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 June 30, 2021

OR

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

For the transition period from _____ to _____

Commission File Number 001-37635

AXSOME THERAPEUTICS, INC.
(Exact name of registrant as specified in its charter)

Delaware	**45-4241907**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
22 Cortlandt Street **16th Floor** **New York, New York**	**10007**
(Address of principal executive offices)	(Zip Code)

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

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

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

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

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

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

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

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

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

There were 37,681,948 shares of the registrant's common stock, $0.0001 par value, outstanding as of August 2, 2021.

AXSOME THERAPEUTICS, INC.
QUARTERLY REPORT ON FORM 10-Q
FOR THE QUARTER ENDED JUNE 30, 2021

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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;
- unforeseen circumstances or other disruptions to normal business operations arising from or related to COVID-19;
- 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

	June 30, 2021 (Unaudited)	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 141,219,090	$ 183,876,453
Prepaid and other current assets	435,804	148,373
Total current assets	141,654,894	184,024,826
Equipment, net	83,444	52,647
Right-of-use asset - operating lease	1,209,037	1,739,475
Other assets	317,375	317,375
Total assets	$ 143,264,750	$ 186,134,323
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 11,611,996	$ 13,504,022
Accrued expenses and other current liabilities	10,162,831	8,713,249
Operating lease liability, current portion	1,088,841	1,220,587
Total current liabilities	22,863,668	23,437,858
Loan payable, long-term	48,882,599	48,321,848
Operating lease liability, long-term	81,863	581,708
Total liabilities	71,828,130	72,341,414
Stockholders' equity:		
Preferred stock, $0.0001 par value per share (10,000,000 shares authorized, none issued and outstanding at June 30, 2021 and December 31, 2020, respectively)	—	—
Common stock, $0.0001 par value per share (150,000,000 shares authorized, 37,648,948 and 37,374,088 shares issued and outstanding at June 30, 2021 and December 31, 2020, respectively)	3,765	3,737
Additional paid-in capital	411,773,127	392,585,265
Accumulated deficit	(340,340,272)	(278,796,093)
Total stockholders' equity	71,436,620	113,792,909
Total liabilities and stockholders' equity	$ 143,264,750	$ 186,134,323

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

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2021	2020	2021	2020
Operating expenses:				
Research and development	$ 14,503,326	$ 10,542,957	$ 31,099,014	$ 38,064,357
General and administrative	16,344,361	7,235,877	27,592,734	12,205,934
Total operating expenses	30,847,687	17,778,834	58,691,748	50,270,291
Loss from operations	(30,847,687)	(17,778,834)	(58,691,748)	(50,270,291)
Interest and amortization of debt discount (expense) income	(1,436,522)	(548,158)	(2,852,431)	(540,847)
Net loss	$ (32,284,209)	$ (18,326,992)	$ (61,544,179)	$ (50,811,138)
Net loss per common share, basic and diluted	$ (0.86)	$ (0.49)	$ (1.64)	$ (1.37)
Weighted average common shares outstanding, basic and diluted	37,595,069	37,100,770	37,512,716	37,081,064

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, 2019	36,933,217	3,693	354,614,189	(175,895,493)	178,722,389
Stock-based compensation	—	—	2,133,530	—	2,133,530
Issuance of common stock upon exercise of options	60,186	6	629,750	—	629,756
Issuance of common stock related to license agreement	82,019	8	7,155,329	—	7,155,337
Net loss	—	—	—	(32,484,146)	(32,484,146)
Balance at March 31, 2020	37,075,422	$ 3,707	$ 364,532,798	$ (208,379,639)	$ 156,156,866
Stock-based compensation	—	—	4,148,025	—	4,148,025
Issuance of common stock upon exercise of options	20,428	2	190,407	—	190,409
Issuance of common stock upon exercise of warrants	29,982	3	—	—	3
Issuance of common stock upon financing	141,678	14	12,074,985	—	12,074,999
Net loss	—	—	—	(18,326,992)	(18,326,992)
Balance at June 30, 2020	**37,267,510**	**$ 3,726**	**$ 380,946,215**	**$ (226,706,631)**	**$ 154,243,310**
Balance at December 31, 2020	37,374,088	3,737	392,585,265	(278,796,093)	113,792,909
Stock-based compensation	—	—	3,731,097	—	3,731,097
Issuance of common stock upon exercise of options	94,000	10	1,913,289	—	1,913,299
Issuance of common stock upon vesting of RSUs	1,917	—	—	—	—
Issuance of common stock upon financing	93,877	9	6,115,855	—	6,115,864
Net loss	—	—	—	(29,259,970)	(29,259,970)
Balance at March 31, 2021	37,563,882	3,756	404,345,506	(308,056,063)	96,293,199
Stock-based compensation	—	—	5,456,242	—	5,456,242
Issuance of common stock upon exercise of options	68,503	7	958,888	—	958,895
Issuance of common stock upon vesting of RSUs	144	0	—	—	—
Issuance of common stock upon financing	16,419	2	1,096,501	—	1,096,503
Shares tendered for withholding taxes	—	0	(84,010)	—	(84,010)
Net loss	—	—	—	(32,284,209)	(32,284,209)
Balance at June 30, 2021	**37,648,948**	**$ 3,765**	**$ 411,773,127**	**$ (340,340,272)**	**$ 71,436,620**

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

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

	Six Months Ended June 30,	
	2021	**2020**
Cash flows from operating activities		
Net loss	$ (61,544,179)	$ (50,811,138)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation expense	9,187,339	6,281,555
Non-cash research and development license expense	—	7,155,337
Amortization of debt discount	560,752	356,664
Amortization of operating lease right-of-use asset	530,437	—
Change in operating lease liability	(631,591)	—
Depreciation	18,075	10,960
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(287,431)	275,914
Accounts payable	(1,892,026)	(1,580,100)
Accrued expenses and other current liabilities	1,449,582	(3,857,658)
Net cash used in operating activities	(52,609,042)	(42,168,466)
Cash flows from investing activities		
Purchases of equipment	(48,872)	(10,759)
Net cash used in investing activities	(48,872)	(10,759)
Cash flows from financing activities		
Proceeds from issuance of common stock upon financing, net	7,212,367	12,074,999
Proceeds from issuance of common stock upon exercise of options	2,872,194	820,165
Proceeds from issuance of common stock upon exercise of warrants	—	3
Payments of tax withholdings on stock award	(84,010)	—
Net cash (used in) provided by financing activities	10,000,551	12,895,167
Net (decrease) increase in cash	(42,657,363)	(29,284,058)
Cash at beginning of period	183,876,453	219,966,167
Cash at end of period	$ 141,219,090	$ 190,682,109
Supplemental disclosures of cash flow information:		
Interest paid	$ 2,312,917	$ 762,501

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 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 five product candidates, AXS-05, AXS-07, AXS-09, AXS-12, and AXS-14, which are being developed for multiple indications. 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.

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, 2020 filed with the SEC on March 1, 2021.

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 six months ended June 30, 2021 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 June 30, 2021, the Company had an accumulated deficit of $340.3 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 may use a combination of public and private equity offerings, debt financings, other third-party funding, strategic alliances, licensing arrangements or marketing and distribution arrangements if market conditions are favorable or in light of other strategic considerations to finance its future cash needs.

The Company's common stock is listed on the Nasdaq Global Market and trades under the symbol "AXSM".

Impact of COVID-19

In December 2019, a novel (new) coronavirus known as SARS-CoV-2 was first detected in Wuhan, Hubei Province, People's Republic of China, causing outbreaks of the coronavirus disease, known as COVID-19, that has now spread globally. On January 30, 2020, the World Health Organization (WHO) declared COVID-19 a public health emergency. The Secretary of Health and Human Services declared a public health emergency in the United States on January 31, 2020, under section 319 of the Public Health Service Act (42 U.S.C. 247d), in response to the COVID-19 outbreak. On March 11, 2020, the WHO declared COVID-19 a pandemic. The full impact of the COVID-19 pandemic is unknown and rapidly evolving. While the potential economic impact brought by and over the duration of the COVID-19 pandemic may be difficult to assess or predict, the COVID-19 pandemic has resulted in significant disruption of global financial markets, which could in the future negatively affect the Company's liquidity. In addition, a recession or market volatility resulting from the COVID-19 pandemic could affect the Company's business. Given the nature and type of the Company's short-term investments, the Company does not believe the COVID-19 pandemic has had or will have a material impact on the Company's current investment liquidity.

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 June 30, 2021, the balance of cash and cash equivalents was $141.2 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 June 30, 2021, 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 on the Company's balance sheet (see Note 6 – 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 costs are expensed as incurred. Research and development expenses consist primarily of personnel costs for our research and development employees, costs incurred to third-party service providers for the conduct of research, preclinical and clinical studies, laboratory supplies, product license fees, consulting and other related expenses. We estimate research, preclinical and clinical study expenses based on services performed, pursuant to contracts with third-party research and development organizations that conduct and manage research, preclinical and clinical activities on our behalf. We estimate these expenses based on discussions with internal management personnel and external service providers as to the progress or stage of completion of services and the contracted fees to be paid for such services. If the actual timing of the performance of services or the level of effort varies from the original estimates, we will adjust the accrual accordingly. Payments associated with licensing agreements to acquire licenses to develop, use, manufacture and commercialize products that have not reached technological feasibility and do not have alternative future use are expensed as incurred. Payments made to third parties under these arrangements in advance of the performance of the related services by the third parties are recorded as prepaid expenses until the services are rendered.

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, 2021 and has not recorded an income tax benefit for the six months ended June 30, 2021 and 2020 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 June 30, 2021, 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, 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 award 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 restricted stock units ("RSUs"), the Company issues them in the form of Company common stock. The fair market value of these awards is based on the market closing price per share on the grant date. Prior to January 1, 2020, the Company only granted stock options. Beginning in 2020, for grants to employees, the Company granted a mix of stock options and RSUs.

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 and RSUs is that shares will be issued as new shares drawing on the Company's 2015 Omnibus Incentive Compensation Plan share pool that was adopted by the stockholders in November 2015.

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, stock options, and RSUs, 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 six months ended June 30, 2021 and 2020.

Leases

The Company determines if an arrangement is a lease at contract inception. Operating lease assets represent the Company's right to use an underlying asset for the lease term and operating lease liabilities represent the Company's obligation to make lease payments arising from the lease. When evaluating whether a contract contains a lease, the Company considers whether (1) the contract explicitly or implicitly identifies assets that are contractually defined and (2) the Company obtains substantially all of the economic benefits from the use of that underlying asset and directs how and for what purpose the asset is used during the term of the contract.

The Company's lease agreement contains lease and non-lease components. Non-lease components primarily include payments for maintenance and utilities. The Company has applied the practical expedient to combine fixed payments for non-lease components with lease payments and account for them together as a single lease component, which increases the amount of lease assets and corresponding liabilities. Payments under the Company's lease arrangement are primarily fixed, however variable payments, are expensed as incurred and not included in the operating lease asset and liability.

Operating lease assets and liabilities are recognized at the commencement date of the lease based upon the present value of lease payments over the lease term. When determining the lease term, the Company includes options to extend or terminate the lease when it is reasonably certain that the Company will exercise that option. The Company uses the implicit interest rate when readily determinable and uses the Company's incremental borrowing rate when the implicit rate is not readily determinable based upon the information available at the commencement date in determining the present value of the lease payments.

The Company's operating leases are reflected in the right-of-use operating asset; operating lease liability, current portion; and operating lease liability, long-term portion in the Company's consolidated balance sheets. Lease expense for minimum lease payments is recognized on a straight-line basis over the lease term. Short-term leases, defined as leases that have a lease term of 12 months or less at the commencement date, and do not include an option to extend the term or purchase the underlying asset that the Company is reasonably certain to exercise, are excluded from this treatment and are recognized on a straight-line basis over the term of the lease.

Recent Accounting Pronouncements

In December 2019, the FASB issued ASU 2019-12, Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes, enhances and simplifies various aspects of the income tax accounting guidance, including requirements such as tax basis step-up in goodwill obtained in a transaction that is not a business combination, ownership changes in investments, and interim-period accounting for enacted changes in tax law. ASU 2019-12 is effective for annual periods, and interim periods within those annual periods, beginning after December 15, 2020. Early adoption is permitted, including adoption in an interim period. The Company adopted this standard on January 1, 2021, and the standard did not have a significant impact on its consolidated financial statements.

In October 2020, the FASB issued ASU 2020-10, Codification Improvements, which clarifies various topics in the Accounting Standards Codification, including the addition of existing disclosure requirements to the relevant disclosure sections. The amendments in ASU 2020-10 do not change GAAP and, therefore, are not expected to result in a significant change in practice. ASU 2020-10 should be applied retrospectively to the beginning of the period that includes the adoption date. ASU 2020-10 is effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2020. The Company adopted this standard on January 1, 2021, and the standard did not have a significant impact on its consolidated financial statements.

Note 3. Accrued Expenses and Other Current Liabilities

At June 30, 2021 and December 31, 2020 accrued expenses and other current liabilities consisted of the following:

	June 30, 2021	December 31, 2020
Accrued research and development	$ 2,195,033	$ 4,293,522
Accrued compensation	3,034,669	2,870,261
Accrued general and administrative	4,551,879	1,155,508
Accrued interest	381,250	393,958
Total	$ 10,162,831	$ 8,713,249

Note 4. Loan and Security Agreement

Hercules Capital, Inc.

In September 2020, the Company entered into a Loan and Security Agreement (the "Loan Agreement") with Hercules Capital, Inc., in its capacity as administrative agent and collateral agent and as a lender (in such capacity, the "Agent" or "Hercules") and the other financial institutions that from time to time become parties to the Loan Agreement as lenders (collectively, the "Lenders"). The Loan Agreement provides for term loans in an aggregate principal amount of up to $225.0 million under multiple tranches (the "2020 Term Loan"). The tranches consist of (i) a first tranche consisting of term loans in an aggregate principal amount of $60.0 million, of which $50.0 million was funded to the Company on the Closing Date (the "First Advance"), and of which the remaining $10.0 million is available at the Company's option at any time through September 15, 2021; (ii) subject to the approval of the Company's AXS-05 product candidate for the treatment of major depressive disorder (the "First Milestone"), a second tranche consisting of additional term loans in an aggregate principal amount of up to $35.0 million, available at the Company's option beginning on the date that the First Milestone is achieved through the earlier of (A) 181 days following such date and (B) June 30, 2022; (iii) subject to the approval of the Company's AXS-07 product candidate for the treatment of migraine (the "Second Milestone"), a third tranche consisting of additional term loans in an aggregate principal amount of up to $20.0 million, available at the Company's option beginning on the date that the Second Milestone is achieved through the earlier of (A) 181 days following such date and (B) June 30, 2022; (iv) subject to the achievement of either the First Milestone or the Second Milestone and so long as the Company is in compliance with a required ratio of Lender indebtedness to net product revenue, a fourth tranche consisting of additional term loans in an aggregate principal amount of up to $60.0 million, available at the Company's option beginning on January 1, 2022 and continuing through March 31, 2023; and (v) subject to approval by the Lenders' in their discretion, a fifth tranche of additional term loans in an aggregate principal amount of up to $50.0 million, available through December 31, 2023. The Company intends to use the proceeds of the Term Loan Advances for working capital and general corporate purposes. In addition, approximately $21.7 million of the proceeds from the First Advance was used to satisfy in full and retire the Company's indebtedness under the 2019 Term Loan (as defined below), as amended.

The outstanding principal balance of the term loans bears interest at an annual rate equal to the greater of either (i) the prime rate as reported in *The Wall Street Journal* plus 5.90% or (ii) 9.15%, subject to an ability by the Company, during certain periods (each, a "PIK Deferral Period"), to request a reduction of the then-effective cash-pay interest rate by up to 1.00% per annum (the "Cash Interest Reduction Amount"). Accrued interest is payable monthly following the funding of each term loan. During each PIK Deferral Period, the term loans will bear cash-pay interest, at the reduced amount, and will accrue paid-in-kind interest at a rate equal to the Cash Interest Reduction Amount multiplied by 1.15, which amount will be capitalized and added to the outstanding principal balance of the term loans on each monthly interest payment date during the PIK Deferral Period.

The Company is required to repay the term loans in equal installments of principal and interest commencing on May 1, 2023 through October 1, 2025 (the "Maturity Date"). However, if either the First Milestone or the Second Milestone are achieved prior to May 1, 2023, and no default exists, the amortization commencement date will be automatically extended to November 1, 2023; if both the First Milestone and the Second Milestone are achieved prior to November 1, 2023, and no default exists, the amortization commencement date will be further automatically extended to May 1, 2024 and if any term loans are funded under the fourth tranche noted above prior to May 1, 2024, and no default exists, the amortization commencement date will be further automatically extended to November 1, 2024. On the Maturity Date, all unpaid term loans will be due and payable.

As collateral for the obligations, the Company has granted to Hercules a senior security interest in all of Company's right, title, and interest in, to and under all of Company's property, inclusive of intellectual property, which includes one of the Company's existing license agreements (the "License Agreement") with Antecip Bioventures II LLC ("Antecip"), an entity owned by Axsome's Chief Executive Officer and Chairman of the Board, Herriot Tabuteau, M.D., subject to limited exceptions. Antecip consented to the collateral assignment of the License Agreement, among other things, under a direct agreement (the "Direct Agreement") with the Company and Hercules.

The Loan Agreement contains customary representations, warranties and covenants, including covenants by the Company limiting additional indebtedness, liens (including a negative pledge on intellectual property and other assets), guaranties, mergers and consolidations, substantial asset sales, investments and loans, certain corporate changes, transactions with affiliates and fundamental changes. At the initial closing, there were no applicable financial covenants contained in the Loan Agreement. Only after additional amounts are drawn down by the Company in the future, if the Company decides to do so, under the terms set forth in the Loan Agreement, there will be certain limited financial covenants that will apply, including:

- Effective upon the date the outstanding principal amount of the advances under the Loan Agreement equals or exceeds $55.0 million, which has not yet occurred, the Company at all times thereafter must maintain cash in an account or accounts in which Hercules has a first priority security interest, in an aggregate amount greater than or equal to $15.0 million, plus the amount of the Company's accounts payable under U.S. GAAP not paid after the 180th day following the invoice for such account payable (such amount, the "Qualified Cash A/P Amount").
- Effective upon the later of (i) the last calendar month of the calendar quarter that is twelve months following the earlier of (x) the date that the First Milestone is achieved and (y) the date that the Second Milestone is achieved, or (ii) the date on which the outstanding principal amount of the term loan advances under the Loan Agreement is equal to or greater than $65.0 million, neither of which have occurred yet, the Company is required to (A) ensure that at all times its market capitalization exceeds $2.0 billion, and that it maintains cash in an account which Hercules has a first priority security interest in an amount not less than 65% of the sum of the outstanding principal amount of the term loan advances *plus* the Qualified Cash A/P Amount, (B) ensure that at all times that it maintains cash in an account which Hercules has a first priority security interest in an amount not less than 100% of the sum of the outstanding principal amount of the term loan advances *plus* the Qualified Cash A/P Amount, or (C) achieve at least 60% of the net product revenue per the board of directors approved forecast solely from the sale of AXS-05 and AXS-07 (which may include royalty, profit sharing, or sales-based milestone revenue recognized in accordance with GAAP, but will not include any upfront or non-sales-based milestone payments under business development or licensing transactions), measured on a trailing six-month basis as of the date of the Company's most recent quarterly financial statement, determined on a quarterly basis.
- Restrictions on the Company's ability to incur additional indebtedness, pay dividends, encumber its intellectual property, or engage in certain fundamental business transactions, such as mergers or acquisitions of other businesses, with certain exceptions.

The Company's obligations under the Loan Agreement are subject to acceleration upon the occurrence of specified events of default, including payment default, insolvency and a material adverse change in the Borrower's business, operations or financial or other condition.

In addition, the Company is required to pay a final payment fee equal to the greater of (A) $2,910,000 and (B) 4.85% of the aggregate amount of all term loan advances minus the aggregate amount of repayments made. The final payment fee is being accreted and amortized into interest expense using the effective interest rate method over the term of the loan.

The Company may, at its option prepay the term loans in full or in part, subject to a prepayment penalty equal to (i) 2.0% of the principal amount prepaid if the prepayment occurs prior to the first anniversary of the Closing Date, (ii) 1.5% of the principal amount prepaid if the prepayment occurs on or after the first anniversary and prior to the second anniversary of the Closing Date, and (iii) 1.0% of the principal amount prepaid if the prepayment occurs on or after the second anniversary and prior to the third anniversary of the Closing Date.

Silicon Valley Bank

In March 2019, the Company entered into a $24.0 million growth capital term loan facility (the "2019 Term Loan") with Silicon Valley Bank, or SVB and West River Innovation Lending Fund VIII, L.P., or WestRiver. In September 2020, the Company used a portion of the 2020 Term Loan to terminate and repay all amounts outstanding under the 2019 Term Loan and recorded a loss on extinguishment of the 2019 Term Loan.

Loan Interest Expense and Amortization

The Company incurred interest expense of $1,156,458 and $2,300,208 for the three and six months ended June 30, 2021 and 379,167 and 758,334 three and six months ended June 30, 2020, respectively. In addition, amortization of the final payment fee was $149,281 and $292,870 for the three and six months ended June 30, 2021 and $119,014 and $238,028 three and six months ended June 30, 2020, respectively.

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

	June 30, 2021	December 31, 2020
Total Outstanding Debt	$ 50,000,000	$ 50,000,000
Add: accreted liability of final payment fee	444,783	151,912
Less: unamortized debt discount, long-term	(1,562,184)	(1,830,064)
Less: current portion of long-term debt	—	—
Loan payable, long-term	$ 48,882,599	$ 48,321,848

In connection with the entry into the Hercules Term Loan, the Company issued to Hercules a warrant to purchase a number of shares of the Company's common stock equal to 2.5% of the aggregate amount of the Term Loan Advances that are funded. Further information on warrants issued related to this loan and prior debt financings and amendments are disclosed in Note 7 - Stockholders' Equity under the "Warrants" section.

Amortization of the debt discount in relation to warrants issued as described above was $132,508 and $267,882 for the three and six months ended June 30, 2021 and $59,998 and $118,636 for the three and six months ended June 30, 2020, respectively.

Scheduled Principal Payments on Outstanding Debt, as of June 30, 2021, are as follows:

2021	—
2022	—
2023	12,193,153
2024	19,761,468
2025	18,045,379
Total principal payments outstanding	$ 50,000,000

The Company was in compliance with all covenants and requirements of its financing arrangements as of and during the six months ended June 30, 2021.

Note 5. Net Loss per Common Share

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2021	2020	2021	2020
Basic and diluted net loss per common share:				
Net loss	$ (32,284,209)	$ (18,326,992)	$ (61,544,179)	$ (50,811,138)
Weighted average common shares outstanding—basic and diluted	37,595,069	37,100,770	37,512,716	37,081,064
Net loss per common share—basic and diluted	$ (0.86)	$ (0.49)	$ (1.64)	$ (1.37)

The following potentially dilutive securities outstanding at June 30, 2021 and 2020 have been excluded from the computation of diluted weighted average shares outstanding, as they would be anti-dilutive:

	June 30,	
	2021	2020
Stock options	4,461,985	3,979,607
Restricted stock units	309,126	150,143
Warrants	15,541	37,042
Total	4,786,652	4,166,792

Note 6. Commitments and Contingencies

Operating Leases

For the three and six months ended June 30, 2021, the Company had the following operating lease expense:

	Statement of Operations Location	Three Months Ended June 30, 2021	Three Months Ended June 30, 2020	Six Months Ended June 30, 2021	Six Months Ended June 30, 2020
Operating lease expense	General and administrative and Research and development	$ 286,923	$ —	$ 573,846	$ —
Total operating lease expense		$ 286,923	$ —	$ 573,846	$ —

Future minimum lease payments of the Company's operating leases as of June 30, 2021 were as follows:

2021	$ 575,000
2022	630,000
2023	—
2024	—
2025	—
Thereafter	—
Total lease payments	1,205,000
Less imputed interest	(34,296)
Present value of operating lease liabilities	$ 1,170,704

As of June 30, 2021, the remaining lease term for our operating lease was 1.1 years with a discount rate of 6.0%. The interest rate implicit in lease contracts is typically not readily determinable and as such, the Company uses its incremental borrowing rate based on the information available at the lease commencement date, which represents an internally developed rate that would be incurred to borrow, on a collateralized basis, over a similar term, an amount equal to the lease payments in a similar economic environment.

Note 7. Stockholders' Equity

Capital Structure

In May 2019, the Company entered into the May 2019 Sales Agreement with SVB Leerink, pursuant to which the Company may sell up to $50 million in shares of the Company's common stock from time to time through SVB Leerink, acting as the Company's sales agent, in one or more at-the-market offerings utilizing the 2016 Shelf Registration Statement. SVB Leerink is entitled to receive a commission of 3.0% of the gross proceeds for any shares sold under the May 2019 Sales Agreement. Due to expiration of the 2016 Shelf Registration Statement, at the Company's option, the shares that were unsold of approximately $29.9 million under the May 2019 Sales Agreement, may be rolled over to the December 2019 Sales Agreement (see below).

In December 2019, the Company entered into the December 2019 Sales Agreement with SVB Leerink, pursuant to which the Company may sell up to $80 million in shares of the Company's common stock from time to time through SVB Leerink, acting as the Company's sales agent, in one or more at-the-market offerings utilizing the 2019 Shelf Registration Statement. SVB Leerink is entitled to receive a commission of 3.0% of the gross proceeds for any shares sold under the December 2019 Sales Agreement. For the six months ended June 30, 2021, the Company received approximately $7.4 million in gross proceeds through the sale of 110,296 shares, of which net proceeds were approximately $7.2 million. For the six months ended June 30, 2020, the Company received approximately $12.4 million in gross proceeds through the sale of 141,678 shares, of which net proceeds were approximately $12.1 million.

In December 2019, the Company completed an underwritten public offering, whereby the Company sold 2,300,000 shares of our common stock at a public offering price of $87.00 per share. The Company received gross proceeds of approximately $200.1 million and net proceeds of approximately $187.1 million, net of underwriting discounts and offering expenses.

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.

Shelf Registration Statement

On December 5, 2019, the Company filed an automatic shelf registration statement ("2019 Shelf Registration") with the Securities and Exchange Commission ("SEC") for the issuance of common stock, preferred stock, warrants, rights, debt securities and units. It became effective upon filing with the SEC and is currently the Company's only active shelf registration. Through the date of this report, the Company has issued common stock of approximately $229.3 million pursuant to such shelf registration statement.

Under SEC rules, the 2019 Shelf Registration Statement allows for the potential future offer and sale by the Company, from time to time, in one or more public offerings, of an indeterminate amount of the Company's common stock, preferred stock, debt securities, and units at indeterminate prices. At the time any of the securities covered by the 2019 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 4,572,808 shares available for the issuance of stock options or stock-based awards under the Company's 2015 Omnibus Incentive Compensation Plan at June 30, 2021.

Stock Options

The following table sets forth the stock option activity for the six months ended June 30, 2021:

	Number of shares	Weighted average exercise price	Weighted average contractual term	Aggregate intrinsic value
Outstanding at December 31, 2020	3,725,648	$ 16.36		
Granted	955,213	66.05		
Exercised	(162,503)	17.67		
Forfeited	(55,727)	63.58		
Expired	(646)	87.76		
Outstanding at June 30, 2021	4,461,985	$ 26.35	7.3	$ 186,299,331
Vested and expected to vest at June 30, 2021	4,455,816	$ 26.38	7.3	$ 185,891,183
Exercisable at June 30, 2021	2,670,402	$ 13.19	5.8	$ 145,918,708

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 $48.74 per option for the six months ended June 30, 2021. As of June 30, 2021, there was $57.0 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 8,647 options outstanding as of June 30, 2021, which are performance-based and vest upon the achievement of certain corporate milestones. Stock-based compensation will be measured and recorded if and when it is probable that the milestone will occur.

Restricted Stock Units

In 2020, the Company began granting RSUs covering an equal number of its shares of common stock to employees. The fair value of RSUs is determined on the date of the grant based on the market price of its shares of common stock as of that date. The fair value of the RSUs is recognized as an expense ratably over the vesting period of four years. As of June 30, 2021, total compensation cost not yet recognized related to unvested RSUs was $11.5 million, which is expected to be recognized over a weighted-average period of 3.4 years.

The following table sets forth the RSU activity for the six months ended June 30, 2021:

	Number of shares	Weighted average grant date fair value
Outstanding at December 31, 2020	136,067	$ 36.82
Granted	182,187	49.92
Vested	(3,378)	47.54
Forfeited	(5,750)	71.48
Outstanding at June 30, 2021	309,126	$ 43.78

Stock-based compensation expense recognized for the three and six months ended June 30, 2021 and 2020 was allocated as follows:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2021	2020	2021	2020
Research and development	$ 2,302,504	$ 1,037,530	$ 3,836,899	$ 1,671,905
General and administrative	$ 3,153,738	3,110,495	5,350,440	4,609,650
Total	$ 5,456,242	$ 4,148,025	$ 9,187,339	$ 6,281,555

Warrants

The following table summarizes warrant activity for the six months ended June 30, 2021:

	Number of warrants	Weighted average exercise price
Outstanding at December 31, 2020	15,541	$ 80.43
Issued	—	—
Exercised	—	—
Outstanding at June 30, 2021	15,541	$ 80.43

Outstanding Warrants

In connection with the first advance of the 2020 Term Loan, Hercules Capital Inc. received warrants to purchase an aggregate 15,541 shares of the Company's common stock at an exercise price of $80.43 per share, which was the volume weighted average price of the Company's common stock over the ten-day trading period immediately preceding the initial closing, subject to certain limited adjustments as specified in the warrant. The warrants are exercisable for seven years from the date of issuance. The warrants were classified as a component of stockholders' equity. The relative fair value of the warrants of approximately $0.9 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.

Note 8. License Agreements

Exclusive License Agreement with Pfizer

In January 2020, the Company entered into an exclusive license agreement with Pfizer Inc. ("Pfizer") for Pfizer's clinical and nonclinical data, and intellectual property for reboxetine, the active pharmaceutical ingredient in AXS-12 which the Company is developing for the treatment of narcolepsy. The agreement also provides the Company exclusive rights to develop and commercialize esreboxetine, a new late-stage product candidate now referred to as AXS-14, in the U.S. for the treatment of fibromyalgia.

Under the terms of the agreement, Pfizer received 82,019 shares of the Company's common stock having a stated value of $8.0 million, based on the average closing price of the Company's common stock for the ten prior trading days of $97.54, in consideration for the license and rights and also received an upfront cash payment of $3.0 million. The Company determined that the fair value of each share of common stock granted to Pfizer on the closing date of January 9, 2020 was $87.24, based on the closing price of the Company's stock on that date. As a result, the fair value of the stock issued was $7.2 million and therefore, the total research and development expense recognized was $10.2 million related to the Pfizer license agreement during the six months ended June 30, 2020.

Pfizer can also receive up to $323 million in regulatory and sales milestones, and tiered mid-single to low double-digit royalties on future sales. Pfizer will also have a right of first negotiation on any potential future strategic transactions involving AXS-12 and AXS-14. During the three months ended June 30, 2021, no milestone payments or royalties were paid to Pfizer by the Company.

Exclusive License Agreements with Antecip

In 2012, the Company entered into three exclusive license agreements with Antecip, in which it was granted exclusive licenses to develop, manufacture, and commercialize Antecip's patents and applications related to the development of AXS-02, AXS-05, and AXS-04, a product candidate that is currently in early stage development, anywhere in the world for human therapeutic, veterinary, and diagnostic use. Pursuant to the agreements, the Company is 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, the Company is 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 the Company, its 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 the Company for convenience, the agreements shall remain in effect on a product-by-product and country-by-country basis until the later to occur of (i) the applicable product is no longer covered by a valid claim in that country or (ii) 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, the Company's 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 the Company exercises its right to terminate any of the agreements for convenience, the rights granted to the Company under such terminated agreement will revert to Antecip. To date, the Company has not been required to make any payments to Antecip under any of the license agreements.

In connection with the 2020 Term Loan, the Company entered into a Direct Agreement with Antecip pursuant to which Antecip consented to the collateral assignment of the License Agreement to Hercules, among other things.

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, 2020 which was *filed with the Securities and Exchange Commission, or SEC, on March 1, 2021*.

Overview

We are a biopharmaceutical company developing novel therapies for the management of central nervous system, or CNS, conditions that have 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 five CNS product candidates, AXS-05, AXS-07, AXS-09, AXS-12, and AXS-14 which are being developed for multiple indications. AXS-05 is being developed for the treatment of major depressive disorder, or MDD, for which we have completed a Phase 2 controlled trial and Phase 3 controlled trial, which we refer to as the ASCEND study and the GEMINI study, respectively, and a Phase 3 long-term open-label study, which we refer to as the COMET study. A New Drug Application, or NDA, has been submitted and accepted for filing for AXS-05 for the treatment of MDD. The FDA has set a Prescription Drug User Fee Act (PDUFA) target action date for the AXS-05 NDA of August 22, 2021. AXS-05 is also under development for the treatment of Alzheimer's disease agitation, or AD agitation. We have completed one Phase 2/3 controlled trial, which we refer to as the ADVANCE-1 study, for this indication. We are conducting a Phase 3 placebo-controlled, randomized withdrawal trial in AD agitation, which we refer to as the ACCORD study, and one open-label long-term safety study in AD agitation. AXS-05 is also being developed for smoking cessation and a Phase 2 trial in this indication has been completed. AXS-07 is being developed for the acute treatment of migraine, for which we have completed two Phase 3 controlled trials, which we refer to as the MOMENTUM study and the INTERCEPT study, and one Phase 3 long-term open-label trial, which we refer to as the MOVEMENT study. An NDA has been submitted for filing for AXS-07 for the acute treatment of migraine. AXS-09 is being developed for the treatment of CNS disorders. AXS-12 is being developed for the treatment of narcolepsy. We have completed a Phase 2 trial with AXS-12, which we refer to as the CONCERT study. A Phase 3 trial with AXS-12 in narcolepsy is planned. AXS-14 is being developed for the treatment of fibromyalgia. We plan to submit an NDA for AXS-14 in fourth quarter of 2022 for the management of fibromyalgia following a pre-NDA meeting with the FDA. 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 increase available treatment options and improve the lives of patients living with CNS disorders.

AXS-05 is a novel, oral, investigational NMDA, or N-methyl-D-aspartate, receptor antagonist with multimodal activity under development for the treatment of CNS disorders. AXS-05 consists of a proprietary formulation and dose of bupropion and dextromethorphan and utilizes our metabolic inhibition technology. The dextromethorphan component of AXS-05 is an uncompetitive NMDA, receptor antagonist, also known as a glutamate receptor modulator. The dextromethorphan 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 are seeking U.S. Food and Drug Administration, or FDA, approval for AXS-05 utilizing the 505(b)(2) regulatory development pathway. AXS-05 has been granted FDA Breakthrough Therapy designation for both the treatment of MDD and the treatment of Alzheimer's disease agitation, as well as Fast Track designations for the treatment of Alzheimer's disease agitation and treatment resistant depression.

We have completed two pivotal trials, one Phase 2 and one Phase 3, of AXS-05 in MDD, which we refer to as the ASCEND and GEMINI trials, respectively. AXS-05 achieved the primary endpoint in both the ASCEND and GEMINI trials. A Phase 3, open-label, long-term safety study with AXS-05 in patients with MDD and TRD known as the COMET trial has also been completed. Additionally, three Phase 2 open-label efficacy sub-studies of the COMET trial have been completed. These sub-studies evaluated the efficacy and safety of AXS-05 in three clinically pertinent MDD patient populations: the COMET-TRD trial in treatment resistant MDD (TRD), the COMET-AU trial in antidepressant unresponsive MDD, and the COMET-SI trial in MDD with suicidal ideation. In the overall COMET trial, AXS-05 treatment resulted in rapid, substantial, and durable improvement in depressive symptoms, measured using the MADRS, which was sustained or increased with long-term treatment. Additionally, AXS-05 was well tolerated with long-term dosing. Similar findings of rapid and durable improvements in depressive symptoms were demonstrated in the COMET-AU and COMET-TRD sub-studies. In the COMET-SI trial, a rapid reduction in suicidal ideation was observed with AXS-05 treatment, as demonstrated by reductions in the MADRS-SI score. We have completed a Phase 3 trial of AXS-05 in TRD, which we refer to as the STRIDE-1 trial, which met key secondary endpoints but did not reach statistical significance on the primary endpoint. Additionally, we have completed a Phase 2, double-blind, placebo-controlled, multi-center, relapse prevention study in patients with TRD, which we call the MERIT trial. In the MERIT trial, AXS-05 achieved its primary and secondary endpoints by delaying time to relapse and preventing relapse as compared to placebo. We have also completed a Phase 2/3 trial of AXS-05 in AD agitation, which we refer to as the ADVANCE-1 trial. AXS-05 achieved the primary endpoint in the ADVANCE-1 trial. We are conducting the ACCORD trial, a Phase 3, double blind, placebo-controlled, randomized withdrawal trial in patients with AD agitation, and one open-label long-term safety study in AD agitation. AXS-05 is also being developed as an aid to smoking cessation treatment and a positive Phase 2 trial in this indication has been completed under a research collaboration between us and Duke University. We have submitted a New Drug Application, or NDA, for AXS-05 for the treatment of MDD supported by the positive results from the ASCEND and GEMINI trials which has been accepted for filing by the FDA and has granted the application Priority Review resulting in a Prescription Drug User Fee Act (PDUFA) target action date of August 22, 2021.

AXS-07 is a novel, oral, rapidly absorbed, multi-mechanistic, investigational medicine under development for the acute treatment of migraine. AXS-07 consists of MoSEIC™, or Molecular Solubility Enhanced Inclusion Complex, meloxicam and rizatriptan. 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-$HT_{1B/1D}$ agonist that inhibits calcitonin gene-related peptide (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.

We have completed two Phase 3 trials of AXS-07 for the acute treatment of migraine, which we refer to as the MOMENTUM and INTERCEPT trials. AXS-07 achieved the co-primary endpoints in both the MOMENTUM and INTERCEPT trials. An NDA has been submitted for filing for AXS-07 for the acute treatment of migraine supported by the positive results from the MOMENTUM and INTERCEPT trials. An open-label, long-term, safety study of AXS-07 in patients with migraine known as the MOVEMENT trial has also been completed. In the MOVEMENT trial, administration of AXS-07 resulted in rapid, and substantial relief of migraine pain and associated symptoms and was well tolerated with long term dosing.

AXS-09 is an oral, investigational NMDA receptor antagonist with multimodal activity consisting of esbupropion and dextromethorphan, 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 dextromethorphan 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 the treatment of narcolepsy. AXS-12 is a highly selective and potent norepinephrine reuptake inhibitor. AXS-12 has been granted FDA Orphan Drug Designation for the treatment of narcolepsy. We have completed a Phase 2 trial with AXS-12, which we refer to as the CONCERT trial. AXS-12 achieved the primary endpoint in the CONCERT trial. We plan to initiate a Phase 3 trial with AXS-12 in narcolepsy in the third quarter of 2021.

AXS-14, esreboxetine, is a novel, oral, investigational medicine in development for the treatment of fibromyalgia. AXS-14 is a highly selective and potent norepinephrine reuptake inhibitor. We are initially developing esreboxetine for the treatment of fibromyalgia. Esreboxetine, the SS-enantiomer of reboxetine, is more potent and selective than racemic reboxetine. We have in-licensed data from Pfizer which includes a completed Phase 2 trial and Phase 3 trial in fibromyalgia, both of which were positive. We plan to submit an NDA for AXS-14 in the fourth quarter of 2022 for the management of fibromyalgia.

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 $61.5 million and $50.8 million for the six months ended June 30, 2021 and 2020, respectively. Our accumulated deficit as of June 30, 2021 was $340.3 million, and we expect to incur significant expenses and increasing operating losses for the foreseeable future. We expect to continue to incur expenses in connection with the development of our product candidates, including with respect to conducting clinical trials and seeking regulatory approval for our current product candidates and any other product candidates that we develop or in-license and advance to clinical development. In preparation for obtaining regulatory approval for our product candidates, we expect to incur significant expenses in order to create an infrastructure and market readiness 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 and/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

AXS-05

In April 2021, we announced that the FDA has accepted for filing the NDA for AXS-05 for the treatment of MDD, and has granted the application Priority Review resulting in a PDUFA target action date of August 22, 2021.

In August 2021, we announced that AXS-05 achieved primary and key secondary endpoints in the MERIT Phase 2 Trial in treatment resistant depression.

AXS-07

In June 2021, we submitted an NDA for filing for AXS-07 for the acute treatment of migraine.

AXS-12

In July 2021, we announced that we were notified by the FDA that the FDA has rescinded our Breakthrough Therapy Designation for our AXS-12 product candidate for the treatment of cataplexy in narcolepsy, due to the FDA approving an additional drug product for the treatment of cataplexy in narcolepsy subsequent to granting AXS-12 Breakthrough Therapy Designation.

AXS-14

In June 2021, we announced that we plan to submit an NDA for AXS-14 for the management of fibromyalgia following a pre-NDA meeting with the U.S. Food and Drug Administration.

Financial Overview

Revenue

We have not generated any revenue and have incurred significant operating losses since inception, and we do not expect to generate any revenue from the sale of any products unless or until we obtain regulatory approval. 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. If we enter into licensing or collaboration arrangements, such agreements may generate revenue in the future.

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 have and will incur substantial costs beyond our present and planned clinical trials in order to file a new drug application, or 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 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.

The following table summarizes our research and development expenses for our primary programs for the three and six months ended June 30, 2021 and 2020:

	Three Months Ended June 30,		Six months ended June 30,	
	2021	2020	2021	2020
AXS-05	$ 2,184,776	$ 5,257,477	$ 12,228,922	$ 14,575,299
AXS-07	7,290,067	2,920,493	9,821,616	8,930,771
AXS-12	819,569	153,901	1,553,427	5,710,963
AXS-14	4,039	—	4,039	5,077,669
Other research and development	1,902,371	1,173,556	3,654,111	2,097,750
Stock-based compensation	2,302,504	1,037,530	3,836,899	1,671,905
Total research and development expenses	$ 14,503,326	$ 10,542,957	$ 31,099,014	$ 38,064,357

Other research and development expenses primarily consist of employee salaries and benefits, facilities, and overhead costs.

General and Administrative Expenses

General and administrative expenses primarily consist of salaries and related costs for personnel in executive, commercial, finance, and operational functions, including stock based compensation and travel expenses. Also included in general and administrative expenses are pre-commercialization costs, facility-related costs, insurance expense, 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) income

Interest and amortization of debt discount (expense) income primarily consists of cash interest and non-cash costs related to our term loans (see "Liquidity and Capital Resources" below for a further discussion). We amortize these costs over the term of our debt agreements as interest expense in our consolidated statement of operations. Interest and amortization of debt discount (expense) income also includes interest income earned on cash.

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.

There have been no material changes to our critical accounting policies since the beginning of our fiscal year. Our critical accounting policies are described in "Management's Discussion and Analysis of Financial Condition and Results of Operations" included in our Annual Report on Form 10-K for the year ended December 31, 2020 and in the notes to the condensed consolidated financial statements appearing elsewhere in this Quarterly Report on Form 10-Q.

Results of Operations

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

	Three Months Ended June 30,		Six months ended June 30,	
	2021	2020	2021	2020
Operating expenses:				
Research and development	$ 14,503,326	$ 10,542,957	$ 31,099,014	$ 38,064,357
General and administrative	16,344,361	7,235,877	27,592,734	12,205,934
Total operating expenses	30,847,687	17,778,834	58,691,748	50,270,291
Loss from operations	(30,847,687)	(17,778,834)	(58,691,748)	(50,270,291)
Interest and amortization of debt discount (expense) income	(1,436,522)	(548,158)	(2,852,431)	(540,847)
Net loss	$ (32,284,209)	$ (18,326,992)	$ (61,544,179)	$ (50,811,138)

Comparison of the three months ended June 30, 2021 and 2020

Research and Development Expenses. Our research and development expenses for the three months ended June 30, 2021 were $14.5 million, compared to $10.5 million for the three months ended June 30, 2020, an increase of $4.0 million. The increase was driven by costs to support the NDA filings and personnel expense which includes an increase in headcount along with an increase in stock compensation expense.

General and Administrative Expenses. Our general and administrative expenses for the three months ended June 30, 2021 were $16.3 million, compared to $7.2 million for the three months ended June 30, 2020, an increase of $9.1 million. The increase was primarily due to pre-commercial activities and personnel expense which includes an increase in headcount along with an increase in stock compensation expense.

Interest and amortization of debt discount (expense) income. Interest and amortization of debt discount expense for the three months ended June 30, 2021 was $1.4 million, compared to $0.5 million for the three months ended June 30, 2020, an increase of $0.9 million. The change is mainly due to a higher outstanding principal amount on our debt in 2021 as compared to the comparable period in 2020.

Comparison of the six months ended June 30, 2021 and 2020

Research and Development Expenses. Our research and development expenses for the six months ended June 30, 2021 were $31.1 million, compared to $38.1 million for the six months ended June 30, 2020, a decrease of $7.0 million. The decrease was driven by a one-time charge of $10.2 million for the Pfizer license agreement in the comparable period in 2020, offset by costs to support the NDA filings.

General and Administrative Expenses. Our general and administrative expenses for the six months ended June 30, 2021 were $27.6 million, compared to $12.2 million for the six months ended June 30, 2020, an increase of $15.4 million. The increase was primarily due to pre-commercial activities and personnel expense which includes an increase in headcount along with an increase in stock compensation expense.

Interest and amortization of debt discount (expense) income. Interest and amortization of debt discount expense for the six months ended June 30, 2021 was $2.9 million, compared to $0.5 million for the six months ended June 30, 2020, an increase of $2.4 million. The change is mainly due to a higher outstanding principal amount on our debt in 2021 as compared to the comparable period in 2020.

Liquidity and Capital Resources

Since our inception through June 30, 2021, we have financed our operations primarily through proceeds from equity offerings and debt borrowings. See discussion below.

In November 2015, we completed our IPO, in which we sold 5,666,667 shares of common stock at an offering price to the public of $9.00 per share. We received gross proceeds of approximately $51.0 million and net proceeds of approximately $45.5 million, after deducting underwriting discounts and commissions and offering-related transaction costs.

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 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 loan and security agreement with SVB to provide an additional $4 million growth capital loan, related to our narcolepsy clinical program with AXS-12. We refer to this amendment as the First Amendment to the Original Term Loan. The additional capital was available to be drawn, at our option, subject to the achievement of a specified clinical milestone. Our obligations under the loan and security agreement, as amended, along with our ability to draw down on the additional $4.0 million tranche, were subsequently extinguished in connection with the establishment of a new term loan facility with SVB during March 2019 (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, completed a registered direct offering priced at the market in December 2017 and September 2018, entered into a sales agreement in May 2019 pursuant to which we sold shares of our common stock from time to time in an at-the-market offering each utilizing the 2016 Shelf Registration Statement. The 2016 Shelf Registration expired in December 2019.

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 Sales Agreement, with Leerink Partners LLC, or now known as SVB Leerink, pursuant to which we could sell up to $30 million in shares of our common stock from time to time through SVB Leerink, acting as our sales agent, in one or more at-the-market offerings. In January 2019, we raised approximately $25.8 million in gross proceeds through the sale of 3,164,015 shares under the Sales Agreement. Upon completion of this final sale, the Sales Agreement was automatically terminated. SVB Leerink received a commission of 3.0% of the gross proceeds for all shares sold under the Sales Agreement.

In December 2017, we completed a registered direct offering priced at the market, 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 offering for gross proceeds of approximately $9.5 million and net proceeds of approximately $8.8 million, net of underwriting discounts 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.

In September 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 a loan and security agreement, the 2019 Term Loan with SVB and WestRiver, for a term loan up to $24.0 million. The initial tranche of $20.0 million was funded shortly after executing the loan agreement. The second tranche of $4.0 million was 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 then ongoing Phase 2 clinical trial for AXS-12 in narcolepsy, sufficient to submit a Phase 3 protocol to FDA, provided that we had not received any objections from the FDA within thirty days after submission of such Phase 3 protocol A portion of the initial tranche was used to satisfy our existing obligations under our November 2016 term loan facility with SVB, as amended in November 2018, and such obligations are considered fully repaid and extinguished. In September 2020, we terminated and repaid all amounts outstanding under 2019 Term Loan in connection with our entry into the Loan Agreement (see below).

In May 2019, we entered into the May 2019 Sales Agreement with SVB Leerink, pursuant to which we may sell up to $50 million in shares of our common stock from time to time through SVB Leerink, acting as our sales agent, in one or more at-the-market offerings utilizing the 2016 Shelf Registration Statement. SVB Leerink is entitled to receive a commission of 3.0% of the gross proceeds for any shares sold under the May 2019 Sales Agreement. Due to expiration of the 2016 Shelf Registration Statement, the shares that were unsold under the May 2019 Sales Agreement, were rolled over to the December 2019 Sales Agreement (see below).

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 could have been 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.

On December 5, 2019, we filed an automatic shelf registration statement with the SEC for the issuance of common stock, preferred stock, warrants, rights, debt securities and units up to an unlimited amount, which we refer to as the 2019 Shelf Registration Statement. It was declared effective by the SEC upon filing. As discussed in greater detail below, we entered into a sales agreement in December 2019 pursuant to which we sold shares of our common stock from time to time in an at-the-market offering and completed an offering of common stock in December 2019, each utilizing the 2019 Shelf Registration Statement. In the future, we may conduct additional offerings of one or more of these securities utilizing the 2019 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 2019 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 December 2019, we entered into the December 2019 Sales Agreement with SVB Leerink, pursuant to which we may sell up to $80 million in shares of our common stock from time to time through SVB Leerink, acting as our sales agent, in one or more at-the-market offerings utilizing the 2019 Shelf Registration Statement. SVB Leerink is entitled to receive a commission of 3.0% of the gross proceeds for any shares sold under the December 2019 Sales Agreement. For the six months ended June 30, 2021, we received approximately $7.4 million in gross proceeds through the sale of 110,296 shares, of which net proceeds were approximately $7.2 million. For the year ended December 31, 2020, we received approximately $14.6 million in gross proceeds through the sale of 167,243 shares, of which net proceeds were approximately $14.1 million. For the year ended December 31, 2019, we received approximately $7.3 million in gross proceeds through the sale of 89,390 shares, of which net proceeds were approximately $7.1 million.

In September 2020, we entered into the Loan Agreement with Hercules for the 2020 Term Loan, which consists of several tranches in an aggregate amount of up to $225.0 million. The first tranche consists of term loans in the amount of $60.0 million, of which $50.0 million was funded shortly after executing the Loan Agreement and the remaining $10.0 million is available at our option at any time through September 15, 2021. A portion of the initial tranche was used to repay the 2019 Term Loan along with associated final payment fees. The remaining $115 million may be drawn at our option, in three separate tranches, as described below under “Contractual Obligations - September 2020 Loan and Security Agreement – Hercules.” An additional $50 million is available, subject to the approval of Hercules, to support future strategic initiatives, including further pipeline advancement or expansion. The 2020 Term Loan bears interest at a calculated prime-based variable rate currently at 9.15%. It matures in October 2025 and has an initial interest-only payment period of 30 months, which may be extended to up to 48 months upon the drawing of future tranches.

In the future, we may conduct additional offerings of one or more of the securities covered by the 2019 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 2019 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.

We believe our current cash, along with the committed capital from the term loan facility, will be sufficient to fund our anticipated operations, based on our current operating plans which includes costs for the commercial launch of AXS-05 in MDD

and AXS-07 in migraine into at least 2024. Because the process of commercializing products and 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:

	Six Months Ended June 30,	
	2021	**2020**
Net cash (used in) provided by:		
Operating activities	$ (52,609,042)	$ (42,168,466)
Investing activities	(48,872)	(10,759)
Financing activities	10,000,551	12,895,167
Net increase (decrease) in cash	$ (42,657,363)	$ (29,284,058)

Operating Activities. Cash used in operating activities for the six months ended June 30, 2021 was $52.6 million as compared to $42.2 million for the six months ended June 30, 2020. The increase of $10.4 million in net cash used was mainly due the build-out of the commercial function and related commercialization costs.

Investing Activities. Cash used in investing activities for the purchase of property and equipment was less than $0.1 million for the six months ended June 30, 2021 and 2020.

Financing Activities. Cash provided by financing activities was $10.0 million for the six months ended June 30, 2021, which included net proceeds from the sale of common stock through our Sales Agreement with Leerink of $7.2 million and proceeds from the issuance of common stock upon exercise of employee stock options of $2.9 million, offset by cash paid out related to tax withholdings on stock awards of $0.08 million. Cash provided by financing activities was $12.9 million for the six months ended June 30, 2020, which included net proceeds from the sale of common stock through our Sales Agreement with Leerink of $12.1 million and proceeds from the issuance of common stock upon exercise of employee stock options of $0.8 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 may need to raise additional financing in the future to fund our operations. In the event that we need additional financing, we may incur additional 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 agreement with Pfizer

In January 2020, we entered into a license agreement with Pfizer. Under the terms of our exclusive license agreement with Pfizer, Pfizer received 82,019 shares of our common stock having a stated value of $8.0 million, based on the average closing price of our common stock for the ten prior trading days of $97.54, in consideration for the license and rights. Pfizer also received an upfront cash payment of $3.0 million. We determined that the fair value of each share of common stock granted to Pfizer on the closing date of January 9, 2020 was $87.24, based on the closing price of our common stock on that date. As a result, the fair value of the stock issued was $7.2 million.

Pfizer can also receive up to $323 million upon the achievement of certain regulatory and sales milestones, and tiered mid-single to low double-digit royalties on future sales. Pfizer will also have a right of first negotiation on any potential future strategic transactions involving AXS-12 and AXS-14.

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.

In connection with the 2020 Term Loan, Antecip consented to the collateral assignment of one of the license agreements, among other things, under a direct agreement with us and Hercules.

September 2020 Loan and Security Agreement – Hercules

In September 2020, we entered into the Loan Agreement with Hercules, in its capacity as administrative agent and collateral agent and as a lender, and the other financial institutions that may from time to time become parties to the Loan Agreement as lenders, which we collectively refer to as the Lenders. The Loan Agreement provides for term loans in an aggregate principal amount of up to $225.0 million under multiple tranches. The tranches consist of (i) a first tranche consisting of term loans in an aggregate principal amount of $60.0 million, of which $50.0 million, or the First Advance, was funded at closing, and of which the remaining $10.0 million is available at our option at any time through September 15, 2021; (ii) subject to the FDA approval of our AXS-05 product candidate for the treatment of major depressive disorder, or the First Milestone, a second tranche consisting of additional term loans in an aggregate principal amount of up to $35.0 million, available at our option beginning on the date that the First Milestone is achieved through the earlier of (A) 181 days following such date and (B) June 30, 2022; (iii) subject to the approval of our AXS-07 product candidate for the treatment of migraine, or the Second Milestone, a third tranche consisting of additional term loans in an aggregate principal amount of up to $20.0 million, available at our option beginning on the date that the Second Milestone is achieved through the earlier of (A) 181 days following such date and (B) June 30, 2022; (iv) subject to the achievement of either the First Milestone or the Second Milestone and so long as we are in compliance with a required ratio of Lender indebtedness to net product revenue, a fourth tranche consisting of additional term loans in an aggregate principal amount of up to $60.0 million, available at our option beginning on January 1, 2022 and continuing through March 31, 2023; and (v) subject to approval by the Lenders in their discretion, a fifth tranche of additional term loans in an aggregate principal amount of up to $50.0 million, available through December 31, 2023. We intend to use the proceeds of the Term Loan Advances for working capital and general corporate purposes. In addition, approximately $21.7 million of the proceeds from the First Advance was used to satisfy in full and retire our indebtedness under the 2019 Term Loan, as amended.

The outstanding principal balance of the term loans bears interest at an annual rate equal to the greater of either (i) the prime rate as reported in The Wall Street Journal plus 5.90% or (ii) 9.15%, subject to an ability by us, during certain periods, each such period a PIK Deferral Period, to request a reduction of the then-effective cash-pay interest rate by up to 1.00% per annum, which we refer to as the Cash Interest Reduction Amount. Accrued interest is payable monthly following the funding of each term loan. During each PIK Deferral Period, the term loans will bear cash-pay interest, at the reduced amount, and will accrue paid-in-kind interest at a rate equal to the Cash Interest Reduction Amount multiplied by 1.15, which amount will be capitalized and added to the outstanding principal balance of the term loans on each monthly interest payment date during the PIK Deferral Period. We are required to repay the term loans in equal installments of principal and interest commencing on May 1, 2023 through October 1, 2025, which is the Maturity Date. However, if either the First Milestone or the Second Milestone are achieved prior to May 1, 2023, and no default exists, the amortization commencement date will be automatically extended to November 1, 2023; if both the First Milestone and the Second Milestone are achieved prior to November 1, 2023, and no default exists, the amortization commencement date will be further automatically extended to May 1, 2024 and if any term loans are funded under the fourth tranche noted above prior to May 1, 2024, and no default exists, the amortization commencement date will be further automatically extended to November 1, 2024. On the Maturity Date, all unpaid term loans will be due and payable.

As collateral for the obligations, we have granted to Hercules a senior security interest in all our right, title, and interest in, to and under all of our property, inclusive of intellectual property, which includes one of our existing license agreements with Antecip, subject to limited exceptions. Antecip consented to the collateral assignment of the License Agreement, among other things, under a Direct Agreement with us and Hercules.

The Loan Agreement contains customary representations, warranties and covenants, including covenants by us limiting additional indebtedness, liens (including a negative pledge on intellectual property and other assets), guaranties, mergers and consolidations, substantial asset sales, investments and loans, certain corporate changes, transactions with affiliates and fundamental changes. At the initial closing, there were no applicable financial covenants contained in the Loan Agreement. Only after additional amounts are drawn down by us in the future, if we decide to do so, under the terms set forth in the Loan Agreement, there will be certain limited financial covenants that will apply, including:

- Effective upon the date the outstanding principal amount of the advances under the Loan Agreement equals or exceeds $55.0 million, which has not yet occurred, we at all times thereafter must maintain cash in an account or accounts in which Hercules has a first priority security interest, in an aggregate amount greater than or equal to $15.0 million, plus the amount of our accounts payable under U.S. GAAP not paid after the 180th day following the invoice for such account payable which amount we refer to as the Qualified Cash A/P Amount.

- Effective upon the later of (i) the last calendar month of the calendar quarter that is twelve months following the earlier of (x) the date that the First Milestone is achieved and (y) the date that the Second Milestone is achieved, or (ii) the date on which the outstanding principal amount of the term loan advances under the Loan Agreement is equal to or greater than $65.0 million, neither of which have occurred yet, we are required to (A) ensure that at all times its market capitalization exceeds $2.0 billion, and that it maintains cash in an account which Hercules has a first priority security interest in an amount not less than 65% of the sum of the outstanding principal amount of the term loan advances plus the Qualified Cash A/P Amount, (B) ensure that at all times that it maintains cash in an account which Hercules has a first priority security interest in an amount not less than 100% of the sum of the outstanding principal amount of the term loan advances plus the Qualified Cash A/P Amount, or (C) achieve at least 60% of the net product revenue per the board of directors approved forecast solely from the sale of AXS-05 and AXS-07 (which may include royalty, profit sharing, or sales-based milestone revenue recognized in accordance with GAAP, but will not include any upfront or non-sales-based milestone payments under business development or licensing transactions), measured on a trailing six-month basis as of the date of our most recent quarterly financial statement, determined on a quarterly basis.

- Restrictions on our ability to incur additional indebtedness, pay dividends, encumber its intellectual property, or engage in certain fundamental business transactions, such as mergers or acquisitions of other businesses, with certain exceptions.

Our obligations under the Loan Agreement are subject to acceleration upon the occurrence of specified events of default, including payment default, insolvency and a material adverse change in our business, operations or financial or other condition.

In addition, we are required to pay a final payment fee equal to the greater of (A) $2,910,000 and (B) 4.85% of the aggregate amount of all term loan advances minus the aggregate amount of repayments made. The final payment fee is being accreted and amortized into interest expense using the effective interest rate method over the term of the loan.

We may, at our option prepay the term loans in full or in part, subject to a prepayment penalty equal to (i) 2.0% of the principal amount prepaid if the prepayment occurs prior to the first anniversary of the initial closing, (ii) 1.5% of the principal amount prepaid if the prepayment occurs on or after the first anniversary and prior to the second anniversary of the initial closing, and (iii) 1.0% of the principal amount prepaid if the prepayment occurs on or after the second anniversary and prior to the third anniversary of the initial closing.

Employees and Human Capital Management

As of August 2. 2021, we had 93 full-time employees. None of our employees is represented by a collective bargaining agreement and we have never experienced any work stoppage. We believe that we maintain good relations with our employees. Our employees are highly skilled, and many hold advanced degrees. Most of our employees have experience with drug development. Our future performance depends significantly upon the continued service of our key scientific, technical and senior management personnel and our continued ability to attract and retain highly skilled employees. We provide our employees with competitive salaries and bonuses, opportunities for equity ownership, development programs that enable continued learning and growth and a robust employment package that promotes well-being across all aspects of their lives. In addition to salaries, these programs include potential annual discretionary bonuses, stock awards, healthcare and insurance benefits, health savings and flexible spending accounts, paid time off, family leave, and flexible work schedules, among other benefits. We have taken proactive steps throughout the COVID-19 pandemic to protect the health and safety of our employees. We expect to continue to implement these measures until we determine that the COVID-19 pandemic is adequately contained for purposes of our business. We may take further actions, in compliance with all appropriate government regulations, that we determine to be in the best interest of our employees.

Impact of the CARES Act

On March 27, 2020, the Coronavirus Aid, Relief, and Economic Security Act (the “CARES Act”) was enacted and signed into law, and GAAP requires recognition of the tax effects of new legislation during the reporting period that includes the enactment date. The CARES Act, among other things, includes changes to the tax provisions that benefits business entities and makes certain technical corrections to the 2017 Tax Cuts and Jobs Act, including, permitting net operating losses (“NOLs”), carryovers and carrybacks to offset 100% of taxable income for taxable years beginning before 2021. In addition, the CARES Act allows NOLs incurred in 2018, 2019, and 2020 to be carried back to each of the five preceding taxable years to generate a refund of previously paid income taxes. The CARES Act provides other reliefs and stimulus measures. We have evaluated the impact of the CARES Act, however, at present we do not expect that any provision of the CARES Act would result in a material cash benefit to us or have a material impact on our financial statements or internal controls over financial reporting.

Impact of COVID-19 on our Business

In December 2019, a novel coronavirus known as SARS-CoV-2 was first detected in Wuhan, Hubei Province, People's Republic of China, causing outbreaks of the coronavirus disease, known as COVID-19, that has now spread globally. On January 30, 2020, the World Health Organization (WHO) declared COVID-19 a public health emergency. The Secretary of Health and Human Services declared a public health emergency in the United States on January 31, 2020, under section 319 of the Public Health Service Act (42 U.S.C. 247d), in response to the COVID-19 outbreak. On March 11, 2020, the WHO declared COVID-19 a pandemic.

Operations and Liquidity

The full impact of the COVID-19 pandemic is unknown and rapidly evolving. While the potential economic impact brought by and over the duration of the COVID-19 pandemic may be difficult to assess or predict, the COVID-19 pandemic has resulted in significant disruption of global financial markets, which could in the future negatively affect our liquidity. In addition, a recession or market volatility resulting from the COVID-19 pandemic could affect our business. We have taken proactive, aggressive action throughout the COVID-19 pandemic to protect the health and safety of our employees, and expect to continue to implement these measures until we determine that the COVID-19 pandemic is adequately contained for purposes of our business. We may take further actions as government authorities require or recommend or as we determine to be in the best interests of our employees. To date, the COVID-19 pandemic has not had significant effects on the progression of our clinical trials. Given the nature and type of our short-term investments, we do not believe that the COVID-19 pandemic will have a material impact on our current investment liquidity.

Outlook

Although there is uncertainty related to the anticipated impact of the COVID-19 pandemic on our future results, we believe our current cash reserves, coupled with our access to additional capital through the December 2019 Sales Agreement and the Hercules Loan Agreement, leave us well-positioned to manage our business through this crisis as it continues to unfold. However, the impacts of the COVID-19 pandemic are broad-reaching and continuing and the financial impacts associated with the COVID-19 pandemic are still uncertain.

As a result of the ongoing COVID-19 pandemic and its dynamic nature, including uncertainties relating to the ultimate geographic spread of the virus, the severity of the disease, the duration of the pandemic, and actions that have been or may be taken by governmental authorities to contain the pandemic or to treat its impact, it is difficult to forecast the effects of the COVID-19 pandemic on our results for the fiscal year ending December 31, 2021.

Despite the economic uncertainty resulting from the COVID-19 pandemic, we intend to continue to focus on the development of our product candidates. We continue to monitor the rapidly evolving situation and guidance from international and domestic authorities, including federal, state and local public health authorities and we may take additional actions based on their recommendations. In these circumstances, there may be developments outside of our control requiring us to adjust our operating plan. As such, given the dynamic nature of this situation, we cannot reasonably estimate the impacts of the COVID-19 pandemic on our financial condition, results of operations or cash flows in the future.

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 $141.2 million and $183.9 million as of June 30, 2021 and December 31, 2020, 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 and debt agreement, we do not believe an immediate 100 basis point 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 June 30, 2021 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 three months ended June 30, 2021.

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. In the fourth quarter of 2020, we began the implementation of a new Enterprise Resource Planning system, or ERP system, which will replace our existing core financial systems. The ERP system is designed to accurately maintain our financial records, enhance the flow of financial information, improve data management and user access security, and provide timely information to our management team. Changes to our general ledger and consolidated financial reporting are expected to take place in the second half of 2021. As the phased implementation of the new ERP system progresses, we may change our processes and procedures which, in turn, could result in changes to our internal control over financial reporting. As such changes occur, we will evaluate quarterly whether such changes materially affect our internal control over financial reporting.

As of this reporting period, 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.

Risk Factors Summary

Our business is subject to a number of risks and uncertainties, including those risks discussed at length below. These risks include, among others, the following:

- ***We have incurred significant losses since our inception, anticipate that we will incur substantial losses for the foreseeable future, and may never achieve or maintain profitability.***
- ***We may 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.***
- ***Our operating activities may be restricted as a result of covenants related to the outstanding indebtedness under our loan and security agreement with Hercules 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.***
- ***We have a limited operating history and no history of commercializing products, which may make it difficult to evaluate our business and prospects.***
- ***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.***
- ***If safety and efficacy data for our product candidates, a reference 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 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.***
- ***Although Breakthrough Therapy, Fast Track, and other designations are designed to expedite the development and review of drugs, Breakthrough Therapy designation by the FDA for AXS-05 for the treatment of MDD and for the treatment of AD agitation, for example, may not ultimately lead to a faster development or regulatory review or approval process, and it will not increase the likelihood that these product candidates will receive marketing approval.***
- ***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.***
- ***Even if we obtain FDA approval of an NDA for our product candidates, if we are unable to establish effective marketing, sales and distribution capabilities or enter into agreements with third parties to market, sell and distribute our product candidates, if they are approved, we may be unable to generate product revenues.***

- ***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 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.***

- ***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.***

- ***Our business operations, financial condition, results of operations and cash flows may be adversely affected by the effects of health epidemics, pandemics, or outbreaks of infectious diseases, including the recent COVID-19 pandemic.***

- ***As an NDA applicant (and if an NDA is approved) and as a potential commercial "virtual manufacturer," we may rely in many cases 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 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.***

- ***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.***

- ***We have licensed and may need to license certain intellectual property from third parties in the future, such licenses may not be available or may not be available on commercially reasonable terms, and if the licenses are terminated for any reason our business may be materially harmed.***

- ***If we fail to comply with federal state, and foreign healthcare laws, including fraud and abuse and transparency 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.***

- ***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.***

- ***We will need to significantly increase the size of our organization, and we may experience difficulties in managing growth. If we are unable to implement appropriate controls and procedures to manage our growth, we will not be able to implement our business plan successfully.***

- ***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.***

- ***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.***

- ***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.***

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

RISKS RELATED TO OUR FINANCIAL CONDITION AND CAPITAL REQUIREMENTS

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

We are a 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, AXS-12, and AXS-14, which we refer to herein as our product candidates, with the goal of achieving regulatory approval and commercialization. Since inception, we have incurred significant operating losses. Our net losses were $61.5 million for the six months ended June 30, 2021 and $102.9 for the year ended December 31, 2020. As of June 30, 2021, we had an accumulated deficit of $340.3 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 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:

- seek regulatory approval for any product candidates that successfully complete late-stage clinical trials;
- hire additional commercial, clinical, medical, quality control, and scientific personnel;
- add operational, financial, and management information systems and personnel, including personnel to support our product candidate development and planned future commercialization efforts;
- further establish a sales, marketing, and distribution infrastructure, and expand external manufacturing capabilities and production to commercialize any products for which we may obtain regulatory approval and that we choose not to license to a third-party;
- undertake additional manufacturing activities of our product candidates to satisfy FDA requirements for marketing application submissions;
- continue to conduct our Phase 3 clinical trial with AXS-05 in AD agitation;
- conduct our planned Phase 3 clinical trial with AXS-12 in narcolepsy;
- continue to evaluate, plan for, and conduct, clinical trials for AXS-05 as an aid to smoking cessation treatment and AXS-09 for the treatment of CNS disorders;
- continue to evaluate, plan for, and submit an NDA for AXS-14 in fibromyalgia;
- develop, in-license, or acquire additional product candidates;
- conduct late-stage clinical trials for any product candidates that successfully complete early-stage clinical trials;
- conduct additional non-clinical studies with any product candidates;
- conduct clinical studies with any additional product candidates;
- require larger quantities of product; and
- maintain, expand, and protect our intellectual property portfolio.

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 may 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 along with the committed capital from the term loan facility will be sufficient to fund our anticipated operating cash requirements into at least 2024. 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 clinical and 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 (or having manufactured by third parties) 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 and security agreement with Hercules 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 September 2020, we entered into a Loan and Security Agreement, or the Loan Agreement, for a term loan of up to $225.0 million, which we refer to as the 2020 Term Loan, with Hercules Capital, Inc., or Hercules, in its capacity as administrative agent and collateral agent and as a lender, and the other financial institutions that from time to time become parties to the Loan Agreement, collectively referred to as the Lenders, secured by a lien on substantially all of our assets, including intellectual property. The Loan and Agreement contains various covenants that limit our ability to engage in specified types of transactions. These covenants limit our ability to, among other things, sell, transfer, lease or dispose of certain assets; incur indebtedness; encumber or permit liens on certain assets; make certain investments; make certain restricted payments, including paying dividends on, or repurchasing or making distributions with respect to, our common stock; and enter into certain transactions with affiliates. Our business may be adversely affected by these restrictions on our ability to operate our business.

The covenants also include, to the extent the principal amount of the advances under the Loan Agreement equals or exceeds $55.0 million, maintaining cash in an account or accounts in which the Lenders have a first priority security interest, in an aggregate amount greater than or equal to $15.0 million, plus the amount of our accounts payable under U.S generally accepted accounting principles not paid after the 180th day following the invoice for such account payable, which we refer to as the Qualified Cash A/P Account. Further, effective upon the later of (i) the last calendar month of the calendar quarter that is twelve months following the earlier of (x) the date of approval of our NDA for our AXS-05 product candidate for the treatment of major depressive disorder reasonably satisfactory to the Lenders, and (y) the date of approval of our NDA for our AXS-07 product candidate for the treatment of migraine, or (ii) the date on which the outstanding principal amount of the term loan advances under the Loan Agreement is equal to or greater than $65.0 million, we are obligated to (A) ensure that at all times our market capitalization exceeds $2.0 billion, and that we maintain cash in an account in which the Lenders have a first priority security interest in an amount not less than 65% of the sum of the outstanding principal amount of the term loan advances plus the Qualified Cash A/P Amount, (B) ensure that at all times that we maintain cash in an account in which the Lenders have a first priority security interest in an amount not less than 100% of the sum of the outstanding principal amount of the term loan advances plus the Qualified Cash A/P Amount, or (C) achieve at least 60% of the net product revenue per the board of directors approved forecast solely from the sale of AXS-05 and AXS-07 (which may include royalty, profit sharing, or sales-based milestone revenue recognized in accordance with GAAP, but will not include any upfront or non-sales-based milestone payments under business development or licensing transactions), measured on a trailing six-month basis as of the date of our most recent quarterly financial statement, included in the projections we delivered to Hercules on September 9, 2020, as updated from time to time, determined on a quarterly basis.

A breach of any of the covenants under the Loan Agreement could result in a default under the 2020 Term Loan. Upon the occurrence of an event of default under the 2020 Term Loan, the Lenders could elect to declare all amounts outstanding, if any, to be immediately due and payable and terminate all commitments to extend further credit. If there are any amounts outstanding that we are unable to repay, the Lenders could proceed against the collateral granted to it to secure such indebtedness.

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. A Phase 3 trial with AXS-05 in AD agitation is ongoing and a Phase 3 AXS-12 in narcolepsy is planned. 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.

Although we submitted an NDA to the FDA for AXS-05 for the treatment of MDD and for AXS-07 for the acute treatment of migraine, 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.

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. We conducted one interim analysis for the 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 (or have manufactured by third parties) 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, AXS-12 for the treatment of narcolepsy and AXS-14 for the treatment of fibromyalgia. 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-05, as well as two product candidates that are not currently in active 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 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 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 most of our product candidates using the 505(b)(2) pathway, with the exception of AXS-12 and AXS-14. 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 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, hepatoxicity, hypoglycemia, thrombocytopenia or other hypersensitivity reactions, QT 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-glutamyl transferase, 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, Aplenzin, Forfivo, Zyban, Contrave, and Nuedexta.

Based on the side effects disclosed in FDA product labeling 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, arrythmia, 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 Anjeso, Vivlodex, Mobic, and Maxalt.

Based on the side effects disclosed in EMA required product label for marketed drugs that contain the same active molecule as our product candidate, AXS-12 and AXS-14 may result in decreased appetite, insomnia, agitation, anxiety, dizziness, headache, paresthesia, 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 most of our product candidates under an NDA submitted pursuant to 505(b)(2), we will rely, at least in part, upon a reference 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 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 have submitted an NDA for AXS-05 and plan to submit NDAs for 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.

Under the Hatch Waxman Act, the holder of patents listed in the Orange Book for NDAs that a 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.

In practice, companies that produce branded reference listed drugs often bring patent litigation against applicants that seek regulatory approval to market generic or reformulated versions of their 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 a court finds patents valid and infringed by our product candidates, we may be required to cease selling, relinquish or destroy existing stock, or pay monetary damages 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 have not been finally resolved by the courts, an approach 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. Even though we have recently submitted our first NDA to the FDA 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, although we believe that we are able to rely on the completed Phase 2 ASCEND trial and Phase 3 GEMINI trial in MDD to support an NDA for AXS-05 for the treatment of MDD; the Phase 3 MOMENTUM trial, conducted pursuant to a Special Protocol Assessment, or SPA, and the Phase 3 INTERCEPT trial to support an NDA for AXS-07 for the acute treatment of migraine; the Phase 3 ADVANCE-1 trial and the ongoing ACCORD trial to support an NDA for AXS-05 for the treatment of AD agitation; and the completed Phase 2 trial and Phase 3 trial to support an NDA for AXS-14 for the management of fibromyalgia, the FDA could still require additional studies to support the approval of an NDA for these product candidates. Finally, for AXS-12, we will need to conduct a Phase 3 clinical 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;
- we may experience delays in our clinical trials due to the ongoing COVID-19 pandemic;
- 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 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. 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 filing and approval, 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;

- there may be delays in the FDA's ability to conduct necessary Pre-Approval Inspections, or PAIs, due to the COVID-19 pandemic or for other reasons, and more generally 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 smoking cessation. 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 (incidence of ≥5% of subjects) observed in the completed clinical trials of AXS-05 include dizziness, nausea, headache, dry mouth, and decreased appetite. Some reported adverse events resulted in discontinuations from our trials of AXS-05. The most frequent adverse events (incidence of ≥1% of subjects) resulting in discontinuation included dizziness, nausea, and headache. AXS-05 consists of dextromethorphan 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.

To date, the most commonly reported adverse events observed in the completed clinical trials of AXS-07 include nausea, dizziness, somnolence, and paresthesia. AXS-07 consists of meloxicam and rizatriptan, 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.

To date, the most commonly reported adverse events observed in the completed clinical trial of AXS-12 include anxiety, constipation, and insomnia.

To date, the most commonly reported adverse events observed in the completed clinical trials of AXS-14 include anxiety, constipation, and insomnia.

If any of our other product candidates are 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 identify patients for enrollment and maintain a sufficient level of patient participants in our clinical studies due to the ongoing COVID-19 pandemic;
- 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. We may be required by the FDA to modify the entry criteria for our 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 and meloxicam are subject to restrictive marketing and distribution regulations, which if applied to our product candidates could restrict their use and potentially reduce our ability to generate profits.

Currently approved products containing bupropion and meloxicam 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 in addition to a medication guide. We cannot predict whether what will be required as part of the FDA's approval of our product candidates. 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 single agent product candidates.

Certain of our product candidates, including AXS-05, 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, as we begin scale-up efforts for commercial-size manufacturing batches, formulation changes may be necessary to improve tablet robustness. 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-05 for both the treatment of TRD as well as for the treatment of AD agitation, and we may seek Fast Track designation for other of our current or future product candidates. Receipt of a designation to facilitate expedited review for 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 and for the treatment of AD agitation may not ultimately lead to a faster development or regulatory review or approval process, and it will not increase the likelihood that these product candidates will receive marketing approval.

We received Breakthrough Therapy designation for AXS-05 for both the treatment of MDD and the treatment of AD agitation. 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. Breakthrough Therapy designation also allows the sponsor to request a Priority Review or file sections of the NDA on an ongoing basis for rolling review where the FDA may consider beginning review portions of a marketing application before the full submission is complete. 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 for one or more of our applicable product candidates if such product candidates no longer meet the conditions for qualification of this program. For example, we were initially granted Breakthrough Therapy designation for AXS-12 for the treatment of cataplexy in patients with narcolepsy in August 2020. In July 2021, the FDA rescinded our Breakthrough Therapy designation due to the FDA approving an additional drug product for the treatment of cataplexy in narcolepsy.

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 practice, or GCP, 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 cGMP and GCP. 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 or modify 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: AbbVie Inc.; Amgen Inc.; Avadel Pharmaceuticals plc; Biohaven Pharmaceutical Holding Company Ltd.; Eli Lilly and Company; H. Lundbeck A/S; Harmony Biosciences; Intra-Cellular Therapies, Inc.; Janssen Research & Development, LLC; Jazz Pharmaceuticals plc; Otsuka Pharmaceutical Co. Ltd.; Relmada Therapeutics Inc.; Sage Therapeutics, Inc.; and Takeda Pharmaceutical Company Limited.

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, dextromethorphan, bupropion, meloxicam, rizatripan, reboxetine, and esomeprazole, are available in the United States and abroad 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 meloxicam is not currently approved for the treatment of acute migraine, we would not be able to prevent a physician from prescribing it 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 may 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, since providers are not prohibited from prescribing medications for indications other than the approved indications listed on the label. 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, if another sponsor had received FDA approval for a reboxetine-containing product for the treatment of narcolepsy before we had obtained FDA approval for AXS-12 for the treatment of narcolepsy, 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 reboxetine-containing product for the treatment of narcolepsy before we had obtained EMA approval for AXS-12 for the treatment of narcolepsy, 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.

The FDA may undertake a reevaluation of aspects of its orphan drug regulations and policies at any time, and may possibly do so in response to a recent court decision regarding the plain meaning of the exclusivity provision of the Orphan Drug Act. 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.

Even if we obtain FDA approval of an NDA for our product candidates, if we are unable to establish effective marketing, sales and distribution capabilities or enter into agreements with third parties to market, sell and distribute our product candidates we may be unable to generate product revenues.

We are currently building a commercial infrastructure for the marketing, sale, and distribution of pharmaceutical products. We plan to build a commercial infrastructure, including the creation of a sales force to launch that product candidate throughout the United States, which will require consideration of a range of federal and state laws.. If we commercialize our product candidates outside the United States, we intend to partner with marketing and sales 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. Our role as an NDA holder (if we obtain approval) and a virtual manufacturer, and the establishment and development of our commercial infrastructure and 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 these capabilities. We 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;
- the inability of sales personnel to travel and/or arrange in-person meetings with physicians due to the ongoing COVID-19 pandemic;
- our inability to effectively oversee a geographically dispersed sales and marketing team;
- the application of federal and state drug distribution and supply chain requirements to our business;
- 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.

As we build our commercial infrastructure prior to approval of a product candidate being approved by the FDA, we will incur expenses prior to product launch in recruiting this sales force and developing a compliant 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.

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. Third-party payors may also implement onerous access controls, which could further impede our efforts to effectively transition eligible patients to our therapies.

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 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 dextromethorphan 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 $8.0 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 practice, or GCP, for conducting, monitoring, 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 GCP, 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. The FDA must verify our contract manufacturers' compliance with cGMP requirements and comparable foreign regulatory authorities will similarly inspect our contract manufacturers' facilities 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.

Our business operations, financial condition, results of operations and cash flows may be adversely affected by the effects of health epidemics, pandemics, or outbreaks of infectious diseases, including the recent COVID-19 pandemic.

Our business could be adversely affected by health epidemics in regions where we have concentrations of clinical trial sites or other business operations, and could cause significant disruption in the operations of third-party manufacturers and CROs upon whom we rely.

For example, in December 2019, a novel strain of coronavirus, COVID-19, was identified in Wuhan, China. This virus continues to spread globally and in March 2020, the World Health Organization declared COVID-19 a pandemic. The COVID-19 pandemic has negatively impacted the global economy, disrupted global supply chains and created significant volatility and disruption of financial markets. Currently, the COVID-19 pandemic is having a significant adverse impact on the conduct of oncology clinical trials in the US. The evolving COVID-19 pandemic has impacted the pace of enrollment in clinical trials and we may be affected by similar delays as patients may avoid or may not be able to travel to healthcare facilities and physicians' offices unless due to a health emergency and clinical trial staff can no longer get to the clinic. Such facilities and offices have been and may continue to be required to focus limited resources on non-clinical trial matters, including treatment of COVID-19 patients, thereby decreasing availability, in whole or in part, for clinical trial services. In addition, employee disruptions and remote working environments related to the COVID-19 pandemic and the federal, state and local responses to such virus, has impacted and could continue to impact the efficiency and pace with which we work and develop our product candidates and our manufacturing capabilities. In addition, the COVID-19 pandemic has affected and may continue to affect the operations of the FDA and other health authorities, which could result in delays of reviews and approvals.

We may utilize contract manufacturers to manufacture our investigational products and plan to utilize contract manufacturers if and when we obtain FDA approval. The FDA announced it would resume domestic facility inspections, after a previous temporary delay, and more recently the agency stated that it is transitioning back to standard operations for conducting domestic facility inspections. The agency continues its general suspension of foreign facility inspections (other than "mission-critical" inspections). Because of the global pandemic, decision-making around facility inspections by the FDA (including Pre-Approval and for cause inspections) continues to evolve, , especially given the recent report from the Government Accountability Office noting that the FDA had a significant backlog of domestic and foreign inspections resulting from the COVID-19 pandemic. Depending on the length of the COVID-19 pandemic and FDA's related internal policies, this could impact future applications and product candidates. The FDA has indicated that it will utilize interim measures such as reviewing a firm's previous compliance history, using information shared from foreign governments as part of mutual recognition and confidentiality agreements and requesting records "in advance of or in lieu of" on-site drug inspections. Nevertheless, we cannot predict at this time whether this or other developments will cause delays or cause other situations that may impact our business.

The FDA continues to update its guidance, Conduct of Clinical Trials of Medical Products During the COVID-19 Public Health Emergency, which was implemented to assist sponsors in assuring the safety of trial participants, maintaining compliance with GCP, and minimizing risks to trial integrity during the COVID-19 Pandemic, or the COVID-19 Guidelines. The policy is intended to remain in effect only for the duration of the public health emergency related to COVID-19 declared by the Department of Health and Human Services on January 31, 2020. We have implemented several procedures in accordance with the COVID-19 Guidelines to address patient safety and clinical trial conduct during the COVID-19 pandemic, including remote monitoring of patients through telemedical visits, remote monitoring of sites by our clinical trial monitors, remote data entry, and follow-up visits at sites other than the site where the patient was initially treated. Our implementation of the COVID-19 Guidelines and potential disruptions to patient follow up, site monitoring or the timely completion of our trials may have a negative effect on our ability to complete trials and associated regulatory filings.

The ultimate impact of the COVID-19 pandemic is highly uncertain and subject to change. We do not yet know the full extent of potential delays or impacts on our business, financing or clinical trial activities or on healthcare systems or the global economy as a whole. However, these effects may have a material impact on our liquidity, capital resources, operations and business and those of the third parties on which we rely and a recession or market correction resulting from the spread of COVID-19 could materially affect our business and the value of our common stock. We will continue to monitor the COVID-19 situation closely.

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, which could expose us to significant False Claims Act liability and other civil monetary penalties.

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.

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, patent and trade secret protection for our current and future product candidates that we may develop, license, or acquire, as well as the related manufacturing methods. We will be able to protect our technologies from unauthorized use by third parties to the extent that the technologies are covered by valid and enforceable patents or trade secrets.

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 patent applications and patents. Therefore, these patents and patent 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 and patent applications or in third-party patents and patent applications. 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 conceive of and reduce to practice 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 requirements of governmental patent agencies 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 U.S. Patent and Trademark Office, or 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 are 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, may allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or may 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 any of our current or future product candidates can be challenged by third parties during prosecution before 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. 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 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 against 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 their intellectual property rights, 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 have licensed and may need to license certain intellectual property from third parties in the future, such licenses may not be available or may not be available on commercially reasonable terms, and if the licenses are terminated for any reason our business may be materially harmed.

We are a party to certain license agreements under which we are granted rights to intellectual property, including patent rights that are important to our business. We expect that we may need to enter into additional license agreements in the future to commercialize our products, in which case we would be required to obtain a license from additional third parties. Such licenses 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 rely on these licenses to use intellectual property that may be material to our business and important or necessary to the development or commercialization of our products. Our existing license agreements impose, and we expect that future license agreements will impose on us, various exclusivity obligations. If we fail to comply with our obligations under these agreements, the applicable licensor may have the right to terminate our license, in which case we may not be able to develop or commercialize the products covered by such license.

In January 2020, we entered into an agreement with Pfizer Inc., or Pfizer, for an exclusive U.S. license to Pfizer's clinical and nonclinical data, and intellectual property for reboxetine, the active pharmaceutical ingredient in AXS-12 which Axsome is developing for the treatment of narcolepsy. The agreement also provides Axsome exclusive rights to develop and commercialize esreboxetine, a new late-stage product candidate now referred to as AXS-14, in the U.S. for the treatment of fibromyalgia. Under the terms of the agreement, we received from Pfizer an exclusive U.S. license to Pfizer data for reboxetine and esreboxetine encompassing a full range of nonclinical studies, and short-term and long-term clinical trials involving more than five thousand patients. The licensed data includes results of a positive Phase 3 trial and a positive Phase 2 trial of esreboxetine in the treatment of fibromyalgia. We will have the exclusive right and sole responsibility of developing AXS-14 (esreboxetine) in the U.S. for the treatment of fibromyalgia and for other indications. Pfizer received 82,019 shares of our common stock having a value of $8.0 million, based on the average closing price of our common stock for the 10 prior trading days of $97.538, in consideration for the license and rights. Pfizer also received an upfront cash payment of $3.0 million and will receive up to $323 million in regulatory and sales milestones, and tiered mid-single to low double-digit royalties on future sales. Pfizer will also have a right of first negotiation on any potential future strategic transactions involving AXS-12 and AXS-14. Under the agreement, we are obligated to use commercially reasonable efforts to develop, manufacture and commercialize the compounds and products in the United States and to seek and maintain regulatory approvals for the compounds and products The agreement will expire on a product-by-product basis upon expiration of the last-to-expire royalty term for such product. On expiration (but not earlier termination), we will have a perpetual, non-exclusive, fully paid, royalty-free and irrevocable license under the licensed patent rights and related data to develop, manufacture, use, commercialize and otherwise exploit the compounds. Either party may terminate the agreement for the other party's material breach following a cure period. Pfizer may immediately terminate the agreement upon certain insolvency events relating to us. We may terminate the agreement for any reason upon ninety days written notice to Pfizer at any time after the first anniversary of the agreement. If the license agreement with Pfizer is terminated for any reason, our business, financial condition, results of operations, and prospects 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-05, as well as two product candidates that are not currently in development, anywhere in the world for human therapeutic, veterinary, 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-05. Under the terms of the agreements, we are required to pay to Antecip a royalty equal to 3.0% for AXS-05, 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. We are dependent upon the license agreements with Antecip and 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.

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 patent applications and 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 where 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 transparency 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 the filed Annual Report on Form 10-K, 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 Physician Payments Sunshine 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 laws 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. Many private payors employ "new-to-market blocks" for newly launched medications and other products until the payors have had the opportunity to make a coverage decision based upon their internal review of such products. When a medication or other product is not covered, the patient is responsible to pay the full price, which can significantly limit utilization. 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. Additionally, drug pricing is a key state and federal issue within the U.S., with recent legislation and additional proposals designed to bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare and Medicaid, review the relationship between pricing and manufacturer patient programs and reform government program reimbursement methodologies for drugs. We expect continued focus and pressure on drug pricing going forward. 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 or have fewer access restrictions 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, there have been numerous attempts by Congress and the former Trump Administration, through legislation and executive orders, to repeal or materially modify various aspects of ACA. In addition, there have been multiple lawsuits challenging the constitutionality of the ACA as well as various components of the ACA, and it is unclear what impact these various efforts have and will have on our business operations and resulting financial condition. For example, on December 15, 2019, a federal district court in Texas struck down the ACA in its entirety, finding that the Tax Cuts and Jobs Act of 2017, or TCJA, rendered the individual mandate unconstitutional. The judge further concluded in Texas v. Azar that since the individual mandate is "essential" to the ACA, it could not be severed from the rest of the ACA and therefore, the entire ACA was unconstitutional. Despite its decision, however, the court did not issue an injunction and therefore, immediate compliance is not required. Following appeal of the Fifth Circuit's decision, the Supreme Court heard oral arguments in California v. Texas (formerly Texas v. Azar) on November 2, 2020. Thereafter, the Department of Justice under the new Biden Administration did submit a new amicus brief in February 2021 following the oral hearings asserting that they now believe the ACA is constitutional, and the mandate is severable from the rest of the ACA. In June 2021, the Supreme Court upheld the ACA. It is unclear how regulations and sub-regulatory policy, which fluctuate continually, may affect interpretation and further implementation of the ACA and its practical effects on our business, particularly entering an election year. We are unable to predict the future course of federal or state healthcare legislation in the United States directed at broadening the availability of healthcare and containing or lowering the cost of healthcare, including drugs and biologics. The fate of the ACA and any further changes in the law or regulatory framework that reduce our revenue or increase our costs could also have a material and adverse effect on our business, financial condition and results of operations. Furthermore, federal and state elections in 2020 have changed which persons and parties occupy the Office of the President of the United States and control both chambers of Congress and many states' governors and legislatures. These changes will likely result in new agency priorities, rulemakings, and legislation. We anticipate that the new Biden Administration will issue a number of Executive Orders, which may alter the policies of the previous administration. Additionally, certain agency rules and policy statements of the prior four years may be rescinded. Further, the Biden Administration may propose substantial changes to the U.S. healthcare system, including expanding government-funded health insurance options. We are uncertain of the impact or outcome of these potential Executive Orders, rescission of rules and policy statements, or new legislation, especially any relative impact on the healthcare regulatory and policy landscape, or the impact they may have 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 also an increasing focus on the price of drugs, both at the state and federal levels, and it is likely that additional pricing controls will be enacted and could harm our business, financial condition and results of operations. For instance, states such as California have begun enacting transparency laws aimed at curbing drug price increases and with the change in administration it is possible that President Biden may issue Executive Orders with the potential to change a number of prior executive branch actions on drug pricing. We continue to monitor the potential impact of proposals to lower prescription drug costs at the federal and state level. 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 certain 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. Product identifier information (an aspect of the product tracing scheme) is also now required. The DSCSA requirements, development of standards, and the system for product tracing have been and will continue to be phased in over a period of years, with the FDA indicating enforcement discretion on certain aspects due to the COVID-19 pandemic. The distribution of product samples continues to be regulated under the PDMA, and some states also impose regulations on drug sample distribution.

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. Further, even if we are successful in mounting a defense, we may incur substantial costs in preparing and maintaining our defense and any such action would be time- and resource-intensive and potentially divert management's attention from the business, which could adversely affect our ability to operate our business and our results of operations.

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 August 2, 2021, we had 93 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. Further, the value to employees of stock options or restricted stock units that vest over time is significantly affected by movements in our stock price that are beyond our control, and may at any time be insufficient to counteract more lucrative offers from other companies. 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.

Our continued growth could strain our personnel resources and infrastructure, and if we are unable to implement appropriate controls and procedures to manage our growth, we will not be able to implement our business plan successfully.

As we continue to complete our clinical trials and prepare for commercialization of our product candidates, and as our company continues to grow, we may experience significant strains on our resources, including to our administrative, operational and financial infrastructure, which will result in additional burdens on management. Our success will depend in part upon the ability of our senior management to manage this growth effectively. To do so, we must continue to hire, train and manage new employees as needed. If our new hires perform poorly, or if we are unsuccessful in hiring, training, managing and integrating these new employees, or if we are not successful in retaining our existing employees, our business would be harmed. To manage the expected growth of our operations and personnel, we will need to continue to improve our operational, financial and management controls and our reporting systems and procedures.

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.

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 securities. Further, 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.

The Sarbanes-Oxley Act requires, among other things, that we maintain effective internal controls for financial reporting and disclosure controls and procedures. Under Section 404(a) of the Sarbanes-Oxley Act, we are required to furnish a report by management on, among other things, the effectiveness of our internal control over financial reporting. This report must include disclosure of any material weaknesses identified by our management during its periodic assessment of our internal control over financial reporting. A material weakness is a deficiency, or combination of deficiencies, in internal control over financial reporting that results in more than a reasonable possibility that a material misstatement of annual or interim financial statements will not be prevented or detected on a timely basis. Section 404(b) of the Sarbanes-Oxley Act also requires our independent auditors to attest to, and report on, this management assessment. Ensuring that we have adequate internal controls in place so that we can produce accurate financial statements on a timely basis is a costly and time-consuming effort. If we are not able to comply with the requirements of Section 404 or if we or our independent registered public accounting firm are unable to attest to the effectiveness of our internal control over financial reporting, investors may lose confidence in the accuracy and completeness of our financial reports, the market price of our stock could decline and we could be subject to sanctions or investigations by Nasdaq, the SEC, or other regulatory authorities, which would require additional financial and management resources.

During the evaluation and testing process, if we identify one or more material weaknesses in our internal control over financial reporting, we would be required to implement remediation procedures aimed at mitigating the control weakness or weaknesses. Until such remediation procedures succeed in mitigating the control weakness or weaknesses, we would be unable to assert that our internal control over financial reporting is effective. We cannot assure you that there will not be material weaknesses in our internal control over financial reporting in the future. Any failure to maintain internal control over financial reporting could severely inhibit our ability to timely and accurately report our financial condition, results of operations or cash flows. The cost of compliance with Section 404 requires us to incur substantial accounting expense and expend significant management time on compliance related issues as we implement additional corporate governance practices and comply with reporting requirements. Although we currently use the services of a third-party accounting firm to assist us with internal controls, 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, we could lose investor confidence in the accuracy and completeness of our financial reports, 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. 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.

In addition, as discussed above, the Sarbanes-Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal control over financial reporting. In particular, Section 404 of the Sarbanes-Oxley Act requires us to perform system and process evaluation and testing of our internal control over financial reporting to allow management to report on, and our independent registered public accounting firm to attest to, the effectiveness of our internal control over financial reporting. Pursuant to Section 404, we are required to provide an annual management report on the effectiveness of our internal control over financial reporting and we will also be required to include with such annual report an attestation report on internal controls over financial reporting issued by our independent registered public accounting firm. In the future, our independent registered public accounting firm may issue a report that is adverse in the event that we have not maintained effective internal controls over financial reporting, in all material respects. Any failure to maintain effective disclosure controls and internal control over financial reporting could have a material and adverse effect on our business, results of operations and financial condition and could cause a decline in the trading price of our common stock.

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 and security laws apply more broadly than the Health Insurance Portability and Accountability Act (HIPAA) and its implementing regulations. For example, California recently enacted legislation – the California Consumer Privacy Act, or CCPA – effective 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. Further, many data privacy and security laws within the U.S. have concurrent jurisdiction, which could subject us to enforcement by multiple agencies under multiple statutes for the same conduct (e.g., FTC enforcement under Section 5, HHS-Office for Civil Rights enforcement under HIPAA, and actions by state Attorneys General for violation of applicable state laws).

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 highly volatile. For example, in 2019, we experienced an extraordinary level of appreciation in our stock price. Such levels of gain are unlikely to continue in the future. For example, throughout the course of fiscal year 2020 and already during the first half of 2021, we have seen both significant appreciations and depreciations in our stock price. 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;
- operating and stock price performance of other companies that investors deem comparable to ours;
- recommendations by securities analysts;
- news relating to our industry as a whole and news relating to trends in our markets;
- 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 mid-cap 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. 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 August 2, 2021, our executive officers, directors, and 5% stockholders and their affiliates beneficially owned an aggregate of approximately 43% 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 our other stockholders. 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 August 2, 2021, we have outstanding 37,681,948 shares of common stock and 5,020,267 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, as well as outstanding restricted stock units. Of our currently outstanding shares of common stock, 29,693,124 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 10,453,341 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 2019 public offering and the proceeds from sales pursuant to our Sales Agreement, 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 2019 public offering and the proceeds from sales pursuant to our December 2019 “at-the-market” sales agreement with SVB Leerink, which provides for the sale of up to $80.0 million 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. Our stockholders may not agree with our decisions, and our use of the proceeds may not yield any return on investment for our stockholders. 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. Our stockholders 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.

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. As of December 31, 2020, we had U.S. federal net operating loss, NOL, carryforwards of approximately $249 million. Net operating loss carry forwards amounting to $60 million generated before the 2018 tax year will start expiring beginning 2032, if we have not used them prior to that time, and the net operating losses of approximately $189 million generated in 2018 and later have an indefinite carryforward period. Net operating loss carry forwards arising in taxable years ending after December 31, 2017 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 other public and private Capital Raises, and other transactions that have occurred, may trigger, or may have already triggered, such an ownership change. In addition, since we may need to raise 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.

On March 27, 2020, the Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act, was enacted and signed into law, and GAAP requires recognition of the tax effects of new legislation during the reporting period that includes the enactment date. The CARES Act, among other things, includes changes to the tax provisions that benefits business entities and makes certain technical corrections to the 2017 Tax Cuts and Jobs Act including permitting NOLs, carryovers and carrybacks to offset 100% of taxable income for taxable years beginning before 2021. In addition, the CARES Act allows NOLs incurred in 2018, 2019, and 2020 to be carried back to each of the five preceding taxable years to generate a refund of previously paid income taxes. The CARES Act provides other reliefs and stimulus measures. We have evaluated the impact of the CARES Act, however, at present we do not expect that any provision of the CARES Act would result in a material cash benefit to us or have a material impact on our financial statements or internal controls over financial reporting.

Because we do not intend to pay dividends on our common stock, returns for our stockholders 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. In addition, the terms of our existing credit facility with Hercules preclude us from paying cash dividends without Hercules' consent. 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. We do not currently have any preferred stock outstanding. 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

Exhibit Number	Description
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.INS	Inline XBRL Instance Document (the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document)
101.SCH	Inline XBRL Taxonomy Extension Schema Document
101.CAL	Inline XBRL Taxonomy Extension Calculation Database Document
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104	Cover Page Interactive Data File (formatted as inline XBRL with applicable taxonomy extension information contained in Exhibits 101.)

**Filed herewith.

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: August 9, 2021

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

Date: August 9, 2021

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

Exhibit 31.1

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: August 9, 2021

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

Exhibit 31.2

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: August 9, 2021

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

Exhibit 32.1

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 June 30, 2021 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: August 9, 2021

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

Exhibit 32.2

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 June 30, 2021 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: August 9, 2021

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