics, 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 and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
 - a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
 - c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
 - a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
 - b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: November 7, 2019

/s/ Herriot Tabuteau, M.D.
Herriot Tabuteau, M.D.
Chief Executive Officer
(Principal Executive Officer)

**CERTIFICATION OF PERIODIC REPORT PURSUANT TO SECTION 302 OF THE
SARBANES-OXLEY ACT OF 2002**

I, Nick Pizzie, certify that:

1. I have reviewed this quarterly report on Form 10-Q of Axsome Therapeutics, 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 and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
 - a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
 - c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
 - a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
 - b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: November 7, 2019

/s/ Nick Pizzie
Nick Pizzie
Chief Financial Officer
(Principal Financial and Accounting Officer)

**STATEMENT OF PRINCIPAL EXECUTIVE OFFICER OF
AXSOME THERAPEUTICS, INC.
PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the quarterly report of Axsome Therapeutics, Inc. (the "Company") on Form 10-Q for the quarter ended September 30, 2019 as filed with the Securities and Exchange Commission (the "Report"), I, Herriot Tabuteau, M.D., Chief Executive Officer of the Company, certify, pursuant to 18 U.S.C. §1350, as adopted pursuant to §906 of the Sarbanes-Oxley Act of 2002, that, based on my 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.

Date: November 7, 2019

/s/ Herriot Tabuteau, M.D.
Herriot Tabuteau, M.D.
Chief Executive Officer
(Principal Executive Officer)

**STATEMENT OF PRINCIPAL FINANCIAL OFFICER OF
AXSOME THERAPEUTICS, INC.
PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the quarterly report of Axsome Therapeutics, Inc. (the "Company") on Form 10-Q for the quarter ended September 30, 2019 as filed with the Securities and Exchange Commission (the "Report"), I, Nick Pizzie, Chief Financial Officer of the Company, certify, pursuant to 18 U.S.C. §1350, as adopted pursuant to §906 of the Sarbanes-Oxley Act of 2002, that, based on my 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.

Date: November 7, 2019

/s/ Nick Pizzie

Nick Pizzie

Chief Financial Officer

(Principal Financial and Accounting Officer)
