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, 2022

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 40,304,124 shares of the registrant's common stock, $0.0001 par value, outstanding as of August 1, 2022.

AXSOME THERAPEUTICS, INC.
QUARTERLY REPORT ON FORM 10-Q
FOR THE QUARTER ENDED JUNE 30, 2022

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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 future revenue projections, sales forecasts, and potential peak market data;
- 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 expand our own commercial infrastructure to manufacture, market and sell our products;
- our expected losses;
- our ability to obtain and maintain intellectual property protection for our products;
- 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, 2022 (Unaudited)	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 73,394,640	$ 86,472,854
Accounts receivables, net	16,167,927	—
Inventories, net	10,323,746	—
Prepaid and other current assets	4,091,369	45,286
Total current assets	103,977,682	86,518,140
Equipment, net	634,611	283,846
Right-of-use asset - operating lease	667,582	660,162
Goodwill	11,897,407	—
Intangible asset, net	62,874,350	—
Other assets	507,464	322,910
Total assets	$ 180,559,096	$ 87,785,058
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 19,430,961	$ 13,149,329
Accrued expenses and other current liabilities	16,480,322	9,295,180
Operating lease liability, current portion	709,120	620,675
Contingent consideration, current	5,950,000	—
Total current liabilities	42,570,403	23,065,184
Contingent consideration, non-current	29,330,407	—
Loan payable, long-term	93,458,824	49,089,522
Total liabilities	165,359,634	72,154,706
Stockholders' equity:		
Preferred stock, $0.0001 par value per share (10,000,000 shares authorized, none issued and outstanding at June 30, 2022 and December 31, 2021, respectively)	—	—
Common stock, $0.0001 par value per share (150,000,000 shares authorized, 39,914,411 and 37,816,794 shares issued and outstanding at June 30, 2022 and December 31, 2021, respectively)	3,991	3,782
Additional paid-in capital	505,465,383	424,825,655
Accumulated deficit	(490,269,912)	(409,199,085)
Total stockholders' equity	15,199,462	15,630,352
Total liabilities and stockholders' equity	$ 180,559,096	$ 87,785,058

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

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

	Three Months June 30,		Six Months Ended June 30,	
	2022	2021	2022	2021
Revenues:				
Product sales, net	$ 8,819,786	$ —	$ 8,819,786	$ —
Operating expenses:				
Cost of product sales (excluding amortization and depreciation)	982,836	—	982,836	—
Research and development	15,792,202	14,503,326	28,377,343	31,099,014
Selling, general and administrative	31,160,140	16,344,361	56,863,871	27,592,734
Gain in fair value of contingent consideration	(860,000)	—	(860,000)	—
Intangible asset amortization	925,650	—	925,650	—
Total operating expenses	48,000,828	30,847,687	86,289,700	58,691,748
Loss from operations	(39,181,042)	(30,847,687)	(77,469,914)	(58,691,748)
Interest income (expense)	(2,257,474)	(1,436,522)	(3,600,913)	(2,852,431)
Net loss	$ (41,438,516)	$ (32,284,209)	$ (81,070,827)	$ (61,544,179)
Net loss per common share, basic and diluted	$ (1.06)	$ (0.86)	$ (2.09)	$ (1.64)
Weighted average common shares outstanding, basic and diluted	39,081,100	37,595,069	38,704,227	37,512,716

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, 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	—	—	—	—
Issuance of warrants upon debt financing	—	—	—	—	—
Issuance of common stock upon financing	16,419	2	1,096,501	—	1,096,503
Shares tendered for withholding taxes	—	—	(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**
Balance at December 31, 2021	37,816,794	3,782	424,825,655	(409,199,085)	15,630,352
Stock-based compensation			7,598,329	—	7,598,329
Issuance of common stock upon exercise of options	18,015	2	181,635	—	181,637
Issuance of common stock upon vesting of RSUs	4,555	—	—	—	—
Issuance of common stock upon financing	1,044,081	104	31,008,497	—	31,008,601
Shares tendered for withholding taxes	—	—	(88,594)	—	(88,594)
Net loss	—	—	—	(39,632,311)	(39,632,311)
Balance at March 31, 2022	**38,883,445**	**3,888**	**463,525,522**	**(448,831,396)**	**14,698,014**
Stock-based compensation	—	—	10,161,678	—	10,161,678
Issuance of common stock upon exercise of options	6,691	—	176,412	—	176,412
Issuance of common stock upon vesting of RSUs	1,122	—	—	—	—
Issuance of common stock upon financing	1,023,153	103	30,794,544	—	30,794,647
Issuance of warrants upon debt financing	—	—	826,153	—	826,153
Shares tendered for withholding taxes	—	—	(18,926)	—	(18,926)
Net loss	—	—	—	(41,438,516)	(41,438,516)
Balance at June 30, 2022	**39,914,411**	**3,991**	**505,465,383**	**(490,269,912)**	**15,199,462**

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,	
	2022	**2021**
Cash flows from operating activities		
Net loss	$ (81,070,827)	$ (61,544,179)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation expense	17,760,007	9,187,339
Amortization of intangible asset	925,650	—
Amortization of debt discount	683,022	560,752
Depreciation	104,430	18,075
Gain in fair value of contingent consideration	(860,000)	—
Amortization of operating lease right-of-use asset	553,960	530,437
Change in operating lease liability	(472,935)	(631,591)
Changes in operating assets and liabilities:		
Accounts receivable, net	(16,167,927)	—
Inventories, net	277,254	—
Prepaid expenses and other current assets	(1,204,490)	(287,431)
Accounts payable	6,281,632	(1,892,026)
Accrued expenses and other current liabilities	7,185,142	1,449,582
Other assets	(184,554)	—
Net cash used in operating activities	(66,189,636)	(52,609,042)
Cash flows from investing activities		
Purchases of equipment	(455,195)	(48,872)
Cash paid for business combination	(53,000,000)	—
Net cash used in investing activities	(53,455,195)	(48,872)
Cash flows from financing activities		
Proceeds from draw down of debt	45,000,000	—
Payment of debt issuance costs	(487,160)	—
Proceeds from issuance of common stock upon financing, net	61,803,248	7,212,367
Proceeds from issuance of common stock upon exercise of options	358,049	2,872,194
Payments of tax withholdings on stock award	(107,520)	(84,010)
Net cash (used in) provided by financing activities	106,566,617	10,000,551
Net (decrease) increase in cash	(13,078,214)	(42,657,363)
Cash at beginning of period	86,472,854	183,876,453
Cash at end of period	$ 73,394,640	$ 141,219,090
Supplemental disclosures of cash flow information:		
Interest paid	$ 2,586,375	$ 2,312,917
Operating lease right-of-use asset obtained in exchange for operating lease liability	561,380	—
Supplemental non-cash investing activities:		
Fair value of contingent consideration in a business combination	35,280,407	—

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 and delivering novel therapies for central nervous system (“CNS”) conditions that have 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 was incorporated on January 12, 2012 in the State of Delaware. The Company’s CNS portfolio includes four product candidates, AXS-05, AXS-07, AXS-12, and AXS-14, which are being developed for multiple indications. In May 2022, the Company acquired the U.S. rights to Sunosi® from Jazz Pharmaceuticals ("Jazz"), a product approved by FDA and marketed in the U.S. to improve wakefulness in adult patients with EDS associated with narcolepsy or obstructive sleep apnea, and also recently approved in Europe in January 2020 by the European Commission. 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 refers herein to its four product candidates and Sunosi, collectively, as the Company’s products.

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, 2021 filed with the SEC on March 1, 2022.

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, 2022 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, 2022, the Company had an accumulated deficit of $490.3 million.

The Company’s primary sources of cash have been proceeds from the issuance and sale of its common stock in public offerings and the issuance of debt. Sales for Sunosi were recently initiated and the Company has not yet commercialized any of its other product candidates. 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 additional revenues from its products.

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. During that time, we expect that our expenses will increase due primarily to the commercialization of Sunosi while continuing to further develop the Company's pipeline assets. 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 as a result 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 global pandemic. The full impact of the ongoing COVID-19 pandemic is still 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 products, it will be unable to generate sufficient additional recurring product revenue to 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; accounting for acquisitions; impairments goodwill and intangible assets; contingent consideration; chargebacks, cash discounts, sales rebates, returns and other adjustments; and the recoverability of the Company's net deferred tax assets and related valuation allowance.

Revenue Recognition

Effective January 1, 2018, the Company adopted FASB ASC Topic 606, Revenue from Contracts with Customers ("ASC Topic 606"). The Company did not generate any product related revenue until the Sunosi acquisition, and therefore the adoption of ASC Topic 606 did not have an impact to the Company's financial statements for any prior periods or upon adoption. In accordance with ASC Topic 606, the Company recognizes revenue when the customer obtains control of a promised good or service, in an amount that reflects the consideration that the Company expects to receive in exchange for the good or service. Transfer of control is based on contractual performance obligations, this occurs upon transfer of the title along with the physical transfer of the Company's goods to the Company's third-party logistics provider ("3PL") as that is when the customer has obtained control of significantly all of the economic benefits. The reported results for the three and six months ended June 30, 2022 reflect the application of ASC Topic 606.

To determine revenue recognition for arrangements that the Company determines are within the scope of ASC Topic 606, the Company performs the following five steps: (i) identify the contract(s) with a customer, (ii) identify the performance obligations in the contract, (iii) determine the transaction price, (iv) allocate the transaction price to the performance obligations in the contract, and (v) recognize revenue when (or as) the entity satisfies a performance obligation. The Company only applies the five-step model to arrangements that meet the definition of a contract under ASC Topic 606, including when it is probable that the Company will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of ASC Topic 606, the Company assesses the goods or services promised within each contract and determines those that are performance obligations and assesses whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied. For a complete discussion of accounting for product sales, see Product Sales, net (below).

Product Sales, net

The Company sells Sunosi in the United States through a single 3PL, which takes title and control of the goods. The 3PL distributes the product to wholesale distributors (collectively the "Distributors") with whom we have entered into formal agreements for delivery to retail

pharmacies.

Reserves for Variable Consideration

Our estimates of variable consideration and determination of whether to include estimated amounts in the transaction price are based largely on an assessment of its anticipated performance and all information (historical, current and forecasted) that is reasonably available. These reserves reflect our best estimate of the amount of consideration to which we are entitled based on the terms of the contracts. The amount of variable consideration that is included in the transaction price may be constrained and is included in the net sales price only to the extent that is considered probable that a significant reversal in the amount of the cumulative revenue recognized will not occur in a future period. Actual amounts of consideration ultimately received may differ from our estimates. If actual results in the future vary from our estimates, we will adjust these estimates, which would affect net product revenue and earnings in the period such variances become known.

Trade Discounts and Allowances - The Company generally provides discounts which include incentive fees that are explicitly stated in the Company's contracts and are recorded as a reduction of revenue in the period the related product revenue is recognized. In addition, the Company compensates (through trade discounts and allowances) its distributors for distribution services and data. These payments have been recorded as a reduction of net sales within the consolidated statements of operations through June 30, 2022, as well as a reduction to accounts receivable, net on the consolidated balance sheets.

Product Returns - Consistent with industry practice, the Company generally offers a limited right of return for product that has been purchased from the Company based on the product's expiration date. The Company estimates the amount of its product sales that may be returned and records this estimate as a reduction of revenue in the period the related product revenue is recognized, as well as a component of accrued expense and other current liabilities on the consolidated balance sheets. The Company currently estimates product return liabilities using available industry data and its own sales information.

Provider Chargebacks and Discounts - Chargebacks for fees and discounts to providers represent the estimated obligations resulting from contractual commitments to sell products at prices lower than the list prices charged to distributors. Distributors charge the Company for the difference between what they pay for the product and the ultimate selling price. These reserves are established in the same period that the related revenue is recognized, resulting in a reduction of product revenue and accounts receivables, net.

Rebates - Rebates apply to: Medicaid, managed care, and supplemental rebates to all applicable states as defined by the statutory government pricing calculation requirements under the Medicaid Drug Rebate Program. Tricare rebates to the TRICARE third party administrator based on the statutory calculation defined in the Agreement with Defense Health Agency. Part D and Commercial Managed Care rebates are paid based on the contracts with PBMs and Managed Care Organizations. Rebates are paid to these entities upon receipt of an invoice from the contracted entity which is based on the utilization of the product by the members of the contracted entity. The Company estimates these rebates and records such estimates in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability recorded as an accrued expenses and other current liabilities on the consolidated balance sheets.

Coverage Gap - The Medicare Part D coverage gap is a period of consumer payment for prescription medication costs which lies between the initial coverage limit and the catastrophic-coverage threshold, when the patient is a member of a Medicare Part D prescription-drug program administered by the Centers for Medicare & Medicaid Services. The Company estimates the percentage of goods sold under Coverage Gap and adjusts the transaction price for such discount at the time of sale resulting in a reduction of product revenue and the establishment of a current liability recorded as an accrued expenses and other current liabilities on the consolidated balance sheets.

Other Incentives - Other incentives which the Company offers include voluntary patient assistance programs, such as the co-pay assistance program, which are intended to provide financial assistance to qualified commercially-insured patients with prescription drug co-payments required by payers. The calculation of the accrual for co-pay assistance is based on an estimate of claims and the cost per claim that the Company expects to receive associated with product that has been recognized as revenue. The adjustments are recorded in the same period the related revenue is recognized, resulting in a reduction of product sales and the establishment of a current liability which is included as a component of accrued expenses and other current liabilities on the consolidated balance sheets.

The Company makes significant estimates and judgments that materially affect its recognition of net product revenue. Claims by third-party payors for rebates, chargebacks and discounts frequently are submitted to the Company significantly after the related sales, potentially resulting in adjustments in the period in which the new information becomes known. The Company will adjust its estimates based on new information, including information regarding actual rebates, chargebacks and discounts for its products, as it becomes available.

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 and delivering 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, 2022, the balance of cash and cash equivalents was $73.4 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, 2022, 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. At the time of contract inception or customer account set-up, the Company performs a collectability assessment on the creditworthiness of such customer. In 2022, all of the Company's accounts receivable arose from product sales in the U.S. and all customers have standard payment terms. The Company's accounts receivable balance as of June 30, 2022 is compromised solely from transactions with the Company's 3PL.

Business Combination

The Company accounted for the Sunosi acquisition as a business combination using the acquisition method of accounting, which requires that all identifiable assets acquired, and liabilities assumed be recorded at their estimated fair values. The excess of the fair value of purchase consideration over the fair values of identifiable assets and liabilities is recorded as goodwill. When determining the fair values of assets acquired and liabilities assumed, management makes significant estimates and assumptions. Critical estimates in valuing certain intangible assets include but are not limited to future expected cash flows from acquired patented technology. Management's estimates of fair value are based upon assumptions believed to be reasonable, but are inherently uncertain and unpredictable and, as a result, actual results may differ from estimates.

As a result of the acquisition of Sunosi from Jazz, the Company recorded goodwill and an intangible asset.

Goodwill

Goodwill is deemed to have an indefinite life and therefore not amortized. The Company tests the carrying amounts of goodwill for recoverability on an annual basis or more frequently if events or changes in circumstances indicate that the asset might be impaired. The Company performs a one-step test in its evaluation of the carrying value of goodwill if qualitative factors determine it is necessary to complete a goodwill impairment test. In the evaluation, the fair value of the relevant reporting unit is determined and compared to its carrying value. If the fair value is greater than the carrying value, then the carrying value is deemed to be recoverable, and no further action is required. If the fair value estimate is less than the carrying value, goodwill is considered impaired for the amount by which the carrying amount exceeds the reporting unit's fair value, and a charge is reported in impairment of goodwill in the Company's consolidated statements of operations. As of June 30, 2022, the Company has determined that it has one reporting unit. The Company has not identified any events or changes in circumstances that indicate the existence of potential impairment of goodwill during the six months ended June 30, 2022.

Intangible Assets

All of our intangible assets are amortized using the straight-line method over their estimated period of benefit of ten years. The Company evaluates the recoverability of intangible assets periodically by considering events or changes in circumstances that may warrant revised estimates of useful lives or that indicate the asset may be impaired.

Contingent Consideration

Consideration paid in a business combination may include potential future payments that are contingent upon the acquired business achieving certain milestones in the future ("contingent consideration"). The royalty payments due to Jazz are a high single-digit royalty on the Company's U.S. net sales of Sunosi in the current indication and a mid single-digit royalty on the Company's U.S. net sales of Sunosi for future indications. Contingent consideration liabilities are measured at their estimated fair value as of the date of acquisition, with subsequent changes in fair value recorded in the consolidated statements of operations during such period a change is recognized. The Company estimates the fair value of the contingent consideration as of the acquisition date using the estimated future cash outflows based on future sales. Contingent consideration liabilities expected to be settled within 12 months after the balance sheet date are presented in current liabilities, with the non-current portion recorded under long term liabilities in the consolidated balance sheets.

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—Unobservable inputs for which there is little or no market data, which require the reporting entity to develop its own assumptions.

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. An asset's or liability'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 receivable, accounts payable, accrued liabilities, current and long-term debt, current and non-current contingent consideration. 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. The key assumptions used to determine the fair value of acquisition-related assets and liabilities are estimated by management, not observable in the market and, therefore considered Level 3 inputs within the fair value hierarchy.

Accounts Receivable, net

The Company's accounts receivable, net, arise from product sales. They are generally stated at the invoiced amount and do not bear interest. Accounts receivable allowances result from chargebacks, prompt pay discounts, and distribution fees.

The Company monitors the financial performance and creditworthiness of its customers so that it can properly assess and respond to changes in the customers' credit profiles. In 2022, 100% were generated from the Company's 3PL. The Company estimated the current expected credit losses of its accounts receivable by assessing the risk of loss and available relevant information about collectability, including historical credit losses, existing contractual payment terms, actual payment patterns of its customers, individual customer circumstances, and reasonable and supportable forecast of economic conditions expected to exist throughout the contractual life of the receivable. The Company has not historically experienced significant credit losses. Based on its assessment, as of June 30, 2022, we have not recorded any allowances on receivables.

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.

Inventories, net

The Company values its inventories at the lower of cost or estimated net realizable value. The inventory associated with the Sunosi acquisition is stated at fair value due to purchase accounting. The Company determines the cost of its inventories, which includes amounts related to materials, labor, manufacturing overhead, and shipping and handling costs on a first-in, first-out ("FIFO") basis. The Company performs an assessment of the recoverability of capitalized inventory during each reporting period, and it writes down any excess and obsolete inventories to their estimated net realizable value in the period in which the impairment is first identified. Such impairment charges, if they occur, are recorded within cost of product sales.

The Company capitalizes inventory costs associated with the Company's products after regulatory approval when, based on management's judgment, future commercialization is considered probable and the future economic benefit is expected to be realized. Inventory acquired and manufactured prior to receipt of regulatory approval of a product candidate is expensed as research and development expense as incurred. Inventory that can be used in either the production of clinical or commercial product is expensed as research and development expense when selected for use in a clinical manufacturing campaign.

Equipment, net

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.

Cost of Product Sales

The Company's cost of product sales relates to sales of Sunosi. Cost of product sales primarily includes product royalty fees, overhead, and direct costs (inclusive of material, shipping, handling, and manufacturing costs). Cost of product sales excludes depreciation and amortization. Cost of product sales were approximately $1.0 million and $0 for the three and six months ended June 30, 2022 and 2021, respectively. There were no sales in 2021.

The Company also assumed the commitments of Jazz to SK Biopharmaceuticals ("SK)" and Aerial Biopharma ("Aerial"). SK is the originator of Sunosi and retains rights in 12 Asian markets, including China, Korea, and Japan. In 2014, Jazz acquired from Aerial worldwide rights to Sunosi excluding those Asian markets stated previously. The assumed commitments to SK and Aerial include single-digit tiered royalties based on the Company's sales of Sunosi, and the Company is committed to pay up to $165 million based on revenue milestones and $1 million based on development milestones. The related royalties are recorded within cost of product sales on the statement of operations.

Research and Development Costs

Research and development costs are expensed as incurred. Research and development expenses consist primarily of employee-related expenses including salaries, benefits, travel, and stock-based compensation expense, contract services, 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, 2022 and has not recorded an income tax benefit for the six months ended June 30, 2022 and 2021 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, 2022, 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 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.

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, 2022 and 2021.

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 October 2021, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") No. 2021-08, Business Combinations (Topic 805) . This update requires that an entity (acquirer) recognize and measure contract assets and contract liabilities acquired in a business combination in accordance with Accounting Standards Codification ("ASC") 606. This differs from the current requirement to measure contract assets and contract liabilities acquired in a business combination at fair value. The amendments in this update should be applied prospectively, and are effective for fiscal years beginning after December 15, 2022, including interim periods within those fiscal years. Early adoption is permitted, including adoption in an interim period. The Company is currently evaluating the impact of this ASU on its consolidated financial statements.

Note 3. Business Combination

Acquisition of Assets of Jazz Pharmaceuticals

On March 25, 2022, the Company entered into an Asset Purchase Agreement (the "Purchase Agreement") with Jazz, pursuant to which the Company will acquire Sunosi from Jazz (the "Acquisition"). The Company accounted for the Acquisition as a business combination using the acquisition method of accounting. The acquisition of Sunosi will occur in two separate closings. The sale and purchase of Specified Initial Assets as defined and contemplated by the Purchase Agreement occurred on May 9, 2022 ("Initial Closing"), following the satisfaction or waiver of the closing conditions under the Purchase Agreement. The sale and purchase of Specified Ex-U.S. Assets contemplated by the Purchase Agreement is expected to occur during the fourth quarter of 2022 ("Final Closing" or "Ex-U.S. Closing").

Under the terms of the Asset Purchase Agreement, the Company received from Jazz worldwide commercial, development, manufacturing, and intellectual property rights to Sunosi, except for certain Asian markets. Jazz received from the Company a total upfront payment of $53 million. In addition, Jazz will receive a high single-digit royalty on the Company's U.S. net sales of Sunosi in the current indication, and a mid single-digit royalty on the Company's U.S. net sales of Sunosi in future indications. The Company also assumed the commitments of Jazz to SK Biopharmaceuticals ("SK)" and Aerial Biopharma ("Aerial"). SK is the originator of Sunosi and retains rights in 12 Asian markets, including China, Korea, and Japan. In 2014, Jazz acquired from Aerial worldwide rights to Sunosi excluding those Asian markets as stated previously. The assumed commitments to SK and Aerial include single-digit tiered royalties based on the Company's sales of Sunosi, and additionally, the Company is committed to pay up to $165 million based on revenue milestones and $1 million based on development milestones. The Company financed the transaction via its existing $300 million term loan facility with Hercules Capital, Inc.

In conjunction with the Acquisition, the Company incurred approximately $0.5 million in transaction costs, which were expensed as selling, general, and administrative expense in the consolidated statement of operations during the six months ended June 30, 2022.

Our Consolidated Statement of Operations for the three and six months ended June 30, 2022, include $8.8 million of Product sales and $4.6 million of Net Loss associated with the result of operations of Sunosi from the acquisition date to June 30, 2022.

Preliminary purchase consideration consisted of the following:

Cash at settlement	$	53,000,000
Fair value of contingent consideration		36,140,407
Total	$	89,140,407

The preliminary allocation of the fair value of the Sunosi acquisition is shown in table below:

		Estimated fair value
Inventory	$	10,601,000
Other current assets		3,551,000
Developed technology		63,800,000
Goodwill		11,897,407
Accrued expenses and other current liabilities		(709,000)
Total	$	89,140,407

The above allocation of the purchase price is based upon certain preliminary valuations and other analyses that have not been finalized as of the date of this filing. As such, the purchase price amount and allocations for this transaction are preliminary estimates including developed technology, goodwill and contingent consideration, which may be subject to change within the measurement period.

The net assets were recorded at their estimated fair value. In valuing acquired assets and liabilities, fair value estimates were based primarily on future expected cash flows, market rate assumptions for contractual obligations, and appropriate discount rates.

Inventories acquired included raw materials, work in process and finished goods for Sunosi. Inventories were recorded at their estimated fair values categorized as Level 3. The fair value of finished goods was determined based on the estimated selling price, net of selling costs and a margin on the selling activities. The fair value of work in process was determined based on estimated selling price, net of selling costs and costs to complete the manufacturing, and a margin on the selling and

manufacturing activities. The fair value of raw materials was estimated to equal the replacement cost. A step-up in the value of inventory of $1.1 million was originally recorded in connection with the Acquisition.

Other current assets acquired were sample inventory and the rebates for Sunosi sales by the Company after the Initial Closing to be covered by Jazz.

Intangible assets include acquired developed technology. The fair value of the acquired developed technology asset was determined by applying the income approach, which recognizes that the fair value of an asset is premised upon the expected receipt of future economic benefits such as earnings and cash inflows based on current sales projections and estimated direct costs, using a discount rate of 43.5 % that reflects the return requirements of the market. This intangible asset is being amortized over an estimated useful life of 10 years.

Goodwill is considered an indefinite-lived asset and relates primarily to intangible assets that do not qualify for separate recognition, such as the assembled workforce and synergies between the entities. Goodwill of $ 11.9 million was established as a result of the Acquisition. The Company expects that the entire amount of the purchase price allocated to goodwill will be deductible for U.S. income tax purposes over a 15-year period.

Accrued expense and other current liabilities acquired were the Company's assumed sales returns liability for Sunosi after the transaction close date related to Jazz sales prior to the Initial Closing

Pro Forma Consolidated Financial Information

The following unaudited pro forma summary presents consolidated information of the Company, including Sunosi, as if the business combination had occurred on January 1, 2021, the earliest period presented herein:

	Six Months Ended	
	June 30, 2022	June 30, 2021
Net revenues	$ 32,848,000	$ 21,328,000
Net Loss	(108,332,000)	(169,365,000)

These pro forma results are illustrative only and not indicative of the actual results of operations that would have been achieved nor are they indicative of future results of operations.

Note 4. Goodwill

Goodwill of $11.9 million was recorded in connection with the Sunosi acquisition as described in Note 3 Business Combination. The Company will perform an annual impairment test unless condition exist where an interim impairment analysis is necessary.

The following table provides the Company’s goodwill as of June 30, 2022. There was no goodwill impairment during six months ended June 30, 2022.

	Goodwill
Balance at December 31, 2021	$ —
Goodwill from Sunosi Acquisition	11,897,407
Goodwill impairment	—
Balance at June 30, 2022	**$ 11,897,407**

Note 5. Intangible Asset

The gross carrying amount and net book value of our intangible asset are as follows:

	Estimated fair value	Remaining Weighted-Average Useful Life
Balance at December 31, 2021	$ —	
Gross Carrying Amount	63,800,000	10-years
Accumulated Amortization	(925,650)	
Net Book Value at June 30, 2022	**$ 62,874,350**	

Based on finite-lived intangible assets recorded as of June 30, 2022, and assuming the underlying assets will not be impaired and that we will not change the expected lives of the assets, future amortization expenses were estimated as follows:

	Estimated Amortization Expense
2022	3,213,578
2023	6,374,760
2024	6,392,226
2025	6,374,760
2026	6,374,760
Thereafter	34,144,266
Total	$ 62,874,350

Note 6. Fair Value of Financial Instruments

In connection with the Sunosi acquisition, we pay a royalty on net sales of Sunosi. The discounted cash flow method used to value this contingent consideration includes inputs of not readily observable market data, which are Level 3 inputs. As of the May 9, 2022 acquisition date, the contingent consideration had a fair value of $36.1 million. The fair value of the contingent consideration was $35.3 million as of June 30, 2022 and is reflected as current accrued contingent consideration of $6.0 million and non-current contingent consideration liability of $29.3 million in the consolidated balance sheet.

The fair value of financial instruments measured on a recurring basis is as follows:

May 9, 2022	Level 1	Level 2	Level 3	Total
Liabilities:				
Contingent consideration	$ —	$ —	$ 36,140,407	$ 36,140,407

June 30, 2022	Level 1	Level 2	Level 3	Total
Liabilities:				
Contingent consideration	$ —	$ —	$ 35,280,407	$ 35,280,407
Total	$ —	$ —	$ 35,280,407	$ 35,280,407

The fair value of the contingent consideration was remeasured at June 30, 2022. The fair value of the financial instruments as of June 30, 2022 is as follows:

	Contingent Consideration
Balance at December 31, 2021	$ —
Initial estimate	36,140,407
Gain in fair value of contingent consideration	(860,000)
Balance at June 30, 2022	**$ 35,280,407**

The recurring Level 3 fair value measurements of contingent consideration for which a liability is recorded include the following significant unobservable inputs:

			As of June 30, 2022	As of May 9, 2022
	Valuation Methodology	Significant Unobservable Input	Weighted Average (range, if applicable)	Weighted Average (range, if applicable)
Contingent Consideration	Probability weighted income approach	Discount rate	13.2%	11.7%
		Revenue Discount rate	20.9%	20.8%

The fair value measurement of the contingent consideration is sensitive to the change in discount rate. As of June 30, 2022, if the discount rate increases or decreases by approximately 1%, the fair value of the contingent consideration would range

from $33.6 million to $37.0 million. As of June 30, 2022, if the revenue discount rate increases or decreases by approximately 1%, the fair value of the contingent consideration would range from $34.1 million to $36.6 million.

Note 7. Inventory

Inventory consists of the following:

	June 30, 2022
Raw materials	$ 1,307,000
Work in process	8,430,000
Finished goods	586,746
Total	$ 10,323,746

As of June 30, 2022, inventories included $1.1 million related to the purchase accounting inventory fair value step-up on inventory acquired in the Sunosi Acquisition for the U.S. Territory.

Note 8. Accrued Expenses and Other Current Liabilities

At June 30, 2022 and December 31, 2021 accrued expenses and other current liabilities consisted of the following:

	June 30, 2022	December 31, 2021
Accrued research and development	$ 2,792,715	$ 2,416,897
Accrued compensation	3,871,439	4,050,236
Accrued selling, general and administrative	3,496,776	2,442,700
Accrued sales discounts, rebates and allowances	4,816,205	—
Accrued royalties	705,583	—
Accrued interest	797,604	385,347
Total	$ 16,480,322	$ 9,295,180

Note 9. Loan and Security Agreement

Hercules Capital, Inc.

Second Amendment to the Loan Agreement

On March 27, 2022, in connection with the Acquisition (as described above), the Company entered into a Second Amendment to the Loan and Security Agreement (the "Second Amendment") with Hercules Capital, Inc., or Hercules. The Second Amendment closed on May 9, 2022 concurrently with the closing of the Acquisition.

The Second Amendment amends the terms of that certain Loan and Security Agreement, dated as of September 25, 2020 (as amended by the First Amendment to the Loan and Security Agreement, dated of October 14, 2021) (the "Loan Agreement"). The changes in the Term Loan Advances (as defined in the Loan Agreement) amounts and dates are as follows: (i) increasing the Tranche 1 (as defined in the Loan Agreement) from $60.0 million to $95.0 million, whereby $45.0 million was drawn upon the Second Amendment closing date (ii) changing the Tranche 2 Advances to three sub-tranches of $35.0 million, $35.0 million and $30.0 million, respectively, for a same total value of $100.0 million, upon Approval of AXS-05 (iii) changing the Tranche 3 Advance to two sub-tranches of $15.0 million and $5.0 million, respectively, for the same total value of $20.0 million, upon Approval of AXS-07 (iv) decreasing the Tranche 4 Advance from $55.0 million to $50.0 million, available upon achievement of certain combined sales and outstanding debt criteria and (v) decreasing the Tranche 5 Advance from $75.0 million to $35.0 million, subject to the approval from Hercules. The outstanding balance of the debt bears interest at a floating rate based on the greater of (a) 8.95% or (b) US WSJ Prime + 5.70%) to not exceed 10.70%.

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 closing of the Second Amendment of the Loan Agreement, 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 $40.0 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"). The $40.0 million threshold decreases to $25.0 million upon achievement of the AXS-05 milestone.
- Effective upon the (i) the last calendar month of the calendar quarter that is nine months following the earlier of (x) the date that the First Milestone is achieved (y) the date that the Second Milestone is achieved, or (z) the final closing date of the Sunosi acquisition (A) ensure that at all times its market capitalization exceeds $1.0 billion, and that it maintains cash in an account which Hercules has a first priority security interest in an amount not less than 50% 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 85% 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, AXS-07, and Sunosi (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 (A) $2,910,000 in connection with the drawn amount of Tranche 1A plus (B) 4.5% on the draw down of Tranche 1B and the aggregate amount of all term future loan advances. 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 First Amendment 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 First Amendment 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 First Amendment Closing Date. These percentages are unchanged from the First Amendment to the Loan Agreement.

The Company evaluated whether the Hercules Term Loan entered into in March 2022 represented a debt modification or extinguishment in accordance with ASC 470-50, Debt – Modifications and Extinguishments. As the present value of the cash flows under the terms of the Second Amendment to the Hercules Agreement is less than 10% different from the remaining cash flows under the terms of the First amendment, the Second Amendment was accounted for as a debt modification. The unamortized balance of debt discount costs incurred in connection with those loans and additional debt discount costs incurred in connection with entry into the Hercules Second Amendment to the Loan Agreement, are being amortized through maturity in October 2026 utilizing the effective interest rate method.

Loan Interest Expense and Amortization

The interest expense, amortization expense for the final payment fee and debt discount related to the issuance costs and warrants for our debt is as follows:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2022	2021	2022	2021
Interest Expense	$ 1,874,674	$ 1,156,458	$ 2,998,632	$ 2,300,208
Amortization of final payment fee	160,179	149,281	258,039	292,870
Amortization of debt discount related issuance costs and warrants	299,486	132,508	424,983	267,882

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

	June 30, 2022	December 31, 2021
Total Outstanding Debt	$ 95,000,000	$ 50,000,000
Add: accreted liability of final payment fee	952,722	706,407
Less: unamortized debt discount, long-term	(2,493,898)	(1,616,885)
Less: current portion of long-term debt	—	—
Loan payable, long-term	$ 93,458,824	$ 49,089,522

Scheduled Principal Payments on Outstanding Debt, as of June 30, 2022, are as follows:

2022	—
2023	—
2024	—
2025	15,202,884
2026	79,797,116
Total principal payments outstanding	$ 95,000,000

The Company was in compliance with all covenants and requirements of its financing arrangements as of and during the six months ended June 30, 2022.

Note 10. 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,	
	2022	2021	2022	2021
Basic and diluted net loss per common share:				
Net loss	$ (41,438,516)	$ (32,284,209)	$ (81,070,827)	$ (61,544,179)
Weighted average common shares outstanding—basic and diluted	39,081,100	37,595,069	38,704,227	37,512,716
Net loss per common share—basic and diluted	$ (1.06)	$ (0.86)	$ (2.09)	$ (1.64)

The following potentially dilutive securities outstanding at June 30, 2022 and 2021 have been excluded from the computation of diluted weighted average shares outstanding, as they would be anti-dilutive:

	June 30,	
	2022	2021
Stock options	6,522,561	4,461,985
Restricted stock units	713,311	309,126
Warrants	50,796	15,541
Total	7,286,668	4,786,652

Note 11. Commitments and Contingencies

Operating Leases

For the three and six months ended June 30, 2022 and 2021, the Company had the following operating lease expense:

	Statement of Operations Location	Three Months Ended June 30, 2022	Three Months Ended June 30, 2021	Six Months Ended June 30, 2022	Six Months Ended June 30, 2021
Operating lease expense	General and administrative	290,769	286,923	581,538	573,846
Total operating lease expense		290,769	286,923	581,538	573,846

Future minimum lease payments of the Company's operating leases as of June 30, 2022 were as follows:

2022	$ 615,000
2023	105,000
2024	—
2025	—
Thereafter	—
Total lease payments	720,000
Less imputed interest	(10,880)
Present value of operating lease liabilities	$ 709,120

In January 2022, the Company entered into an agreement to extend the lease of 22 Cortlandt Street for a term of six months from August 1, 2022 through January 31, 2023. As of June 30, 2022, the remaining lease term for our operating lease was 0.6 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 12. Stockholders' Equity

Capital Structure

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. The December 2019 Sales Agreement was replaced by the March 2022 Sales Agreement (see below).

In March 2022, the Company entered into the March 2022 Sales Agreement with SVB Leerink, pursuant to which the Company may sell up to $200 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 March 2022 Sales Agreement. The March 2022 Sales Agreement supersedes the December 2019 Sales Agreement, dated December 5, 2019, by and between the Company and SVB Leerink LLC.

Under the December 2019 Sales Agreement and March 2022 Sales Agreement, for the six months ended June 30, 2022, the Company received approximately $58.6 million in gross proceeds through the sale of 1,914,747 shares, of which net proceeds were approximately $56.8 million.

Upon the closing of the Second Amendment, Hercules also purchased 152,487 of the Company's unregistered common stock for a total consideration of $5.0 million at a share price equal to $32.79 per share, pursuant to a share transfer agreement.

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 $292.9 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 3,341,813 shares available for the issuance of stock options or stock-based awards under the Company's 2015 Omnibus Incentive Compensation Plan at June 30, 2022.

Stock Options

The following table sets forth the stock option activity for the six months ended June 30, 2022:

	Number of shares	Weighted average exercise price	Weighted average contractual term	Aggregate intrinsic value
Outstanding at December 31, 2021	5,090,377	$ 28.89		
Granted	1,590,426	31.62		
Exercised	(24,706)	14.49		
Forfeited	(111,376)	41.51		
Expired	(22,160)	46.50		
Outstanding at June 30, 2022	6,522,561	$ 28.98	7.5	$ 95,081,479
Vested and expected to vest at June 30, 2022	6,522,561	$ 28.98	7.5	$ 95,081,479
Exercisable at June 30, 2022	3,170,564	$ 17.70	5.8	$ 76,800,643

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 $23.70 per option for the six months ended June 30, 2022. As of June 30, 2022, there was $90.3 million of total unrecognized compensation cost related to non-vested stock options which is expected to be recognized over a weighted average period of 3.1 years. These amounts do not include 6,169 options outstanding as of June 30, 2022, 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, 2022, total compensation cost not yet recognized related to unvested RSUs was $19.2 million, which is expected to be recognized over a weighted-average period of 3.3 years.

The following table sets forth the RSU activity for the six months ended June 30, 2022:

	Number of shares	Weighted average grant date fair value
Outstanding at December 31, 2021	302,764	$ 42.93
Granted	482,793	23.85
Vested	(63,330)	42.19
Forfeited	(8,916)	40.51
Outstanding at June 30, 2022	713,311	$ 30.12

Stock-based compensation expense recognized for the three and six months ended June 30, 2022 and 2021 was allocated as follows:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2022	2021	2022	2021
Research and development	$ 2,679,848	$ 2,302,504	$ 4,489,325	$ 3,836,899
General and administrative	7,481,830	3,153,738	13,270,682	5,350,440
Total	$ 10,161,678	$ 5,456,242	$ 17,760,007	$ 9,187,339

Warrants

The following table summarizes warrant activity for the six months ended June 30, 2022:

	Warrants	Weighted average exercise price
Outstanding at December 31, 2021	15,541	$ 80.43
Issued	35,255	31.91
Exercised	—	—
Outstanding at June 30, 2022	50,796	$ 46.75

Outstanding Warrants

In connection with the entry into the Second Amendment, Hercules received warrants to purchase an aggregate 35,255 shares of the Company's common stock at an exercise price of $31.91 per share ("2022 warrants") and in connection with the first advance of the 2020 Term Loan, Hercules received warrants to purchase an aggregate 15,541 shares of the Company's common stock at an exercise price of $80.43 per share ("2020 warrants").

Both the 2022 warrants and 2020 warrants were priced using 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 $0.8 million for the 2022 warrants and $0.9 million for the 2020 warrants 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 13. 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 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 year ended 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 related to the licensed products. Pfizer will also have a right of first negotiation on any potential future strategic transactions involving AXS-12 and AXS-14. During the three and six months ended June 30, 2022 and 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, 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.

Note 14. Royalty Agreements

Pursuant to the Purchase Agreement, the Company agreed to make non-refundable, non-creditable royalty payments to Jazz equal to a (A) high-single digit royalty for any Current Indication (as defined in the Purchase Agreement), or (B) mid-single digit royalty for any Future Indication (as defined in the Purchase Agreement), of Net Sales (as defined in the Purchase Agreement) in the U.S. Territory (as defined in the Purchase Agreement) made during the applicable Royalty Term (as defined in the Purchase Agreement). There are no royalty payments due to Jazz for Net Sales outside of the U.S. Territory.

At the initial closing, the Company assumed all of the commitments of Jazz to SK and Aerial. SK is the originator of the Product and retains rights in twelve Asian markets, including China, Korea, and Japan. In 2014, Jazz acquired from Aerial worldwide rights to Sunosi excluding those Asian markets stated previously. The assumed commitments to SK and Aerial include single-digit tiered royalties based on the Company's sales of Sunosi, and additionally, the Company is committed to pay up to $165 million based on revenue milestones and $1 million based on development milestones.

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, 2021 which was *filed with the Securities and Exchange Commission, or SEC, on March 1, 2022*.

Overview

We are a biopharmaceutical company developing and delivering 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 CNS portfolio includes Sunosi® and four CNS product candidates, AXS-05, AXS-07, AXS-12, and AXS-14 which are being developed for multiple indications.

In May 2022, we acquired the U.S. rights to Sunosi® from Jazz Pharmaceuticals, ("Jazz"). Sunosi was launched in the U.S. in 2019 as a therapy to improve wakefulness in adult patients with EDS associated with narcolepsy or OSA. Sunosi was approved in Europe in 2020, and the rolling launch is ongoing. Sunosi was approved in Canada in 2021. Sunosi® is the first and only dual-acting dopamine and norepinephrine reuptake inhibitor, or DNRI approved by the FDA to treat EDS in narcolepsy or OSA
. It is synergistic with the rest of our late-stage psychiatry and neurology pipeline
.
We intend to develop Sunosi for a new indication in ADHD with a Phase 3 trial initiation planned in 2022.

We refer herein to our four product candidates and Sunosi, collectively, as our products.

AXS-05 is being developed for the treatment of major depressive disorder, or MDD, for which a New Drug Application, or NDA, has been submitted and accepted for filing by the FDA. The FDA had set a Prescription Drug User Fee Act (PDUFA) target action date for the AXS-05 NDA of August 22, 2021, which was not completed on such date and therefore the review of the application is ongoing. AXS-05 is also under development for the treatment of Alzheimer's disease agitation, or AD agitation. AXS-05 is also being developed for smoking cessation. AXS-07 is being developed for the acute treatment of migraine, for which an NDA was submitted and had a PDUFA target action date of April 30, 2022. On April 29, 2022, we received a Complete Response Letter (CRL) from the FDA regarding the NDA for AXS-07 for the acute treatment of migraine. AXS-12 is being developed for the treatment of narcolepsy. AXS-14 is being developed for the treatment of fibromyalgia. 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 dextromethorphan and bupropion and utilizes our metabolic inhibition technology. The dextromethorphan component of AXS-05 is an uncompetitive antagonist of the NMDA, an ionotropic glutamate receptor. The dextromethorphan component of AXS-05 is also a sigma-1 receptor agonist. The bupropion component of AXS-05 serves to increase the bioavailability of dextromethorphan and is a norepinephrine and dopamine reuptake inhibitor. We are seeking 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 trial. AXS-05 achieved the primary endpoint in the ADVANCE 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 with Duke University.

We have submitted an NDA for AXS-05 for the treatment of MDD supported by the positive results from the ASCEND and GEMINI trials which was accepted for filing by the FDA and was granted Priority Review, resulting in a PDUFA target action date of August 22, 2021. On August 20, 2021, the FDA informed us that its review would not be completed by the PDUFA target action date and the review of the application is ongoing.

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 Tmax, 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-HT1B/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 are seeking 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 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. We have submitted an NDA for AXS-07 for the acute treatment of migraine supported by the positive results from the MOMENTUM and INTERCEPT trials which was accepted for filing by the FDA with a PDUFA target action date of April 30, 2022. On April 29, 2022, the Company received a CRL from the FDA regarding its NDA for AXS-07 for the acute treatment of migraine. The CRL did not identify or raise any concerns about the clinical efficacy or safety data in the NDA, and the FDA did not request any new clinical trials to support the approval of AXS-07. The principal reasons given in the CRL relate to chemistry, manufacturing, and controls considerations. The Company believes that the issues raised in the CRL are addressable and intends to provide potential timing for a resubmission following consultation with the FDA.

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 study. A randomized, placebo-controlled Phase 3 trial with AXS-12 in narcolepsy was initiated in the third quarter of 2021, which we refer to as the SYMPHONY study, and one open-label long-term safety extension study was also initiated.

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 management 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 2023 for the management of fibromyalgia based on a pre-NDA meeting with the FDA which occurred in the second quarter of 2021.

Since our incorporation in January 2012, our operations to date have included organizing and staffing our company, business planning, raising capital, developing our compounds, engaging in other discovery and preclinical activities and commencing the commercialization of Sunosi. Subsequent to our IPO, we have raised capital 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 have recently begun commercial sales of Sunosi but we do not expect to generate significant revenue unless and until we successfully commercialize Sunosi and/or at least one of our product candidates.

We have incurred significant operating expenses and net losses since inception. We incurred net losses of $81.1 million and $61.5 million for the six months ended June 30, 2022 and 2021, respectively. Our accumulated deficit as of June 30, 2022 was $490.3 million, and we expect to incur significant expenses and increasing operating losses for the foreseeable future. We expect to incur commercialization expenses for Sunosi as we look to continue to support the growth of the product. 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. As we continue to seek regulatory approval for our product candidates, we expect to incur significant expenses in order to continue to create an infrastructure and support market readiness for the commercialization of our product candidates, 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

Acquisition of Assets of Jazz Pharmaceuticals

In March 2022, we entered into an Asset Purchase Agreement (the “Purchase Agreement”) with Jazz, pursuant to which the Company was to acquire Sunosi from Jazz (the "Acquisition"), a dual-acting dopamine and norepinephrine reuptake inhibitor indicated to improve wakefulness in adult patients living with excessive daytime sleepiness due to narcolepsy or obstructive sleep apnea, which was approved by the FDA in 2019 and by the European Medicines Agency, or EMA, in 2020. On May 9, 2022, we completed the acquisition of the U.S. rights for Sunosi. The sale and purchase of the Specified Ex-U.S. Assets contemplated by the Asset Purchase Agreement is expected to occur during the fourth quarter of 2022.

AXS-05

In January 2022, we provided a response to the FDA addressing the two, previously disclosed, deficiencies related to analytical methods in the Chemistry, Manufacturing, and Controls, or CMC, section of our NDA for AXS-05 for the treatment of major depressive disorder. At this time, we have not been made aware of any other deficiencies related to the NDA by the FDA.

In April 2022, we announced that we have received, and agreed to, Postmarketing Requirements/Commitments proposed by the FDA with respect to the NDA for our AXS-05 product candidate for the treatment of major depressive disorder.

In June 2022, we received from the FDA proposed labeling for AXS-05 with respect to our NDA for the treatment of major depressive disorder.

AXS-07

On February 2022, we entered into a Litigation Discontinuance Agreement with Baudax Bio, Inc. (“Baudax”) pursuant to which Baudax was to voluntarily dismiss, with prejudice, its lawsuit against us in the United States District Court for the District of Delaware (the “Baudax Action”). The Baudax Action, which was never served on us, alleged that our AXS-07 drug product candidate infringes on U.S. Patents 8,512,727 and 10,471,067, both owned by assignment by Baudax. A notice of dismissal with prejudice was filed by Baudax in the Baudax action on February 7, 2022.

In April 2022, we received a Complete Response Letter, or CRL, from the FDA regarding our NDA for AXS-07 for the acute treatment of migraine. The CRL did not identify or raise any concerns about the clinical efficacy or safety data in the NDA, and the FDA did not request any new clinical trials to support the approval of AXS-07. The principal reasons given in the CRL relate to chemistry, manufacturing, and controls (CMC) considerations.

Financial

In March 2022, we entered into a Sales Agreement with SVB Securities LLC, or SVB Securities, with respect to an at the market offering program, under which we may, from time to time in our sole discretion, issue and sell through SVB Securities, acting as sales agent, shares of our common stock of up to $200 million. The Agreement supersedes the prior Sales Agreement, dated December 5, 2019, by and between us and SVB Leerink LLC.

In May 2022, we entered in the Second Amendment to the Loan and Security Agreement (the "Second Amendment"). in connection with the Acquisition (as described above) with Hercules Capital, Inc. The Second Amendment amends the terms of that certain Loan and Security Agreement, dated as of September 25, 2020, by and among the Company, Hercules and the Lenders (as amended by that certain First Amendment to Loan and Security Agreement, dated as of October 14, 2021).

Financial Overview

Revenue

Net revenues from product sales consist of sales of Sunosi, which we acquired in May 2022. We generated approximately $8.8 million in net revenue from product sales in the quarter ended June 30, 2022.

We expect that Sunosi revenues are likely to fluctuate based on demand quarter to quarter. We will not generate revenue from other products unless and until we successfully develop, obtain regulatory approval of, and commercialize one of our current or future product candidates. We have incurred significant operating losses since inception. 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 from such product candidates, 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.

Cost of product sales

Cost of product sales is the fair value of inventory acquired from Jazz and sold during the period. Additionally, it includes royalty expense. In the future, it will be comprised of direct costs of formulating, manufacturing and packaging drug product, overhead costs consisting of labor, customs, stock based compensation, shipping, outside inventory management and other miscellaneous operating costs, and royalty payments on product sales.

Research and Development Expenses

Research and development expenses primarily include preclinical studies, clinical trials, manufacturing costs, employee-related expenses including salaries, benefits, travel, and 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 to what extent we will generate revenue from the commercialization and sale of Sunosi or our product candidates if we obtain 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 products for the three and six months ended June 30, 2022 and 2021:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2022	2021	2022	2021
Sunosi	$ 964,353	$ —	$ 964,353	$ —
AXS-05	6,483,993	2,184,776	12,514,433	12,228,922
AXS-07	2,202,943	7,290,067	4,349,430	9,821,616
AXS-12	1,641,781	819,569	3,523,317	1,553,427
AXS-14	703,102	4,039	944,449	4,039
Other research and development	1,116,182	1,902,371	1,592,036	3,654,111
Stock-based compensation	2,679,848	2,302,504	4,489,325	3,836,899
Total research and development expenses	$ 15,792,202	$ 14,503,326	$ 28,377,343	$ 31,099,014

During the six months ended June 30 2021, the category "Other research and development expenses" primarily consisted of employee salaries and benefits, facilities, and overhead costs. Beginning July 2021, employee salaries and benefits were allocated to specific products.

Selling, general and administrative expenses

Selling, 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. Selling, general and administrative expenses are expensed when incurred.

Interest income (expense)

Interest income (expense) 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 income (expense) 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 material changes to our critical accounting policies since the beginning of our fiscal year. We believe that our most critical accounting policies are those relating to variable consideration associated with revenue recognition, business combinations and contingent consideration. Our critical accounting policies are described in the notes to the 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 June 30,		Six Months Ended June 30,	
	2022	2021	2022	2021
Revenues:				
Product sales, net	$ 8,819,786	$ —	$ 8,819,786	$ —
Operating expenses:				
Cost of product sales (excluding amortization and depreciation)	982,836	—	982,836	—
Research and development	15,792,202	14,503,326	28,377,343	31,099,014
Selling, general and administrative	31,160,140	16,344,361	56,863,871	27,592,734
Gain in fair value of contingent consideration	(860,000)	—	(860,000)	—
Intangible asset amortization	925,650	—	925,650	—
Total operating expenses	48,000,828	30,847,687	86,289,700	58,691,748
Loss from operations	(39,181,042)	(30,847,687)	(77,469,914)	(58,691,748)
Interest income (expense)	(2,257,474)	(1,436,522)	(3,600,913)	(2,852,431)
Net loss	$ (41,438,516)	$ (32,284,209)	$ (81,070,827)	$ (61,544,179)

Comparison of the three months ended June 30, 2022 and 2021

Product sales, net. We acquired the U.S. rights to Sunosi from Jazz on May 9, 2022. We sold Sunosi in the United States through a single 3PL. The 3PL distributes the product to wholesale distributors with whom we have entered into formal distribution agreements.

Cost of product sales. In connection with the Sunosi acquisition, we acquired inventory which was sold through our 3PL as described above. This also includes the royalty expense to SK and Aerial.

Research and Development Expenses. Our research and development expenses for the three months ended June 30, 2022 were $15.8 million, compared to $14.5 million for the three months ended June 30, 2021, an increase of $1.3 million. The increase was driven by expenses related to personnel expense and ongoing clinical trial costs.

Selling, general and administrative Expenses. Our selling, general and administrative expenses for the three months ended June 30, 2022 were $31.2 million, compared to $16.3 million for the three months ended June 30, 2021, an increase of $14.9 million. The increase was primarily related to pre-commercial activities, commercial activities for the Sunosi acquisition, personnel expense, along with an increase in non-cash stock compensation expense.

Gain in Fair Value of Contingent Consideration. The change in fair value of contingent consideration was primarily due to the change in significant unobservable inputs such as the discount rates.

Intangible asset amortization. As part of the preliminary purchase price allocation, we determined the identifiable intangible asset is developed technology. We amortize the intangible asset over its useful life of 10 years.

Interest income (expense). Interest and amortization of debt discount expense for the three months ended June 30, 2022 was $2.3 million, compared to $1.4 million for the three months ended June 30, 2021, an increase of $0.9 million. The increase is mainly due to higher debt balance compared to the prior comparable period since we amended our loan and security agreement with Hercules in May 2022.

Comparison of the six months ended June 30, 2022 and 2021

Product sales, net. We acquired the U.S. rights to Sunosi from Jazz on May 9, 2022. We sold Sunosi in the United States through a single 3PL. The 3PL distributes the product to wholesale distributors with whom we have entered into formal distribution agreements.

Cost of product sale. In connection with the Sunosi acquisition, we acquired inventory which was sold through our 3PL as described above. This also includes the royalty expense to SK and Aerial.

Research and Development Expenses. Our research and development expenses for the six months ended June 30, 2022 were $28.4 million, compared to $31.1 million for the six months ended June 30, 2021, a decrease of $2.7 million. The decrease was driven by NDA fees that were incurred in the prior comparable period.

Selling, general and administrative Expenses. Our selling, general and administrative expenses for the six months ended June 30, 2022 were $56.9 million, compared to $27.6 million for the six months ended June 30, 2021, an increase of $29.3 million. The increase was primarily related to pre-commercial activities, commercial activities for the Sunosi acquisition, personnel expense, along with an increase in non-cash stock compensation expense.

Gain in Fair Value of Contingent Consideration. The change in fair value of contingent consideration was primarily due to the change in significant unobservable inputs such as the discount rates.

Intangible asset amortization. As part of the preliminary purchase price allocation, the Company determined the identifiable intangible asset is developed technology. We amortize the intangible asset over its useful life of 10 years.

Interest income (expense). Interest and amortization of debt discount expense for the six months ended June 30, 2022 was $3.6 million, compared to $2.9 million for the six months ended June 30, 2021, an increase of $0.7 million. The increase is mainly due to higher debt balance compared to the prior comparable period since we amended our loan and security agreement with Hercules in May 2022.

Liquidity and Capital Resources

Since our inception through June 30, 2022, we have financed our operations primarily through proceeds from equity offerings and debt borrowings. See discussion below.

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.

In March 2022, we entered into the March 2022 Sales Agreement with SVB Securities, pursuant to which we may sell up to $200 million in shares of our common stock from time to time through SVB Securities, acting as our sales agent, in one or more at-the-market offerings utilizing the 2019 Shelf Registration Statement. SVB Securities is entitled to receive a commission of 3.0% of the gross proceeds for any shares sold under the March 2022 Sales Agreement. The March 2022 Sales Agreement supersedes the December 2019 Sales Agreement, dated December 5, 2019, by and between the Company and SVB Leerink LLC.

Under both the December 2019 and March 2022 Sales Agreements, for the six months ended June 30, 2022, we received approximately $58.6 million in gross proceeds through the sale of 1,914,747 shares, of which net proceeds were approximately $56.8 million.

In March 2022, we entered into a Second Amendment to Loan and Security Agreement with Hercules Capital, Inc. The Second Amendment amends the terms of that certain Loan and Security Agreement, dated as of September 25, 2020, by and among us, Hercules and the Lenders (as amended by that certain First Amendment to Loan and Security Agreement, dated as of October 14, 2021, and as further amended by the Second Amendment). In connection with the Second Amendment, the parties also clarified certain terms of the Warrant Agreement previously issued to Hercules. The Second Amendment was effective upon the closing of the Acquisition on May 9, 2022. See 'Contractual Obligations and Commitments - March 2022 Second Amendment to the Loan and Security Agreement – Hercules' section below for more information.

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 that our current available cash, along with the remaining committed capital from the $300 million term loan facility, is sufficient to fund anticipated operations into 2024, based on the current operating plan, which includes the potential launch of AXS-05 in MDD and the commercialization of Sunosi. 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,	
	2022	**2021**
Net cash (used in) provided by:		
Operating activities	$ (66,189,636)	$ (52,609,042)
Investing activities	(53,455,195)	(48,872)
Financing activities	106,566,617	10,000,551
Net increase (decrease) in cash	$ (13,078,214)	$ (42,657,363)

Operating Activities. Cash used in operating activities for the six months ended June 30, 2022 was $66.2 million as compared to $52.6 million for the six months ended June 30, 2021. The increase of $13.6 million in net cash used was mainly due to the commercialization activities.

Investing Activities. Cash used in investing activities for the six months ended June 30, 2022 was $53.5 million and was less than $0.1 million for the six months ended June 30, 2021. The increase was due to the Sunosi acquisition for $53 million.

Financing Activities. Cash provided by financing activities was $106.6 million for the six months ended June 30, 2022, which included net proceeds from Tranche 1B related to the Second Amendment of the Loan and Security Agreement with Hercules of $45.0 million along with the purchase of 152,487 shares of our common stock for a total consideration of $5.0 million by Hercules, the sale of common stock through our Sales Agreement with SVB Securities of $56.8 million and proceeds from the issuance of common stock upon exercise of employee stock options of $0.4 million. 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 SVB Securities 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.

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 product, including Sunosi. 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.

March 2022 Second Amendment to the Loan and Security Agreement – Hercules

In March 2022, we entered into a Second Amendment to Loan and Security Agreement with Hercules Capital, Inc. The Second Amendment amends the terms of that certain Loan and Security Agreement, dated as of September 25, 2020, by and among us, Hercules and the Lenders (as amended by that certain First Amendment to Loan and Security Agreement, dated as of October 14, 2021, and as further amended by the Second Amendment). In connection with the Second Amendment, the parties also clarified certain terms of the Warrant Agreement previously issued to Hercules. The Second Amendment was effective upon the closing of the Acquisition on May 9, 2022.

The Second Amendment changed the Term Loan Advance (as defined in the Loan Agreement) amounts and dates available under Tranche 1 through Tranche 5, including increasing the Tranche 1 Advance (as defined in the Loan Agreement) from $60.0 million to $95.0 million, changing the Tranche 2 Advances (as defined in the Loan Agreement) from two sub-tranches of $50.0 million each to three sub-tranches of $35.0 million, $35.0 million and $30.0 million, respectively, changing the Tranche 3 Advance (as defined in the Loan Agreement) from one tranche of $20.0 million to two sub-tranches of $15.0 million and $5.0 million, respectively, decreasing the Tranche 4 Advance (as defined in the Loan Agreement) from $55.0 million to $50.0 million, and decreasing the Tranche 5 Advance (as defined in the Loan Agreement) from $75.0 million to $35.0 million; (iii) modified the interest rate (a floating rate based on the greater of (a) 8.95% or (b) US WSJ Prime + 5.70%) to not exceed 10.70%; and (iv) changed the minimum cash requirement of the Company from $15,000,000 (plus certain accounts payable amounts) to $40,000,000 (plus certain accounts payable amounts), provided that upon U.S. Food and Drug Administration (the "FDA") approval of the Company's AXS-05 product candidate for the treatment of major depressive disorder, the minimum cash requirement shall be $25.0 million (plus certain accounts payable amounts).

Royalty Agreements

Pursuant to the Purchase Agreement, we agreed to make non-refundable, non-creditable royalty payments to Jazz equal to a (A) high-single digit royalty for any Current Indication or (B) mid-single digit royalty for any Future Indication, of Net Sales in the U.S. Territory made during the applicable Royalty Term (in each case, as those terms are defined in the Purchase Agreement). There are no royalty payments due to Jazz for Net Sales outside of the U.S. Territory.

At the initial closing, we assumed all of the commitments of Jazz to SK and Aerial. SK is the originator of Sunosi and retains rights in twelve Asian markets, including China, Korea, and Japan. In 2014, Jazz acquired from Aerial worldwide rights to Sunosi excluding those Asian markets stated previously. The assumed commitments to SK and Aerial include single-digit tiered royalties based on our sales of Sunosi, and we are committed to pay up to $165 million based on revenue milestones and $1 million based on development milestones.

Employees and Human Capital Management

As of August 1, 2022, we had 198 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. Many 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 took 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, which has 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 global pandemic.

Operations and Liquidity

The full impact of the COVID-19 pandemic is still unknown and constantly 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 continuous 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 March 2022 Sales Agreement and debt facility, 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, 2022.

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 $73.4 million and $86.5 million as of June 30, 2022 and December 31, 2021, 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 manufactures located in Europe and certain invoices are denominated in foreign currencies. 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, 2022 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 six months ended June 30, 2022.

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. During the quarter ended June 30, 2022, other than continuing changes to our internal control process resulting from acquisition of Sunosi, there have been no changes in internal controls over financial reporting that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

PART II. OTHER INFORMATION

ITEM 1. LEGAL PROCEEDINGS.

Except as described herein, 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 also become involved in various claims and legal actions arising in the ordinary course of business.

Securities Class Action

On May 13, 2022, Evy Gru filed a putative class action complaint captioned Gru v. Axsome Therapeutics, Inc., et. al., in the U.S. District Court for the Southern District of New York against the Company and certain of its current and former officers and one director (the "Securities Class Action"). The complaint asserts claims under Sections 10(b) and 20(a) of the Securities Exchange Act of 1934, as amended, and Rule 10b-5 promulgated thereunder, and alleges, among other things, that the defendants made false statements and omissions concerning the Company's Chemistry Manufacturing and Controls practices, and its New Drug Application with the FDA, with respect to one of its product candidates, AXS-07. The plaintiff seeks unspecified damages, fees, interest, and costs. The Company has not yet answered or otherwise responded to the complaint.

Shareholder Derivative Action

On July 21, 2022, Daniel Engel filed a stockholder derivative complaint captioned Engel v. Herriot Tabuteau, et. al., in the U.S. District Court for the Southern District of New York against the Company's current directors, certain of the Company's current and former officers, and the Company (as nominal defendant). The complaint arises out of similar allegations as those made in the Securities Class Action. The plaintiff asserts claims for breach of fiduciary duties against all of the defendants and for contribution for violations of Section 10(b) and 21D of the Securities Exchange Act of 1934. The plaintiff seeks unspecified damages, fees, interest, and costs, as well as corporate governance changes. The Company has not yet answered or otherwise responded to the complaint.

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 a minimal history of commercializing products, which may make it difficult to evaluate our business and prospects.***

- ***We are substantially dependent on the success of our products and cannot guarantee that any of our products will successfully complete any planned or ongoing 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, they may not ultimately lead to a faster approval process or faster development of regulatory review and they will not increase the likelihood that our product candidates will receive marketing approval, for example, Breakthrough Therapy designation by the FDA for AXS-05 for the treatment of MDD and for the treatment of AD agitation.***

- ***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 by 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 products 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 ongoing COVID-19 pandemic.***

- ***As an NDA applicant and 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 products effectively, including by making 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. Our business may be materially harmed if the licenses are not available or terminated for any reason.***

- ***If we fail to comply with federal, state, and foreign healthcare laws, including fraud and abuse and transparency and health and other data protection, 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 health maintenance organization (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.***

- ***If we fail to maintain an effective system of internal controls over financial reporting, 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 may 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-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 $81.1 million for the six months ended June 30, 2022 and $130.4 million for the year ended December 31, 2021. As of June 30, 2022, we had an accumulated deficit of $490.3 million. To date, we have not received regulatory approvals for any of our product candidates. We recently acquired the U.S. rights to Sunosi and have begun commercial sale of Sunosi in the US. We refer herein to our four product candidates and Sunosi, collectively, as our products. 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 Sunosi and our current and future product candidates, if they are approved by the 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, regulatory, 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;
- 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;
- conduct our clinical trials with AXS-05 in depression and AD agitation;
- conduct our clinical trials 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 other CNS disorders;
- continue to evaluate, plan for, and potentially submit an NDA for AXS-14 in fibromyalgia;
- continue to expand commercial sales of Sunosi;
- 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/or 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, or if we are able to successfully commercialize approved commercial products that we have acquired, such as Sunosi. 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 may 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 that our current available cash, along with the remaining committed capital from the $300 million term loan facility, is sufficient to fund anticipated operations into 2024, based on the current operating plan, which includes the potential launch of AXS-05 in MDD, and the acquisition and commercialization of Sunosi. We have based this estimate on the assumption that AXS-05 will be approved in 2022, which will give us access to additional funds under the 2020 Term Loan. However, if AXS-05 is not approved, or such approval is delayed, we believe our current available cash is sufficient to fund our anticipated operations, based on the current operating plan, for at least 12 months. Our assumptions 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 expanding 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 an 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 third parties manufacture, 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. In October 2021, we entered into a First Amendment to the Loan Agreement to, among other things, increase the size of the 2020 Term Loan to $300.0 million. In March 2022, we entered into a Second Amendment to the 2020 Term Loan that among other things, changed the terms of the Term Loan Advances (as defined in the 2020 Term Loan) upon the consummation of the Acquisition. 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, upon the Second Amendment closing date, 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 $40.0 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. The $40.0 million threshold decreases to $25.0 million upon achievement of the AXS-05 milestone. Further, effective upon the later of (i) the last calendar month of the calendar quarter that is nine months following the earlier of (x) the date that the AXS-05 Milestone is achieved (y) the date that the AXS-07 Milestone is achieved, or (z) the final closing date of the Sunosi acquisition, we are obligated to (A) ensure that at all times our market capitalization exceeds $1.0 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 50% 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 85% 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 our board of directors approved forecast solely from the sale of AXS-05, AXS-07, and Sunosi (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.

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 a minimal 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, developing our product candidates, including undertaking preclinical studies and conducting clinical trials of our product candidates, and our recent acquisition and commercialization of Sunosi. We have not yet demonstrated an ability to obtain regulatory approval for, or successfully commercialize, a product candidate and we have only recently begun commercial sales of Sunosi. In addition, as a relatively nascent business, we may encounter unforeseen expenses, difficulties, complications, delays, and other known and unknown difficulties. If any of 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.

We are currently operating in a period of economic uncertainty and capital markets disruption, which has been significantly impacted by geopolitical instability due to the ongoing military conflict between Russia and Ukraine. Our business, financial condition and results of operations could be materially adversely affected by any negative impact on the global economy and capital markets resulting from the conflict in Ukraine or any other geopolitical tensions.

U.S. and global markets are experiencing volatility and disruption following the escalation of geopolitical tensions and the start of the military conflict between Russia and Ukraine. On February 24, 2022, a full-scale military invasion of Ukraine by Russian troops was reported. Although the length and impact of the ongoing military conflict is highly unpredictable, the conflict in Ukraine could lead to market disruptions, including significant volatility in commodity prices, credit and capital markets, as well as supply chain interruptions. We are continuing to monitor the situation in Ukraine and globally and assessing its potential impact on our business.

Additionally, the recent military conflict in Ukraine has led to sanctions and other penalties being levied by the United States, European Union and other countries against Russia. Additional potential sanctions and penalties have also been proposed and/or threatened. Russian military actions and the resulting sanctions could adversely affect the global economy and financial

markets and lead to instability and lack of liquidity in capital markets, potentially making it more difficult for us to obtain additional funds.

Although our business has not been materially impacted by the ongoing military conflict between Russian and Ukraine to date, it is impossible to predict the extent to which our operations, or those of our suppliers and manufacturers, will be impacted in the short and long term, or the ways in which the conflict may impact our business. The extent and duration of the military action, sanctions and resulting market disruptions are impossible to predict, but could be substantial. Any such disruptions may also magnify the impact of other risks described herein.

Climate change or legal, regulatory or market measures to address climate change may negatively affect our business, results of operations, cash flows and prospects.

We believe that climate change has the potential to negatively affect our business and results of operations, cash flows and prospects. We are exposed to physical risks (such as extreme weather conditions or rising sea levels), risks in transitioning to a low-carbon economy (such as additional legal or regulatory requirements, changes in technology, market risk and reputational risk) and social and human effects (such as population dislocations and harm to health and well-being) associated with climate change. These risks can be either acute (short-term) or chronic (long-term).

The adverse impacts of climate change include increased frequency and severity of natural disasters and extreme weather events such as hurricanes, tornados, wildfires (exacerbated by drought), flooding, and extreme heat. Extreme weather and sea-level rise pose physical risks to our facilities as well as those of our suppliers. Such risks include losses incurred as a result of physical damage to facilities, loss or spoilage of inventory, and business interruption caused by such natural disasters and extreme weather events. Other potential physical impacts due to climate change include reduced access to high-quality water in certain regions and the loss of biodiversity, which could impact future product development. These risks could disrupt our operations and its supply chain, which may result in increased costs.

New legal or regulatory requirements may be enacted to prevent, mitigate, or adapt to the implications of a changing climate and its effects on the environment. These regulations, which may differ across jurisdictions, could result in us being subject to new or expanded carbon pricing or taxes, increased compliance costs, restrictions on greenhouse gas emissions, investment in new technologies, increased carbon disclosure and transparency, upgrade of facilities to meet new building codes, and the redesign of utility systems, which could increase our operating costs, including the cost of electricity and energy used by us. Our supply chain would likely be subject to these same transitional risks and would likely pass along any increased costs to us.

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

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

We currently have one recently acquired product, Sunosi, 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, including our ability to generate revenue, depends entirely on the successful commercialization of Sunosi and the successful development and commercialization of our product candidates, which may never occur. Furthermore, given the nature of our business, the biopharmaceutical industry in general and the uncertainty and costs associated with developing and commercializing our products within a complicated and costly regulatory regime, our goals, plans and assumptions with respect to our products 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 products. 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 products.

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 and a Phase 3 trial with AXS-12 in narcolepsy are ongoing. 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 NDAs 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 2/3 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;
- 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 labeling 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 certain 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 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 NDAs for AXS-05 and AXS-07 pursuant to the 505(b)(2) process, we have not conducted certain additional clinical trials for these product candidates and, as such, we will have less experience with actual testing of the product candidate.

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

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

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

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

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 and the availability and prioritization of regulatory agency resources. 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 submitted two NDAs 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 limited experience in filing and supporting the applications necessary to gain marketing approvals and 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 fundswe may decide, or regu 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 ADVANCE trial and one additional Phase 3 trial to support an NDA for AXS-05 for the treatment of AD agitation; the Phase 2 CONCERT trial and ongoing SYMPHONY trial to support an NDA for AXS-12 for the treatment of cataplexy and narcolepsy; 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. 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 Alzheimer's disease agitation or 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 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 that 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 product candidates of ours including AXS-05 and AXS-07 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 products 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 Breakthrough Therapy, Fast Track, and other designations are designed to expedite the development and review of drugs, they may not ultimately lead to a faster approval process or faster development of regulatory review and they will not increase the likelihood that our product candidates will receive marketing approval, for example, Breakthrough Therapy designation by the FDA for AXS-05 for the treatment of MDD and for the treatment of AD agitation.

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 products 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 products, 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 will continue to be subject to, ongoing obligations and continued regulatory review, which may result in significant additional expense. Additionally, any of our products, 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.

Our product(s) are and 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 products; 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 GCP, for any clinical trials that we conduct post approval. Even if marketing approval of a product 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 products, 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 our products. 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.

Timelines for the review of our regulatory submissions, including our NDA for AXS-05, by the FDA and other regulatory agencies are subject to change and uncertainty, which may delay the potential approval of any product candidates we seek to develop or commercialize.

We cannot predict the timeline for review of submissions to any regulatory authorities or when any of our product candidates will receive marketing approval, if at all. The timeline for regulatory approval can be affected by a variety of factors, including disruptive effects of the COVID-19 pandemic, budget and funding levels, agency staffing, and statutory, regulatory and policy changes.

For example, although the FDA set a PDUFA target action date of August 22, 2021, for our NDA for AXS-05 for the treatment of MDD, its review of our NDA was not completed on such date and remains ongoing. Although we believe that we have addressed all deficiencies known to us related to the NDA in our responses to the FDA, the FDA's review process for the NDA is not yet complete. Delays or uncertainty in the timing of regulatory action in response to our submissions could adversely impact our development and commercialization efforts and our business prospects.

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 PRODUCTS

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; Biogen Inc.; Biohaven Pharmaceutical Holding Company Ltd.; Eli Lilly and Company; H. Lundbeck A/S; Harmony Biosciences; Intra-Cellular Therapies, Inc.; Janssen; 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, rizatriptan, 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 products, 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, 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 our 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 products, 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, if they are approved, we may be unable to generate product revenues.

We are currently expanding our commercial infrastructure for the marketing, sale, and distribution of pharmaceutical products, which include the creation of a sales force to launch our product candidates throughout the United States. This may require additional compliance with 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 limited 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 and a virtual manufacturer along with the establishment and development of our commercial infrastructure, 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 revenue from those product candidates. Factors that may inhibit our efforts to commercialize any of our products 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 expand our commercial infrastructure, 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.

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 products 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 products 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 of our products. For example, we may be sued if any products 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 products. 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 including 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.

Sunosi is a controlled substance and may be subject to U.S. federal and state controlled substance laws and regulations, and our failure to comply with these laws and regulations, or the cost of compliance with these laws and regulations, could materially and adversely affect our business, results of operations, financial condition and growth prospects.

Sunosi contains controlled substances as defined in the Federal Controlled Substances Act, or CSA. Controlled substances are subject to a number of requirements and restrictions under the CSA and implementing regulations, including certain registration, security, recordkeeping, reporting, import, export and other requirements administered by the U.S. Drug Enforcement Administration, or DEA. The DEA classifies controlled substances into five schedules: Schedule I, II, III, IV or V substances. Schedule I substances by definition have a high potential for abuse, no currently "accepted medical use" in the U.S., lack accepted safety for use under medical supervision, and may not be prescribed, marketed or sold in the U.S. Pharmaceutical products approved for use in the U.S. which contain a controlled substance are listed as Schedule II, III, IV or V, with
Schedule II substances considered to present the highest potential for abuse or dependence and Schedule V substances the lowest relative risk of abuse among such substances. Schedule I and II drugs are subject to the strictest controls under the CSA, including manufacturing and procurement quotas, heightened security requirements and additional criteria for importation. In addition, dispensing of Schedule II drugs is further restricted. For example, they may not be refilled without a new prescription. Sunosi is a Schedule IV controlled substance.

Individual states have also established controlled substance laws and regulations. Though state-controlled substances laws often mirror federal law, they may separately schedule our products or our product candidates as well. We or our partners may also be required to obtain separate state registrations, permits or licenses in order to be able to manufacture, distribute, administer or prescribe controlled substances for clinical trials or commercial sale, and failure to meet applicable regulatory requirements could lead to enforcement and sanctions by the states in addition to those from the DEA or otherwise arising under federal law.

U.S facilities conducting research, manufacturing, distributing, importing or exporting, or dispensing controlled substances must be registered (licensed) to perform these activities and must comply with the security, control, recordkeeping and reporting obligations under the CSA, DEA regulations and corresponding state requirements. DEA and state regulatory bodies conduct periodic inspections of certain registered establishments that handle controlled substances. Obtaining and maintaining the necessary registrations and complying with the regulatory obligations may result in delay of the importation, manufacturing, distribution or clinical research of our products and products candidates. Furthermore, failure to maintain compliance with the CSA and DEA and state regulations by us or any of our contractors, distributors or pharmacies can result in regulatory action that could have a material adverse effect on our business, financial condition and results of operations. DEA and state regulatory bodies may seek civil penalties, refuse to renew necessary registrations, or initiate proceedings to restrict, suspend or revoke those registrations. In certain circumstances, violations could lead to criminal penalties. Any penalties imposed by the DEA to us or our third-party manufacturers which could have a material adverse effect on our business, results of operations, financial condition and growth 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 by 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 could 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, such as 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, when we submit an NDA for review, we are 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 or to meet the related submission requirements can result in enforcement actions, including civil monetary penalties 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 products 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 products, and we do not currently plan to develop any capacity to do so. We currently outsource all manufacturing of our products 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 products may delay the development or commercialization of our products. Moreover, we do not yet in all cases 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 products and programs. Our products 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 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 products or the drug substances used to manufacture them, it will be more difficult for us to develop our products 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 products 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 products 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 products, 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 products 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 or market our products, or obtain regulatory approval for, our product candidates. 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 our product candidates or successfully commercialize our products.

Any failure or refusal to supply our products 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 ongoing 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. The evolving COVID-19 pandemic may impact 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 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. For example, the FDA recently announced an extension to a previous pause on domestic inspections through February 4, 2022, due to the omicron variant of COVID-19, with the goal of restarting inspections as soon as possible. Due to the uncertainty of the COVID-19 pandemic and the FDA's related internal policies, this could impact future applications and approval of product candidates. The FDA has indicated that under certain circumstances it will utilize remote interactive evaluations which include inspection activities "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 adversely impact our business.

The FDA continues to periodically 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.

As an NDA applicant and 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 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 products, 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 products 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:

- collaborators may not perform their obligations as expected;
- collaborators may not pursue development and commercialization of any product candidates which 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, lead to additional responsibilities for us with respect to product candidates, or 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 products effectively, including by making them readily available at the point of care throughout their networks of pharmacies.

In addition to extensive internal efforts, the successful commercialization of our products will require many third parties, over whom we have no control, to decide to utilize our products, 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 products for its own pharmacies, or a PBM will pay retail network pharmacies on behalf of its health plans, any such products 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 products for use in their institutions or reimbursing retail pharmacies outweighs clinical benefits and will resist efforts to add any such products 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 products.

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 products 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 products 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 products may infringe. There could also be existing patents of which we are not aware that any of our current or future products 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 products 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 products 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 products 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. Our business may be materially harmed if the licenses are not available or terminated for any reason.

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.

In connection with the acquisition of Sunosi, in addition to the upfront purchase price, we assumed certain liabilities in connection with the acquisition and agreed to make non-refundable, non-creditable royalty payments to Jazz Pharmaceuticals on U.S. net sales. There are no royalty payments due to Jazz Pharmaceuticals for net sales outside of the U.S. In addition, we assumed all of the commitments of Jazz Pharmaceuticals to SK Biopharmaceuticals Co., Ltd. (SK) and Aerial Biopharma, LLC (Aerial). The assumed commitments to SK and Aerial include single-digit tiered royalties and certain sales and development milestones. We are dependent on these agreements, and if we breach these agreements, 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 products, 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 products 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 products 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 data protection, 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.

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 enacted legislation – the California Consumer Privacy Act, or CCPA – which went into effect in January 2020. The CCPA, among other things, creates 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).

In addition, 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. Moreover, 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.

If we or our operations are found to be in violation of any federal or state healthcare, data or information privacy 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 health maintenance organization (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. It is unclear what impact these various efforts have and will have on our business operations and resulting financial condition. 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. After proceeding through more recent appellate challenges, 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. 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. 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, we anticipate that the 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. For example, under the Biden Administration's Build Back Better Agenda, Medicare negotiation of prescription drug costs with biopharmaceutical companies is proposed to lower prescription drug costs. 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 it would permit certain exemptions and exclusions, and enforcement discretion on certain aspects due to the COVID-19 pandemic, although this situation may continue to evolve. 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 products 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 products involve the controlled storage, use, and disposal of hazardous materials, including the components of our products, 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. 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 of August 1, 2022, we had 198 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 controls over financial reporting, 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.

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.

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

Governmental authorities, non-governmental organizations, customers, investors, external stakeholders and employees are increasingly sensitive to environmental, social and governance, or ESG, concerns, such as diversity and inclusion, climate change, water use, recyclability or recoverability of packaging, and plastic waste. This focus on ESG concerns may lead to new requirements that could result in increased costs associated with developing, manufacturing and distributing our products. Our ability to compete could also be affected by changing customer preferences and requirements, such as growing demand for more environmentally friendly products, packaging or supplier practices, or by failure to meet such customer expectations or demand. While we strive to improve its ESG performance, we risk negative stockholder reaction, including from proxy advisory services, as well as damage to its brand and reputation, if we do not act responsibly, or if we are perceived to not be acting responsibly in key ESG areas, including equitable access to medicines and vaccines, product quality and safety, diversity and inclusion, environmental stewardship, support for local communities, corporate governance and transparency, and addressing human capital factors in our operations. If we do not meet the ESG expectations of its investors, customers and other stakeholders, we could experience reduced demand for its products, loss of customers, and other negative impacts on our business and results of operations.

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 years 2020, 2021, and thus far in 2022, we saw 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 products, or the products of our competitors; and
- the level of underlying demand for our products

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 may be able to exert significant control over matters subject to stockholder approval.

As of August 1, 2022, our executive officers, directors, and 5% stockholders and their affiliates beneficially owned an aggregate of approximately 32% 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 1, 2022, we have outstanding 40,304,124 shares of common stock and 7,325,815 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, 32,302,124 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 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 the proceeds from sales pursuant to our March 2022 “at-the-market” sales agreement with SVB Securities, which provides for the sale of up to $200.0 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, 2021, we had U.S. federal net operating loss, NOL, carryforwards of approximately $364 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 $304 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
10.1**	Form of Warrant Agreement, dated as of May 9, 2022, between Axsome Therapeutics, Inc. and Hercules Capital, Inc.
10.2**	Share Transfer Agreement, dated as of May 9, 2022, by and between Axsome Therapeutics, Inc., Hercules Capital, Inc., Hercules Private Global Venture Growth Fund I L.P., and Hercules Private Credit Fund I L.P.
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, 2022

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

Date: August 9, 2022

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

THIS WARRANT AND THE SHARES ISSUABLE UPON EXERCISE HEREOF HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "ACT"), OR ANY STATE SECURITIES LAWS, AND MAY NOT BE SOLD, OFFERED FOR SALE, PLEDGED, OR HYPOTHECATED IN THE ABSENCE OF AN EFFECTIVE REGISTRATION STATEMENT RELATED THERETO OR, SUBJECT TO SECTION 11 HEREOF, AN OPINION OF COUNSEL IN A FORM SATISFACTORY TO THE COMPANY THAT SUCH REGISTRATION IS NOT REQUIRED UNDER THE ACT, OR ANY APPLICABLE STATE SECURITIES LAWS.

WARRANT AGREEMENT

To Purchase Shares of the Common Stock of

AXSOME THERAPEUTICS, INC.

Dated as of [ ] (the "Effective Date")

WHEREAS, Axsome Therapeutics, Inc., a Delaware corporation (the "Company"), has entered into a Loan and Security Agreement, dated September 25, 2020 (as amended and in effect from time to time, the "Loan Agreement") with Hercules Capital, Inc., a Maryland corporation (the "Warrantholder"), in its capacity as administrative agent, and the lender parties thereto;

WHEREAS, pursuant to the Loan Agreement and as additional consideration to the Warrantholder for, among other things, its agreements in the Loan Agreement, the Company has agreed to issue to the Warrantholder this Warrant Agreement, evidencing the right to purchase shares of the Company's Common Stock (this "Warrant", "Warrant Agreement", or this "Agreement");

NOW, THEREFORE, in consideration of the Warrantholder having executed and delivered the Loan Agreement and provided the financial accommodations contemplated therein, and in consideration of the mutual covenants and agreements contained herein, the Company and Warrantholder agree as follows:

SECTION 1.GRANT OF THE RIGHT TO PURCHASE COMMON STOCK.

(a) For value received, the Company hereby grants to the Warrantholder, and the Warrantholder is entitled, upon the terms and subject to the conditions hereinafter set forth, to subscribe for and purchase, from the Company, up to the number of fully paid and non-assessable shares of Common Stock (as defined below) as determined pursuant to Section 1(b) below, at a purchase price per share equal to the Exercise Price (as defined below). The number and Exercise Price of such shares are subject to adjustment as provided in Section 8. As used herein, the following terms shall have the following meanings:

"Act" means the Securities Act of 1933, as amended.

"Charter" means the Company's Certificate of Incorporation, as may be amended and in effect from time to time.

"Common Stock" means the Company's common stock, $0.0001 par value per share, as presently constituted under the Charter, and any class and/or series of Company capital stock for or into which such common stock may be converted or exchanged in a reorganization, recapitalization or similar transaction.

"Exercise Price" means $[ ], subject to adjustment from time to time in accordance with the provisions of this Warrant.

"Liquid Sale" means the closing of a Merger Event in which the consideration received by the Company and/or its stockholders, as applicable, consists solely of cash and/or Marketable Securities.

"Marketable Securities" in connection with a Merger Event means securities meeting all of the following requirements: (i) the issuer thereof is then subject to the reporting requirements of Section 13 or Section 15(d) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and is then current in its filing of all required reports and other information under the Act and the Exchange Act; (ii) the class and series of shares or other security of the issuer that would be received by the Warrantholder in connection with the Merger Event were the Warrantholder to exercise this Warrant on or prior to the closing thereof is then traded on a national securities exchange or over-the-counter market, and (iii) following the closing of such Merger Event, Warrantholder would not be restricted from publicly re-selling all of the issuer's shares and/or other securities that would be received by Warrantholder in such Merger Event were Warrantholder to exercise this Warrant in full on or prior to the closing of such Merger Event, except to the extent that any such restriction (x) arises solely under federal or state securities laws, rules or regulations, and (y) does not extend beyond six (6) months from the closing of such Merger Event.

"Merger Event" means any of the following: (i) a sale, lease or other transfer of all or substantially all assets of the Company, (ii) any merger or consolidation involving the Company in which the Company is not the surviving entity or in which the outstanding shares of the Company's capital stock are otherwise converted into or exchanged for shares of capital stock or other securities or property of another entity, or (iii) any sale by holders of the outstanding voting equity securities of the Company in a single transaction or series of related transactions of shares constituting a majority of the outstanding combined voting power of the Company.

"Purchase Price" means, with respect to any exercise of this Warrant, an amount equal to the then-effective Exercise Price multiplied by the number of shares of Common Stock as to which this Warrant is then exercised.

"Warrant Coverage" means [ ].

(b) Number of Shares. This Warrant shall be exercisable for a number of shares of Common Stock equal to the quotient derived by dividing (i) the Warrant Coverage by (ii) the Exercise Price, subject to adjustment from time to time in accordance with the provisions of this Warrant.

SECTION 2.TERM OF THE AGREEMENT.

The term of this Agreement and the right to purchase Common Stock as granted herein shall commence on the Effective Date and, subject to Section 8(a) below, shall be exercisable for a period ending upon the seventh (7th) anniversary of the Effective Date.

SECTION 3.EXERCISE OF THE PURCHASE RIGHTS.

(a) Exercise. The purchase rights set forth in this Agreement are exercisable by the Warrantholder, in whole or in part, at any time, or from time to time, prior to the expiration of the term set forth in Section 2, by tendering to the Company at its principal office a notice of exercise in the form attached hereto as Exhibit I (the "Notice of Exercise"), duly completed and executed. Promptly upon

receipt of the Notice of Exercise and the payment of the Purchase Price in accordance with the terms set forth below, and in no event later than three (3) business days thereafter, the Company shall issue to the Warrantholder , via book entry, the number of shares of Common Stock purchased and shall execute the acknowledgment of exercise in the form attached hereto as Exhibit II (the "Acknowledgment of Exercise") indicating the number of shares which remain subject to future purchases under this Warrant, if any.

The Purchase Price may be paid at the Warrantholder's election either (i) by cash or check, or (ii) by surrender of all or a portion of the Warrant for shares of Common Stock to be exercised under this Agreement and, if applicable, an amended Agreement setting forth the remaining number of shares purchasable hereunder, as determined below ("Net Issuance"). If the Warrantholder elects the Net Issuance method, the Company will issue shares of Common Stock in accordance with the following formula:

$$X = \frac{Y(A-B)}{A}$$

Where: X = the number of shares of Common Stock to be issued to the Warrantholder.

Y = the number of shares of Common Stock requested to be exercised under this Agreement.

A = the then-current fair market value of one (1) share of Common Stock at the time of exercise.

B = the then-effective Exercise Price.

For purposes of the above calculation, the current fair market value of shares of Common Stock shall mean with respect to each share of Common Stock:

(i) at all times when the Common Stock shall be traded on a national securities exchange, inter-dealer quotation system or over-the-counter bulletin board service, the fair market value of one (1) share of Common Stock shall be deemed to be the prior day closing price before the day the current fair market value of the securities is being determined;

(ii) if the exercise is in connection with a Merger Event, the fair market value of a share of Common Stock shall be deemed to be the per share value received by the holders of the outstanding shares of Common Stock pursuant to such Merger Event as determined in accordance with the definitive transaction documents executed among the parties in connection therewith; or

(iii) in cases other than as described in the foregoing clauses (i) and (ii), the current fair market value of a share of Common Stock shall be determined in good faith by the Company's Board of Directors.

Upon partial exercise by either cash or Net Issuance, prior to the expiration or earlier termination hereof, the Company shall promptly amend this Agreement to reflect the remaining number of shares and/or other securities purchasable hereunder. All other terms and conditions of such amended Agreement shall be identical to those contained herein, including, but not limited to the Effective Date hereof.

(b) Exercise Prior to Expiration. To the extent this Warrant is not previously exercised as to all shares subject hereto, and if the then-current fair market value of one share of Common Stock is greater than the Exercise Price then in effect, or, in the case of a Liquid Sale, where the value per share of

Common Stock (as determined as of the closing of such Liquid Sale in accordance with the definitive agreements executed by the parties in connection with such Merger Event) to be paid to the holders thereof is greater than the Exercise Price then in effect, this Agreement shall be deemed automatically exercised on a Net Issuance basis pursuant to Section 3(a) (even if not surrendered) as of immediately before its expiration determined in accordance with Section 2. For purposes of such automatic exercise, the fair market value of one share of Common Stock upon such expiration shall be determined pursuant to Section 3(a). To the extent this Warrant or any portion hereof is deemed automatically exercised pursuant to this Section 3(b), the Company agrees to promptly notify the Warrantholder, upon written request, of the number of shares of Common Stock if any, the Warrantholder is to receive by reason of such automatic exercise, and shall issue the Warrantholder such shares via book entry.

SECTION 4.RESERVATION OF SHARES.

During the term of this Agreement, the Company will at all times have authorized and reserved a sufficient number of shares of its Common Stock to provide for the exercise of the rights to purchase Common Stock as provided for herein.

SECTION 5.NO FRACTIONAL SHARES OR SCRIP.

No fractional shares or scrip representing fractional shares shall be issued upon the exercise of this Agreement, but in lieu of such fractional shares the Company shall make a cash payment therefor upon the basis of the then fair market value of one share of Common Stock.

SECTION 6.NO RIGHTS AS STOCKHOLDER.

Without limitation of any provision hereof, Warrantholder agrees that this Agreement does not entitle the Warrantholder to any voting rights or other rights as a stockholder of the Company prior to the exercise of any of the purchase rights set forth in this Agreement.

SECTION 7.WARRANTHOLDER REGISTRY.

The Company shall maintain a registry showing the name and address of the registered holder of this Agreement. Warrantholder's initial address, for purposes of such registry, is set forth in Section 12(g) below. Warrantholder may change such address by giving written notice of such changed address to the Company.

SECTION 8.ADJUSTMENT RIGHTS.

The Exercise Price and the number of shares of Common Stock purchasable hereunder are subject to adjustment from time to time, as follows:

(a) Merger Event. In connection with a Merger Event that is a Liquid Sale, this Warrant shall, on and after the closing thereof, automatically and without further action on the part of any party or other person, represent the right to receive the consideration payable on or in respect of all shares of Common Stock that are issuable hereunder as of immediately prior to the closing of such Merger Event less the Purchase Price for all such shares of Common Stock (such consideration to include both the consideration payable at the closing of such Merger Event and all deferred consideration payable thereafter, if any, including, but not limited to, payments of amounts deposited at such closing into escrow and payments in the nature of earn-outs, milestone payments or other performance-based payments, subject to the terms of the definitive agreements governing the Merger Event), and such Merger Event consideration shall be paid to Warrantholder as and when it is paid to the holders of the outstanding shares of Common Stock. In connection with a Merger Event that is not a Liquid Sale, the Company shall cause the successor or surviving entity to assume this Warrant and the obligations of the Company hereunder on the closing thereof, and, thereafter this Warrant shall be exercisable for the same

number and type of securities or other property as the Warrantholder would have received in consideration for the shares of Common Stock issuable hereunder had it exercised this Warrant in full as of immediately prior to such closing, at an aggregate Exercise Price no greater than the aggregate Exercise Price in effect as of immediately prior to such closing, and subject to further adjustment from time to time in accordance with the provisions of this Warrant. The provisions of this Section 8(a) shall similarly apply to successive Merger Events.

(b) Reclassification of Shares. Except for Merger Events subject to Section 8(a), if the Company at any time shall, by combination, reclassification, exchange or subdivision of securities or otherwise, change any of the securities as to which purchase rights under this Agreement exist into the same or a different number of securities of any other class or classes of securities, this Agreement shall thereafter represent the right to acquire such number and kind of securities as would have been issuable as the result of such change with respect to the securities which were subject to the purchase rights under this Agreement immediately prior to such combination, reclassification, exchange, subdivision or other change. The provisions of this Section 8(b) shall similarly apply to successive combination, reclassification, exchange, subdivision or other change.

(c) Subdivision or Combination of Shares. If the Company at any time shall combine or subdivide its Common Stock, (i) in the case of a subdivision, the Exercise Price shall be proportionately decreased and the number of shares for which this Warrant is exercisable shall be proportionately increased, or (ii) in the case of a combination, the Exercise Price shall be proportionately increased and the number of shares for which this Warrant is exercisable shall be proportionately decreased.

(d) Stock Dividends. If the Company at any time while this Agreement is outstanding and unexpired shall:

(i) pay a dividend with respect to the outstanding shares of Common Stock payable in additional shares of Common Stock, then the Exercise Price shall be adjusted, to that price determined by multiplying the Exercise Price in effect immediately prior to such date of determination by a fraction (A) the numerator of which shall be the total number of shares of Common Stock outstanding immediately prior to such dividend or distribution, and (B) the denominator of which shall be the total number of shares of Common Stock outstanding immediately after such dividend or distribution, and the number of shares of Common Stock for which this Warrant is exercisable shall be proportionately increased; or

(ii) make any other dividend or distribution on or with respect to Common Stock, except any dividend or distribution (A) in cash, or (B) specifically provided for in any other clause of this Section 8, then, in each such case, provision shall be made by the Company such that the Warrantholder shall receive upon exercise or conversion of this Warrant a proportionate share of any such dividend or distribution as though it were the holder of the Common Stock (or other stock for which the Common Stock is convertible) as of the record date fixed for the determination of the stockholders of the Company entitled to receive such dividend or distribution.

(e) Notice of Certain Events. If: (i) the Company shall declare any dividend or distribution upon its outstanding Common Stock, payable in stock, cash, property or other securities (provided that Warrantholder in its capacity as lender under the Loan Agreement consents to such dividend); (ii) the Company shall offer for subscription pro rata to the holders of its Common Stock any additional shares of stock of any class or other rights; (iii) there shall be any Merger Event; or (iv) there shall be any voluntary dissolution, liquidation or winding up of the Company; then, in connection with

each such event, the Company shall give the Warrantholder notice thereof at the same time and in the same manner as it gives notice thereof to the holders of outstanding Common Stock.

SECTION 9.REPRESENTATIONS, WARRANTIES AND COVENANTS OF THE COMPANY.

(a) Reservation of Common Stock. The Company covenants and agrees that all shares of Common Stock, if any, that may be issued upon the exercise of the rights represented by this Warrant will, upon issuance, be validly issued and outstanding, fully paid and non-assessable. The Company further covenants and agrees that the Company will, at all times during the term hereof, have authorized and reserved, free from preemptive rights, a sufficient number of shares of Common Stock to provide for the exercise of the rights represented by this Warrant. If at any time during the term hereof the number of authorized but unissued shares of Common Stock shall not be sufficient to permit exercise of this Warrant in full, the Company will take such corporate action as may, in the opinion of its counsel, be necessary to increase its authorized but unissued shares of Common Stock to such number of shares as shall be sufficient for such purposes.

(b) Due Authority. The execution and delivery by the Company of this Agreement and the performance of all obligations of the Company hereunder, including the issuance to Warrantholder of the right to acquire the shares of Common Stock, have been duly authorized by all necessary corporate action on the part of the Company. This Agreement: (1) does not violate the Company's Charter or current bylaws; (2) does not contravene any law or governmental rule, regulation or order applicable to it; and (3) does not and will not contravene any provision of, or constitute a default under, any indenture, mortgage, contract or other instrument to which it is a party or by which it is bound. This Agreement constitutes a legal, valid and binding agreement of the Company, enforceable in accordance with its terms, except as may be limited by bankruptcy, insolvency, reorganization, moratorium or similar laws relating to or affecting creditors' rights generally (including, without limitation, fraudulent conveyance laws) and by general principles of equity, regardless of whether considered in a proceeding in equity or at law.

(c) Consents and Approvals. No consent or approval of, giving of notice to, registration with, or taking of any other action in respect of any state, federal or other governmental authority or agency is required with respect to the execution, delivery and performance by the Company of its obligations under this Agreement, except for the filing of notices pursuant to Regulation D under the Act and any filing required by applicable state securities law, which filings will be effective by the time required thereby.

(d) Exempt Transaction. Subject to the accuracy of the Warrantholder's representations in Section 10, the issuance of the Common Stock upon exercise of this Agreement will constitute a transaction exempt from (i) the registration requirements of Section 5 of the Act, in reliance upon Section 4(a)(2) thereof, and (ii) the qualification requirements of the applicable state securities laws.

(e) Information Rights. At all times (if any) prior to the expiration or earlier termination of this Warrant, when the Company shall not be required to file reports pursuant to Section 13 or 15(d) of the Exchange Act or shall not have timely filed all such required reports, Warrantholder shall be entitled to the information rights contained in Sections 7.1(b) and 7.1(c) of the Loan Agreement, provided that the confidentiality provisions contained in Section 11.13 of the Loan Agreement shall apply to any information received under this section, and in any such event Sections 7.1(b), 7.1(c) and 11.13 of the Loan Agreement are hereby incorporated into this Agreement by this reference as though fully set forth herein. In receiving any such information, Warrantholder shall at all times comply with all securities laws applicable to the resale of this Warrant or the shares of Common Stock issuable upon exercise of this Warrant, including relevant insider trading laws.

(f) Rule 144 Compliance. The Company shall, at all times prior to the earlier to occur of (x) the date of sale or other disposition by Warrantholder of this Warrant or all shares of Common Stock issued on exercise of this Warrant, or (y) the expiration or earlier termination of this Warrant if the

Warrant has not been exercised in full or in part on such date, use all commercially reasonable efforts to timely file all reports required under the 1934 Act and otherwise timely take all actions necessary to permit the Warrantholder to sell or otherwise dispose of this Warrant and the shares of Common Stock issued on exercise hereof pursuant to Rule 144 promulgated under the Act as amended and in effect from time to time, provided that the foregoing shall not apply in the event of a Merger Event following which the successor or surviving entity is not subject to the reporting requirements of the 1934 Act. If the Warrantholder proposes to sell Common Stock issuable upon the exercise of this Agreement in compliance with Rule 144, then, upon Warrantholder's written request to the Company, the Company shall furnish to the Warrantholder, within five (5) business days after receipt of such request, a written statement confirming the Company's compliance with the filing and other requirements of such Rule.

SECTION 10.REPRESENTATIONS AND COVENANTS OF THE WARRANTHOLDER.

This Agreement has been entered into by the Company in reliance upon the following representations and covenants of the Warrantholder:

(a) Investment Purpose. This Warrant and the shares issued on exercise hereof will be acquired for investment and not with a view to the sale or distribution of any part thereof in violation of applicable federal and state securities laws, and the Warrantholder has no present intention of selling or engaging in any public distribution of the same except pursuant to a registration or exemption.

(a) Private Issue. The Warrantholder understands (i) that the Common Stock issuable upon exercise of this Agreement is not, as of the Effective Date, registered under the Act or qualified under applicable state securities laws on the grounds that the issuance contemplated by this Agreement will be exempt from the registration and qualifications requirements thereof, and (ii) that the Company's reliance on exemption from such registration is predicated on the representations set forth in this Section 10.

(b) Financial Risk. The Warrantholder has such knowledge and experience in financial and business matters as to be capable of evaluating the merits and risks of its investment, and has the ability to bear the economic risks of its investment.

(c) Accredited Investor. Warrantholder is an "accredited investor" within the meaning of Rule 501 of Regulation D promulgated under the Act, as presently in effect ("Regulation D").

(d) No Short Sales. Warrantholder has not at any time on or prior to the Effective Date engaged in any short sales or equivalent transactions in the Common Stock. Warrantholder agrees that at all times from and after the Effective Date and on or before the expiration or earlier termination of this Warrant, it shall not engage in any short sales or equivalent transactions in the Common Stock.

SECTION 11.TRANSFERS.

Subject to compliance with applicable federal and state securities laws, this Agreement and all rights hereunder are transferable, in whole or in part, without charge to the holder hereof (except for transfer taxes) upon surrender of this Agreement properly endorsed. Each taker and holder of this Agreement, by taking or holding the same, consents and agrees that this Agreement, when endorsed in blank, shall be deemed negotiable, and that the holder hereof, when this Agreement shall have been so endorsed and its transfer recorded on the Company's books, shall be treated by the Company and all other persons dealing with this Agreement as the absolute owner hereof for any purpose and as the person entitled to exercise the rights represented by this Agreement. The transfer of this Agreement shall be recorded on the books of the Company upon receipt by the Company of a notice of transfer in the form attached hereto as Exhibit III (the "Transfer Notice"), at its principal offices and the payment to the Company of all transfer taxes and other governmental charges imposed on such transfer. Until the Company receives such Transfer Notice, the Company may treat the registered owner hereof as the owner for all purposes. Notwithstanding anything herein or in any legend to the contrary, the Company shall not require an opinion of counsel in connection with any sale, assignment or other transfer by Warrantholder

of this Warrant (or any portion hereof or any interest herein) or of any shares of Common Stock issued upon any exercise hereof to an affiliate (as defined in Regulation D) of Warrantholder, provided that such affiliate is an "accredited investor" as defined in Regulation D.

SECTION 12.MISCELLANEOUS.

(a) Effective Date. The provisions of this Agreement shall be construed and shall be given effect in all respects as if it had been executed and delivered by the Company on the date hereof. This Agreement shall be binding upon any successors or assigns of the Company.

(b) Remedies. In the event of any default hereunder, the non-defaulting party may proceed to protect and enforce its rights either by suit in equity and/or by action at law, including but not limited to an action for damages as a result of any such default, and/or an action for specific performance for any default where Warrantholder will not have an adequate remedy at law and where damages will not be readily ascertainable. The Company expressly agrees that it shall not oppose an application by the Warrantholder or any other person entitled to the benefit of this Agreement requiring specific performance of any or all provisions hereof or enjoining the Company from continuing to commit any such breach of this Agreement.

(c) No Impairment of Rights. The Company will not, by amendment of its Charter or through any other means, avoid or seek to avoid the observance or performance of any of the terms of this Agreement, but will at all times in good faith assist in the carrying out of all such terms and in the taking of all such actions as may be necessary or appropriate in order to protect the rights of the Warrantholder against impairment.

(d) Additional Documents. In the event the Company shall not be required to file reports pursuant to Section 13 or 15(d) of the Exchange Act or shall not have timely filed all such required reports, the Company agrees to supply such other documents as the Warrantholder may from time to time reasonably request to value this Warrant for Warrantholder's accounting or reporting requirements and/or to evaluate whether to exercise (in cash or a net issuance basis) this Warrant.

(e) Attorneys' Fees. In any litigation, arbitration or court proceeding between the Company and the Warrantholder relating hereto, the prevailing party shall be entitled to reasonable attorneys' fees and expenses and all costs of proceedings incurred in enforcing this Agreement. For the purposes of this Section 12(e), attorneys' fees shall include without limitation reasonable fees incurred in connection with the following: (i) contempt proceedings; (ii) discovery; (iii) any motion, proceeding or other activity of any kind in connection with an insolvency proceeding; (iv) garnishment, levy, and debtor and third party examinations; and (v) post-judgment motions and proceedings of any kind, including without limitation any activity taken to collect or enforce any judgment.

(f) Severability. In the event any one or more of the provisions of this Agreement shall for any reason be held invalid, illegal or unenforceable, the remaining provisions of this Agreement shall be unimpaired, and the invalid, illegal or unenforceable provision shall be replaced by a mutually acceptable valid, legal and enforceable provision, which comes closest to the intention of the parties underlying the invalid, illegal or unenforceable provision.

(g) Notices. Except as otherwise provided herein, any notice, demand, request, consent, approval, declaration, service of process or other communication that is required, contemplated, or permitted under this Agreement or with respect to the subject matter hereof shall be in writing, and shall be deemed to have been validly served, given, delivered, and received upon the earlier of: (a) personal delivery to the party to be notified, (b) when sent by confirmed telex, electronic transmission or facsimile if sent during normal business hours of the recipient, if not, then on the next business day, (c) five days after having been sent by registered or certified mail, return receipt requested, postage prepaid, or (d) one day after

deposit with a nationally recognized overnight courier, specifying next day delivery, with written verification of receipt, and shall be addressed to the party to be notified as follows:

If to the Warrantholder:

HERCULES CAPITAL, INC.
Legal Department
Attention: Chief Legal Officer and Michael Dutra
400 Hamilton Avenue, Suite 310
Palo Alto, CA 94301
Facsimile: 650-473-9194
Telephone: 650-289-3060

With a copy to (which shall not constitute notice):

LATHAM & WATKINS LLP
505 Montgomery Street, Suite 2000
San Francisco, CA 94111
Attn: Haim Zaltzman
Facsimile: 415-395-8095
Telephone: 415-395-8870

If to the Company:

AXSOME THERAPEUTICS, INC.
Attention: Chief Financial Officer
22 Cortlandt Street, 16th Floor
New York, New York

With a copy to (which shall not constitute notice):

DLA PIPER LLP (US)
51 John F. Kennedy Pkwy, Suite 120
Short Hills, NJ 07078
Attn: Emilio Ragosa, Esq.
Facsimile: 973-215-2804
Telephone: 973-307-3004

or to such other address as each party may designate for itself by like notice.

(h) Entire Agreement; Amendments. This Agreement constitutes the entire agreement and understanding of the parties hereto in respect of the subject matter hereof, and supersedes and replaces in their entirety any prior proposals, term sheets, letters, negotiations or other documents or agreements, whether written or oral, with respect to the subject matter hereof (including the Warrantholder's proposal letter dated September 2, 2020). None of the terms of this Agreement may be amended except by an instrument executed by each of the parties hereto.

(i) Headings. The various headings in this Agreement are inserted for convenience only and shall not affect the meaning or interpretation of this Agreement or any provisions hereof.

(j) Advice of Counsel. Each of the parties represents to each other party hereto that it has discussed (or had an opportunity to discuss) with its counsel this Agreement and, specifically, the provisions of Sections 12(n), 12(o), 12(p), 12(q) and 12(r).

(k) No Strict Construction. The parties hereto have participated jointly in the negotiation and drafting of this Agreement. In the event an ambiguity or question of intent or interpretation arises, this

Agreement shall be construed as if drafted jointly by the parties hereto and no presumption or burden of proof shall arise favoring or disfavoring any party by virtue of the authorship of any provisions of this Agreement.

(l) No Waiver. No omission or delay by Warrantholder at any time to enforce any right or remedy reserved to it, or to require performance of any of the terms, covenants or provisions hereof by Warrantholder at any time designated, shall be a waiver of any such right or remedy to which Warrantholder is entitled, nor shall it in any way affect the right of Warrantholder to enforce such provisions thereafter during the term of this Agreement.

(m) Survival. All agreements, representations and warranties contained in this Agreement or in any document delivered pursuant hereto shall be for the benefit of Warrantholder and shall survive the execution and delivery of this Agreement and the expiration or other termination of this Agreement.

(n) Governing Law. This Agreement has been negotiated and delivered to Warrantholder in the State of California, and shall be deemed to have been accepted by Warrantholder in the State of California. Delivery of Common Stock to Warrantholder by the Company under this Agreement is due in the State of California. This Agreement shall be governed by, and construed and enforced in accordance with, the laws of the State of California, excluding conflict of laws principles that would cause the application of laws of any other jurisdiction.

(o) Consent to Jurisdiction and Venue. All judicial proceedings arising in or under or related to this Agreement may be brought in any state or federal court of competent jurisdiction located in the State of California. By execution and delivery of this Agreement, each party hereto generally and unconditionally: (i) consents to personal jurisdiction in Santa Clara County, State of California; (ii) waives any objection as to jurisdiction or venue in Santa Clara County, State of California; (iii) agrees not to assert any defense based on lack of jurisdiction or venue in the aforesaid courts; and (iv) irrevocably agrees to be bound by any judgment rendered thereby in connection with this Agreement. Service of process on any party hereto in any action arising out of or relating to this Agreement shall be effective if given in accordance with the requirements for notice set forth in Section 12(g), and shall be deemed effective and received as set forth in Section 12(g). Nothing herein shall affect the right to serve process in any other manner permitted by law or shall limit the right of either party to bring proceedings in the courts of any other jurisdiction.

(p) Mutual Waiver of Jury Trial. Because disputes arising in connection with complex financial transactions are most quickly and economically resolved by an experienced and expert person and the parties wish applicable state and federal laws to apply (rather than arbitration rules), the parties desire that their disputes arising under or in connection with this Warrant be resolved by a judge applying such applicable laws. EACH OF THE COMPANY AND WARRANTHOLDER SPECIFICALLY WAIVES ANY RIGHT IT MAY HAVE TO TRIAL BY JURY OF ANY CAUSE OF ACTION, CLAIM, CROSS-CLAIM, COUNTERCLAIM, THIRD PARTY CLAIM OR ANY OTHER CLAIM (COLLECTIVELY, "CLAIMS") ASSERTED BY THE COMPANY AGAINST WARRANTHOLDER OR ITS ASSIGNEE OR BY WARRANTHOLDER OR ITS ASSIGNEE AGAINST THE COMPANY RELATING TO THIS WARRANT. This waiver extends to all such Claims, including Claims that involve persons or entities other the Company and Warrantholder; Claims that arise out of or are in any way connected to the relationship between the Company and Warrantholder; and any Claims for damages, breach of contract, specific performance, or any equitable or legal relief of any kind, arising out of this Agreement.

(q) Judicial Reference. If the waiver of jury trial set forth above is ineffective or unenforceable, the parties agree that all Claims shall be resolved by reference to a private judge sitting without a jury before a mutually acceptable referee.

(r) Pre-arbitration Relief. In the event Claims are to be resolved by arbitration, either party may seek from a court of competent jurisdiction identified in Section 12(o), any prejudgment order, writ or

other relief and have such prejudgment order, writ or other relief enforced to the fullest extent permitted by law notwithstanding that all Claims are otherwise subject to resolution by judicial reference.

(s) Counterparts. This Agreement and any amendments, waivers, consents or supplements hereto may be executed in any number of counterparts (including by facsimile or electronic delivery (PDF), and by different parties hereto in separate counterparts, each of which when so delivered shall be deemed an original, but all of which counterparts shall constitute but one and the same instrument.

(t) Specific Performance. The parties hereto hereby declare that it is impossible to measure in money the damages which will accrue to Warrantholder by reason of the Company's failure to perform any of the obligations under this Agreement and agree that the terms of this Agreement shall be specifically enforceable by Warrantholder. If Warrantholder institutes any action or proceeding to specifically enforce the provisions hereof, any person against whom such action or proceeding is brought hereby waives the claim or defense therein that Warrantholder has an adequate remedy at law, and such person shall not offer in any such action or proceeding the claim or defense that such remedy at law exists.

(u) Lost, Stolen, Mutilated or Destroyed Warrant. If this Warrant is lost, stolen, mutilated or destroyed, the Company may, on such terms as to indemnity or otherwise as it may reasonably impose (which shall, in the case of a mutilated Warrant, include the surrender thereof), issue a new Warrant of like denomination and tenor as this Warrant so lost, stolen, mutilated or destroyed. Any such new Warrant shall constitute an original contractual obligation of the Company, whether or not the allegedly lost, stolen, mutilated or destroyed Warrant shall be at any time enforceable by anyone.

(v) Legends. To the extent required by applicable laws, this Warrant and the shares of Common Stock issuable hereunder (and the securities issuable, directly or indirectly, upon conversion of such shares of Common Stock, if any) may be imprinted with a restricted securities legend in substantially the following form:

> THIS SECURITY HAS NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "ACT"), OR ANY APPLICABLE STATE SECURITIES LAWS, AND MAY NOT BE SOLD, PLEDGED OR OTHERWISE TRANSFERRED WITHOUT AN EFFECTIVE REGISTRATION THEREOF UNDER THE ACT AND ANY APPLICABLE STATE SECURITIES LAWS, OR PURSUANT TO RULE 144 OR AN EXEMPTION FROM THE REGISTRATION REQUIREMENTS OF THE ACT AND ANY APPLICABLE STATE SECURITIES LAWS.

[Remainder of Page Intentionally Left Blank]

IN WITNESS WHEREOF, the parties hereto have caused this Warrant Agreement to be executed by its officers thereunto duly authorized as of the Effective Date.

COMPANY:

AXSOME THERAPEUTICS, INC.

By: _____
Name: _____
Title: _____

WARRANTHOLDER:

HERCULES CAPITAL, INC.

By:_____
Name:
Title:

EXHIBIT I

NOTICE OF EXERCISE

To: Axsome Therapeutics, Inc.

(1) The undersigned Warrantholder hereby elects to purchase [_____] shares of the Common Stock of Axsome Therapeutics, Inc., pursuant to the terms of the Agreement dated [ ] (the "Agreement") between Axsome Therapeutics, Inc. and the Warrantholder, and [CASH PAYMENT: tenders herewith payment of the Purchase Price in full, together with all applicable transfer taxes, if any.] [NET ISSUANCE: elects pursuant to Section 3(a) of the Agreement to effect a Net Issuance.]

(2) Please issue a certificate or certificates representing said shares of Common Stock in the name of the undersigned or in such other name as is specified below.

_____
(Name)

_____
(Address)

WARRANTHOLDER: HERCULES CAPITAL, INC.

By: _____
Name: _____
Title: _____

EXHIBIT II

1. ACKNOWLEDGMENT OF EXERCISE

The undersigned, Axsome Therapeutics, Inc., hereby acknowledge receipt of the "Notice of Exercise" from Hercules Capital, Inc. to purchase [____] shares of the Common Stock of Axsome Therapeutics, Inc. pursuant to the terms of the Agreement, and further acknowledges that [_____] shares remain subject to purchase under the terms of the Agreement.

COMPANY: AXSOME THERAPEUTICS, INC.

By: _____

Title: _____

Date: _____

EXHIBIT III

TRANSFER NOTICE

(To transfer or assign the foregoing Agreement execute this form and supply required information. Do not use this form to purchase shares.)

FOR VALUE RECEIVED, the foregoing Agreement and all rights evidenced thereby are hereby transferred and assigned to

_____
(Please Print)

whose address is_____

_____

Dated: _____

Holder's Signature: _____

Holder's Address: _____

_____

Holder's Taxpayer Identification Number: _____

SHARE TRANSFER AGREEMENT

SHARE TRANSFER AGREEMENT (the "Agreement"), dated as of May 9, 2022, by and between **AXSOME THERAPEUTICS, INC.**, a Delaware corporation (the "Company"), **HERCULES CAPITAL, INC.**, **HERCULES PRIVATE GLOBAL VENTURE GROWTH FUND I L.P.**, and **HERCULES PRIVATE CREDIT FUND I L.P.** (each an "Investor", and collectively the "Investors").

WHEREAS:

Subject to the terms and conditions set forth in this Agreement, in consideration for entering into that certain Loan and Security Agreement, dated as of September 25, 2020, (as amended by the First Amendment to Loan and Security Agreement, dated as of October 14, 2021, and the Second Amendment to Loan and Security Agreement, dated as of March 26, 2022 (the "Second Amendment to Loan")), (the "Loan Agreement"), the Company agrees to issue to the Investors an aggregate of 152,487 unregistered shares (the "Shares") of the Company's common stock, $0.0001 par value per share (the "Common Stock"), based on an assumed issuance price of $32.79 per share, for an aggregate purchase price of $5,000,048.73 (the "Purchase Price") and in the amounts as set forth on Exhibit A hereto.

NOW THEREFORE, in consideration of the mutual covenants contained in this Agreement, and for other good and valuable consideration, the receipt and adequacy of which are hereby acknowledged, the Company and each Investor hereby agree as follows:

1. CERTAIN DEFINITIONS.

For purposes of this Agreement, the following terms shall have the following meanings:

(a) "Bankruptcy Law" means Title 11, U.S. Code, or any similar federal or state law for the relief of debtors.

(b) "Business Day" means any day on which the Principal Market is open for trading, including any day on which the Principal Market is open for trading for a period of time less than the customary time.

(c) "Confidential Information" has the meaning set forth in the Loan Agreement.

(d) "Custodian" means any receiver, trustee, assignee, liquidator or similar official under any Bankruptcy Law.

(e) "DTC" means The Depository Trust Company, or any successor performing substantially the same function for the Company.

(f) "DWAC Shares" means shares of Common Stock that are (i) issued in electronic form, (ii) freely tradable and transferable and without restriction on resale and (iii) timely credited by the Company to the Investor or its designee's specified Deposit/Withdrawal at Custodian (DWAC) account with DTC under its Fast Automated Securities Transfer (FAST) Program or any similar program hereafter adopted by DTC performing substantially the same function.

(g) "Exchange Act" means the Securities Exchange Act of 1934, as amended, and the rules and regulations promulgated thereunder.

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(h) "Material Adverse Effect" means any material adverse effect on (i) the enforceability of any Transaction Document, (ii) the results of operations, assets, business or financial condition of the Company and its Subsidiaries, taken as a whole, other than any material adverse effect that resulted primarily from (A) any change in the United States or foreign economies or securities or financial markets in general that does not have a disproportionate effect on the Company and its Subsidiaries, taken as a whole, (B) any change that generally affects the industry in which the Company and its Subsidiaries operate that does not have a disproportionate effect on the Company and its Subsidiaries, taken as a whole, (C) any change arising in connection with earthquakes, hostilities, acts of war, sabotage or terrorism or military actions or any escalation or material worsening of any such hostilities, acts of war, sabotage or terrorism or military actions existing as of the date hereof, (D) any action taken by the Investor, its affiliates or its successors and assigns with respect to the transactions contemplated by this Agreement, (E) the effect of any change in applicable laws or accounting rules that does not have a disproportionate effect on the Company and its Subsidiaries, taken as a whole, (F) any change resulting from compliance with terms of this Agreement or the consummation of the transactions contemplated by this Agreement, or (G) any change, in and of itself, in the Company's stock price or trading volume from and after the date hereof (provided, however, that the facts and circumstances underlying any such change may, except as provided in subsections (A), (B), (C), (D), (E) or (F) of this definition, be considered in determining whether a Company Material Adverse Effect has occurred), or (iii) the Company's ability to perform in any material respect on a timely basis its obligations under any Transaction Document to be performed as of the date of determination.

(i) "Person" means an individual or entity including but not limited to any limited liability company, a partnership, a joint venture, a corporation, a trust, an unincorporated organization and a government or any department or agency thereof.

(j) "Principal Market" means The Nasdaq Global Market (or any nationally recognized successor thereto); provided, however, that in the event the Company's Common Stock is ever listed or traded on The Nasdaq Capital Market, The Nasdaq Global Select Market, the New York Stock Exchange, the NYSE American, the NYSE Arca, the OTC Bulletin Board, or the OTCQX or the OTCQB operated by the OTC Markets Group, Inc. (or any nationally recognized successor to any of the foregoing), then the "Principal Market" shall mean such other market or exchange on which the Company's Common Stock is then listed or traded.

(k) "SEC" means the U.S. Securities and Exchange Commission.

(l) "Securities Act" means the Securities Act of 1933, as amended, and the rules and regulations promulgated thereunder.

(m) "Subsidiary" means any Person the Company wholly-owns or controls, or in which the Company, directly or indirectly, owns a majority of the voting stock or similar voting interest, in each case that would be disclosable pursuant to Item 601(b)(21) of Regulation S-K promulgated under the Securities Act.

(n) "Transaction Documents" means, collectively, this Agreement and the schedules and exhibits hereto, including the Second Amendment to Loan and each of the other documents, certificates and instruments entered into or furnished by the parties hereto in connection with the transactions contemplated hereby and thereby.

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(o) "Transfer Agent" means American Stock Transfer & Trust Company, LLC, or such other Person who is then serving as the transfer agent for the Company in respect of the Common Stock.

2. ISSUANCE OF COMMON STOCK.

(a) Issuance of Common Stock. Subject to the terms and conditions set forth in this Agreement, on the effective date of the Second Amendment to Loan ("Closing Date"), the Investor shall deliver to the Company the Purchase Price via irrevocable wire transfer of immediately available funds to the account designated by the Company, and the Company shall issue or cause to be issued to the Investor the Shares, free and clear of all liens (other than liens imposed by applicable securities laws or contained herein), with a restrictive legend pursuant to Section 6 below.

(b) Deliveries at Closing. At the Closing, the Company shall deliver or cause to be delivered to the Investor the following items:

(i) a copy of the Irrevocable Transfer Agent Instructions;

(ii) an opinion of DLA Piper LLP, counsel for the Company, addressed to the Investor, and dated the Closing Date, in substantially the form attached hereto as Exhibit D; and

(iii) all such other documents, certificates and instruments as the Investor may reasonably request in order to give effect to the transactions contemplated hereby.

3. INVESTOR'S REPRESENTATIONS AND WARRANTIES.

Each Investor represents and warrants to the Company that as of the date hereof and as of the Closing Date:

(a) Organization, Authority. Investor is an entity duly organized, validly existing and in good standing under the laws of the jurisdiction of its organization, with the requisite power and authority to enter into and to consummate the transactions contemplated by this Agreement and otherwise to carry out its obligations hereunder and thereunder.

(b) Accredited Investor Status. The Investor is an "accredited investor" as that term is defined in Rule 501(a)(3) of Regulation D promulgated under the Securities Act.

(c) Information. The Investor understands that its investment in the Shares involves a high degree of risk. The Investor (i) is able to bear the economic risk of an investment in the Shares including a total loss thereof, (ii) has such knowledge and experience in financial and business matters that it is capable of evaluating the merits and risks of the proposed investment in the Shares and (iii) has had an opportunity to ask questions of and receive answers from the officers of the Company concerning the financial condition and business of the Company and others matters related to an investment in the Shares. Neither such inquiries nor any other due diligence investigations conducted by the Investor or its representatives shall modify, amend or affect the Investor's right to rely on the Company's representations and warranties contained in Section 4 below. The Investor has sought such accounting, legal and tax advice from its own independent advisors as it has considered necessary to make an informed investment decision with respect to its acquisition of the Shares.

(d) Acquisition for Investment. The Investor is acquiring the Shares solely for its own account for the purpose of investment and not with a view to or for sale in connection with the distribution thereof. The Investor does not have a present intention to sell any of the Shares, nor a

present arrangement (whether or not legally binding) or intention to effect any distribution of any of the Shares to or through any Person.

(e) No Governmental Review. The Investor understands that the Shares are being offered and issued in reliance on a transactional exemption from the registration requirements of United States federal and state securities laws and the Company is relying in part upon the truth and accuracy of the representations, warranties, agreements, acknowledgments and understandings of the Investor set forth herein in order to determine the availability of such exemptions and the suitability of the Investor to acquire the Shares. The Investor understands that no U.S. federal or state agency or any other government or governmental agency has passed on or made any recommendation or endorsement of the Shares or the fairness or suitability of an investment in the Shares nor have such authorities passed upon or endorsed the merits of the offering of the Shares.

(f) Validity; Enforcement. This Agreement has been duly and validly authorized, executed and delivered on behalf of the Investor and is a valid and binding agreement of the Investor enforceable against the Investor in accordance with its terms, subject as to enforceability to general principles of equity and to applicable bankruptcy, insolvency, reorganization, moratorium, liquidation and other similar laws relating to, or affecting generally, the enforcement of applicable creditors' rights and remedies.

(g) Residency. The Investor is a corporation existing under the laws of Maryland with offices in the State of California.

(h) Rule 144. The Investor understands that the Shares must be held indefinitely unless such Shares are registered under the Securities Act or an exemption from registration is available. The Investor acknowledges that it is familiar with Rule 144 of the rules and regulations of the SEC, promulgated pursuant to the Securities Act ("Rule 144"), and that the Investor has been advised that Rule 144 permits resales only under certain circumstances. The Investor understands that to the extent that Rule 144 is not available, the Investor will be unable to sell any Shares without either registration under the Securities Act or the existence of another exemption from such registration requirement. Following expiration of the holding periods set forth in Rule 144, provided the Investor otherwise complies with the requirements of Rule 144, the Investor may request, and the Company shall promptly (within two (2) business days) have its legal counsel deliver an opinion to the Transfer Agent requesting removal of the restrictive legend(s) appended to Investor's book-entry statement(s) pursuant to Section 6(c). Any fees (with respect to the Transfer Agent, counsel to the Company or otherwise) associated with the issuance of such opinion shall be borne by the Company.

4. REPRESENTATIONS AND WARRANTIES OF THE COMPANY.

The Company represents and warrants to the Investor that as of the date hereof and as of the Closing Date:

(a) Organization and Qualification. The Company and each of its Subsidiaries is an entity duly incorporated or otherwise organized, validly existing and in good standing under the laws of the jurisdiction of its incorporation or organization, with the requisite corporate power and authority to own and use its properties and assets and to carry on its business as currently conducted. Neither the Company nor any of its Subsidiaries is in violation or default of any of the provisions of its respective certificate or articles of incorporation, bylaws or other organizational or charter

documents. Each of the Company and its Subsidiaries is duly qualified to conduct business and is in good standing as a foreign corporation or other entity in each jurisdiction in which the nature of the business conducted or property owned by it makes such qualification necessary, except where the failure to be so qualified or in good standing, as the case may be, could not have or reasonably be expected to result in a Material Adverse Effect and no proceeding has been instituted in any such jurisdiction revoking, limiting or curtailing or seeking to revoke, limit or curtail such power and authority or qualification. The Company has no Subsidiaries except as set forth on Exhibit 21.1 to the Company's Annual Report on Form 10-K for the year ended December 31, 2021.

(b) Authorization; Enforcement; Validity. (i) The Company has the requisite corporate power and authority to enter into and perform its obligations under this Agreement and each of the other Transaction Documents, and to issue the Shares in accordance with the terms hereof and thereof, (ii) the execution and delivery of this Agreement and each of the other Transaction Documents by the Company and the consummation by it of the transactions contemplated hereby and thereby, including without limitation, the issuance of the Shares pursuant to this Agreement, have been duly authorized by the Company's Board of Directors and no further consent or authorization is required by the Company, its Board of Directors or its stockholders, (iii) this Agreement has been and each of the other Transaction Document shall be on the Closing Date, duly executed and delivered by the Company and (iv) this Agreement constitutes, and each other Transaction Document upon its execution on behalf of the Company on the Closing Date, shall on the Closing Date constitute, the valid and binding obligations of the Company enforceable against the Company in accordance with their terms, except as such enforceability may be limited by general principles of equity or applicable bankruptcy, insolvency, reorganization, moratorium, liquidation or similar laws relating to, or affecting generally, the enforcement of creditors' rights and remedies. Except as set forth in this Agreement, no other approvals or consents of the Company's Board of Directors, any authorized committee thereof, and/or stockholders is necessary under applicable laws and the Company's Certificate of incorporation and/or Bylaws to authorize the execution and delivery of this Agreement or any of the transactions contemplated hereby, including, but not limited to, the issuance of the Shares.

(c) Capitalization. The authorized capital of the Company, immediately prior to the date hereof, consists of 150,000,000 shares of Common Stock, 38,913,550 of which were issued and outstanding, and 10,000,000 shares of preferred stock, $0.0001 par value per share, none of which were issued and outstanding. Immediately prior to the date hereof, (i) options to acquire 2,932,835 shares of Common Stock have been granted and are outstanding, and (ii) 2,187,058 shares of Common Stock remained available for future issuance to directors, employees and consultants of the Company and its Subsidiaries. As of the Closing Date, 15,541 warrants with an exercise price of $80.43 per share were issued and outstanding. Except as disclosed in the SEC Documents (as defined below), (i) no shares of the Company's capital stock are subject to preemptive rights or any other similar rights or any liens or encumbrances suffered or permitted by the Company, (ii) there are no outstanding debt securities, (iii) there are no outstanding options, warrants, scrip, rights to subscribe to, calls or commitments of any character whatsoever relating to, or securities or rights convertible into, any shares of capital stock of the Company or any of its Subsidiaries, or contracts, commitments, understandings or arrangements by which the Company or any of its Subsidiaries is or may become bound to issue additional shares of capital stock of the Company or any of its Subsidiaries or options, warrants, scrip, rights to subscribe to, calls or commitments of any character whatsoever relating to, or securities or rights convertible into, any shares of capital stock of the Company or any of its Subsidiaries, (iv) there are no agreements or arrangements under which the Company or any of its Subsidiaries is obligated to register the sale of any of their securities under

the Securities Act, (v) there are no outstanding securities or instruments of the Company or any of its Subsidiaries which contain any redemption or similar provisions, and there are no contracts, commitments, understandings or arrangements by which the Company or any of its Subsidiaries is or may become bound to redeem a security of the Company or any of its Subsidiaries, (vi) there are no securities or instruments containing anti-dilution or similar provisions that will be triggered by the issuance of the Shares as described in this Agreement and (vii) the Company does not have any stock appreciation rights or "phantom stock" plans or agreements or any similar plan or agreement. The Company has furnished to the Investor true and correct copies of the Company's certificate of incorporation, as amended and as in effect on the date hereof (the "Certificate of incorporation"), and the Company's Bylaws, as amended and as in effect on the date hereof (the "Bylaws"), and summaries of the material terms of all securities convertible into or exercisable for Common Stock, if any, and copies of any documents containing the material rights of the holders thereof in respect thereto that are not disclosed in the SEC Documents.

(d) Issuance of Shares. Upon issuance in accordance with the terms and conditions of this Agreement, the Shares shall be duly authorized, validly issued, fully paid and nonassessable and free from all taxes, liens, charges, restrictions, rights of first refusal and preemptive rights with respect to the issue thereof, and will be issued in compliance with all federal and state securities laws, with the holders being entitled to all rights accorded to a holder of shares of Common Stock. The Shares are being issued in accordance with and in reliance upon the exemption from securities registration afforded by Section 4(a)(2) of the Securities Act, and the rules and regulations promulgated thereunder, including Regulation D ("Regulation D"), and/or upon such other exemption from the registration requirements of the Securities Act as may be available with respect to any or all of the investments to be made hereunder. Upon receipt of the Shares, the Investor will have good and marketable title to such Shares.

(e) No Conflicts. The execution, delivery and performance of the Transaction Documents by the Company and the consummation by the Company of the transactions contemplated hereby and thereby (including, without limitation, the issuance of the Shares) will not (i) result in a violation of the Certificate of incorporation, any Certificate of Designations, Preferences and Rights of any outstanding series of preferred stock of the Company or the Bylaws or (ii) conflict with, or constitute a default (or an event which with notice or lapse of time or both would become a default) under, or give to others any rights of termination, amendment, acceleration or cancellation of, any agreement, indenture or instrument to which the Company or any of its Subsidiaries is a party, or result in a violation of any law, rule, regulation, order, judgment or decree (including federal and state securities laws and regulations and the rules and regulations of the Principal Market applicable to the Company or any of its Subsidiaries) or by which any property or asset of the Company or any of its Subsidiaries is bound or affected, except in the case of conflicts, defaults, terminations, amendments, accelerations, cancellations and violations under clause (ii), which could not reasonably be expected to result in a Material Adverse Effect. Neither the Company nor its Subsidiaries is in violation of any term of or in default under its Certificate of incorporation, any Certificate of Designation, Preferences and Rights of any outstanding series of preferred stock of the Company or Bylaws or their organizational charter or bylaws, respectively. Neither the Company nor any of its Subsidiaries is in violation of any term of or is in default under any material contract, agreement, mortgage, indebtedness, indenture, instrument, judgment, decree or order or any statute, rule or regulation applicable to the Company or its Subsidiaries, except for possible conflicts, defaults, terminations or amendments that could not reasonably be expected to have a Material Adverse Effect. The business of the Company and its Subsidiaries is not being conducted, and shall not be conducted, in violation of any law, ordinance or regulation of any governmental

entity, except for possible violations, the sanctions for which either individually or in the aggregate could not reasonably be expected to have a Material Adverse Effect. Except as required under the Securities Act or applicable state securities laws and the rules and regulations of the Principal Market, the Company is not required to obtain any consent, authorization or order of, or make any filing or registration with, any court or governmental agency or any regulatory or self-regulatory agency in order for it to execute, deliver or perform any of its obligations under or contemplated by the Transaction Documents in accordance with the terms hereof or thereof. Except as set forth elsewhere in this Agreement, all consents, authorizations, orders, filings and registrations which the Company is required to obtain pursuant to the preceding sentence shall be obtained or effected on or prior to the Closing Date. Except as disclosed in the SEC Documents, the Company has not received nor delivered any notices or correspondence from or to the Principal Market, other than notices with respect to listing of additional shares of Common Stock and other routine correspondence. Except as disclosed in the SEC Documents, the Principal Market has not commenced any delisting proceedings against the Company.

(f) SEC Documents; Financial Statements. The Company has filed all reports, schedules, forms, statements and other documents required to be filed by the Company under the Securities Act and the Exchange Act, including pursuant to Section 13(a) or 15(d) thereof, (the foregoing materials, including the exhibits thereto and documents incorporated by reference therein, being collectively referred to herein as the "SEC Documents") on a timely basis or has received a valid extension of such time of filing and has filed any such SEC Documents prior to the expiration of any such extension. As of their respective dates, the SEC Documents complied in all material respects with the requirements of the Securities Act and the Exchange Act, as applicable. None of the SEC Documents, when filed, contained any untrue statement of a material fact or omitted to state a material fact required to be stated therein or necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading. The financial statements of the Company included in the SEC Documents comply in all material respects with applicable accounting requirements and the rules and regulations of the SEC with respect thereto as in effect at the time of filing. Such financial statements have been prepared in accordance with United States generally accepted accounting principles applied on a consistent basis during the periods involved ("GAAP"), except as may be otherwise specified in such financial statements or the notes thereto and except that unaudited financial statements may not contain all footnotes required by GAAP, and fairly present in all material respects the financial position of the Company as of and for the dates thereof and the results of operations and cash flows for the periods then ended, subject, in the case of unaudited statements, to normal, immaterial, year-end audit adjustments. Except as set forth in the SEC Documents, the Company has received no notices or correspondence from the SEC for the one year preceding the date hereof**.** To the Company's knowledge, the SEC has not commenced any enforcement proceedings against the Company.

(g) Absence of Certain Changes. Except as disclosed in the SEC Documents, since December 31, 2021, there has been no material adverse change in the business, properties, operations, financial condition or results of operations of the Company or its Subsidiaries. The Company has not taken any steps, and does not currently expect to take any steps, to seek protection pursuant to any Bankruptcy Law nor does the Company or any of its Subsidiaries have any knowledge or reason to believe that its creditors intend to initiate involuntary bankruptcy or insolvency proceedings. The Company is financially solvent and is generally able to pay its debts as they become due.

(h) Absence of Litigation. There is no action, suit, proceeding, inquiry or investigation before or by any court, public board, government agency, self-regulatory organization or body pending or, to the knowledge of the Company or any of its Subsidiaries, threatened against or affecting the Company, the Common Stock or any of the Company's or its Subsidiaries' officers or directors in their capacities as such, which could reasonably be expected to have a Material Adverse Effect.

(i) Acknowledgment Regarding Investor's Status. The Company acknowledges and agrees that the Investor is acting solely in the capacity of arm's length purchaser with respect to the Transaction Documents and the transactions contemplated hereby and thereby. The Company further acknowledges that the Investor is not acting as a financial advisor or fiduciary of the Company (or in any similar capacity) with respect to the Transaction Documents and the transactions contemplated hereby and thereby and any advice given by the Investor or any of its representatives or agents in connection with the Transaction Documents and the transactions contemplated hereby and thereby is merely incidental to the Investor's purchase of the Shares. The Company further represents to the Investor that the Company's decision to enter into the Transaction Documents has been based solely on the independent evaluation by the Company and its representatives and advisors.

(j) No Integrated Offering. Neither the Company, nor or any of its affiliates, nor any Person acting on their behalf has, directly or indirectly, made any offers or sales of any security or solicited any offers to buy any security, under circumstances that would cause this offering of the Shares to be integrated with prior offerings by the Company in a manner that would require stockholder approval pursuant to the rules of the Principal Market on which any of the securities of the Company are listed or designated. The issuance and sale of the Shares hereunder does not contravene the rules and regulations of the Principal Market.

(k) Intellectual Property Rights. The Company and its Subsidiaries own or possess adequate rights or licenses to use all material trademarks, trade names, service marks, service mark registrations, service names, patents, patent rights, copyrights, inventions, licenses, approvals, governmental authorizations, trade secrets and rights necessary to conduct their respective businesses as now conducted. None of the Company's material trademarks, trade names, service marks, service mark registrations, service names, patents, patent rights, copyrights, inventions, licenses, approvals, government authorizations, trade secrets or other intellectual property rights have expired or terminated, or, by the terms and conditions thereof, could expire or terminate within two years from the date of this Agreement. Except as disclosed in the SEC Documents, the Company and its Subsidiaries do not have any knowledge of any infringement by the Company or its Subsidiaries of any material trademark, trade name rights, patents, patent rights, copyrights, inventions, licenses, service names, service marks, service mark registrations, trade secret or other similar rights of others, or of any such development of similar or identical trade secrets or technical information by others, and there is no claim, action or proceeding being made or brought against, or to the Company's knowledge, being threatened against, the Company or its Subsidiaries regarding trademark, trade name, patents, patent rights, invention, copyright, license, service names, service marks, service mark registrations, trade secret or other infringement, which could reasonably be expected to have a Material Adverse Effect.

(l) Environmental Laws. The Company and its Subsidiaries (i) are in compliance with any and all applicable foreign, federal, state and local laws and regulations relating to the protection of human health and safety, the environment or hazardous or toxic substances or wastes, pollutants or

contaminants ("Environmental Laws"), (ii) have received all permits, licenses or other approvals required of them under applicable Environmental Laws to conduct their respective businesses and (iii) are in compliance with all terms and conditions of any such permit, license or approval, except where, in each of the three foregoing clauses, the failure to so comply could not reasonably be expected to have, individually or in the aggregate, a Material Adverse Effect.

(m) Title. Except as set forth in the SEC Documents, the Company and its Subsidiaries have good and marketable title in fee simple to all real property owned by them and good and marketable title in all personal property owned by them that is material to the business of the Company and its Subsidiaries, in each case free and clear of all liens, encumbrances and defects ("Liens") and, except for Liens as do not materially affect the value of such property and do not materially interfere with the use made and proposed to be made of such property by the Company and its Subsidiaries and Liens for the payment of federal, state or other taxes, the payment of which is neither delinquent nor subject to penalties. Any real property and facilities held under lease by the Company and its Subsidiaries are held by them under valid, subsisting and enforceable leases with which the Company and its Subsidiaries are in compliance with such exceptions as are not material and do not interfere with the use made and proposed to be made of such property and buildings by the Company and its Subsidiaries.

(n) Insurance. The Company and each of its Subsidiaries are insured by insurers of recognized financial responsibility against such losses and risks and in such amounts as management of the Company believes to be prudent and customary in the businesses in which the Company and its Subsidiaries are engaged. Neither the Company nor any such Subsidiary has been refused any insurance coverage sought or applied for and neither the Company nor any such Subsidiary has any reason to believe that it will not be able to renew its existing insurance coverage as and when such coverage expires or to obtain similar coverage from similar insurers as may be necessary to continue its business at a cost that would not materially and adversely affect the condition, financial or otherwise, or the earnings, business or operations of the Company and its Subsidiaries, taken as a whole.

(o) Regulatory Permits. The Company and its Subsidiaries possess all material certificates, authorizations and permits issued by the appropriate federal, state or foreign regulatory authorities necessary to conduct their respective businesses, and neither the Company nor any such Subsidiary has received any notice of proceedings relating to the revocation or modification of any such certificate, authorization or permit.

(p) Tax Status. The Company and each of its Subsidiaries has made or filed all federal and state income and all other material tax returns, reports and declarations required by any jurisdiction to which it is subject (unless and only to the extent that the Company and each of its Subsidiaries has set aside on its books provisions reasonably adequate for the payment of all unpaid and unreported taxes) and has paid all taxes and other governmental assessments and charges that are material in amount, shown or determined to be due on such returns, reports and declarations, except those being contested in good faith and has set aside on its books provision reasonably adequate for the payment of all taxes for periods subsequent to the periods to which such returns, reports or declarations apply. There are no unpaid taxes in any material amount claimed to be due by the taxing authority of any jurisdiction, and the officers of the Company know of no basis for any such claim.

(q) Transactions With Affiliates. Except as set forth in the SEC Documents, none of the officers or directors of the Company and, to the knowledge of the Company, none of the employees of the Company is presently a party to any transaction with the Company or any Subsidiary (other than for services as employees, officers and directors), including any contract, agreement or other arrangement providing for the furnishing of services to or by, providing for rental of real or personal property to or from, or otherwise requiring payments to or from any officer, director or such employee or, to the knowledge of the Company, any entity in which any officer, director, or any such employee has a substantial interest or is an officer, director, trustee or partner, in each case in excess of $120,000 other than for (i) payment of salary or consulting fees for services rendered, (ii) reimbursement for expenses incurred on behalf of the Company and (iii) other employee benefits, including stock option agreements under any stock option plan of the Company.

(r) Application of Takeover Protections. The Company and its board of directors have taken all necessary action, if any, in order to render inapplicable any control share acquisition, business combination, poison pill (including any distribution under a rights agreement) or other similar anti-takeover provision under the Certificate of incorporation or the laws of the state of its incorporation which is or could become applicable to the Investor as a result of the transactions contemplated by this Agreement, including, without limitation, the Company's issuance of the Shares and the Investor's ownership of the Shares.

(s) Disclosure. Except with respect to the material terms and conditions of the transactions contemplated by the Transaction Documents that will be timely publicly disclosed by the Company, subject to terms, conditions and restrictions relating to Confidential Information as set forth in the Loan Agreement, the Company confirms that neither it nor any other Person acting on its behalf has provided the Investor or its agents or counsel with any information that it believes constitutes or might constitute material, non-public information which is not otherwise disclosed in the SEC Documents. All of the disclosure furnished by or on behalf of the Company to the Investor regarding the Company, its business and the transactions contemplated hereby, including the disclosure schedules to this Agreement, is true and correct and does not contain any untrue statement of a material fact or omit to state any material fact necessary in order to make the statements made therein, in light of the circumstances under which they were made, not misleading. The press releases disseminated by the Company during the twelve months preceding the date of this Agreement taken as a whole do not contain any untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary in order to make the statements therein, in light of the circumstances under which they were made and when made, not misleading. The Company acknowledges and agrees that the Investor neither makes nor has made any representations or warranties with respect to the transactions contemplated hereby other than those specifically set forth in Section 3 hereof or in the Loan Agreement.

(t) Foreign Corrupt Practices. Neither the Company, nor to the knowledge of the Company, any agent or other Person acting on behalf of the Company, has (i) directly or indirectly, used any funds for unlawful contributions, gifts, entertainment or other unlawful expenses related to foreign or domestic political activity, (ii) made any unlawful payment to foreign or domestic government officials or employees or to any foreign or domestic political parties or campaigns from corporate funds, (iii) failed to disclose fully any contribution made by the Company (or made by any Person acting on its behalf of which the Company is aware) which is in violation of law, or (iv) violated in any material respect any provision of the Foreign Corrupt Practices Act of 1977, as amended.

(u) DTC Eligibility. The Company, through the Transfer Agent, currently participates in the DTC Fast Automated Securities Transfer (FAST) Program and the Common Stock can be transferred electronically to third parties via the DTC Fast Automated Securities Transfer (FAST) Program.

(v) Sarbanes-Oxley. The Company is in compliance in all material respects with all provisions of the Sarbanes-Oxley Act of 2002, as amended, which are applicable to it as of the date hereof.

(w) Certain Fees. No brokerage or finder's fees or commissions are or will be payable by the Company to any broker, financial advisor or consultant, finder, placement agent, investment banker, bank or other Person with respect to the transactions contemplated by the Transaction Documents. The Investor shall not have any obligation with respect to any fees or with respect to any claims made by or on behalf of other Persons for fees of a type contemplated in this Section 4(w) that may be due in connection with the transactions contemplated by the Transaction Documents.

(x) Investment Company. The Company is not required to be registered as, and immediately following the Closing will not be required to be registered as, an "investment company" within the meaning of the Investment Company Act of 1940, as amended.

(y) Listing and Maintenance Requirements. The Common Stock is registered pursuant to Section 12(b) of the Exchange Act, and the Company has taken no action designed to, or which to its knowledge is likely to have the effect of, terminating the registration of the Common Stock pursuant to the Exchange Act nor has the Company received any notification that the SEC is currently contemplating terminating such registration. Except as disclosed in the SEC Documents, the Company has not, in the twelve (12) months preceding the date hereof, received any notice from any Person to the effect that the Company is not in compliance with the listing or maintenance requirements of the Principal Market. Except as disclosed in the SEC Documents, the Company is, and has no reason to believe that it will not in the foreseeable future continue to be, in compliance with all such listing and maintenance requirements.

(z) Accountants. The Company's accountants are set forth in the SEC Documents and, to the knowledge of the Company, such accountants are an independent registered public accounting firm as required by the Securities Act.

(aa) No Market Manipulation. The Company has not, and to its knowledge no Person acting on its behalf has, (i) taken, directly or indirectly, any action designed to cause or to result in the stabilization or manipulation of the price of any security of the Company to facilitate the sale or resale of any of the Shares, (ii) sold, bid for, purchased, or, paid any compensation for soliciting purchases of, any of the Shares, or (iii) paid or agreed to pay to any Person any compensation for soliciting another to purchase any other securities of the Company.

(bb) Shell Company Status. The Company is not currently, and has never been, an issuer identified in Rule 144(i)(1) under the Securities Act.

5. COVENANTS.

(a) Filing of Current Report. The Company agrees that it shall, within one (1) business day of the Closing Date, file with the SEC a report on Form 8-K relating to the transactions contemplated

by, and describing the material terms and conditions of, the Transaction Documents (the "Current Report"), provided that all such filings shall be in accordance with the terms and conditions relating to Confidential Information as set forth in the Loan Agreement.

(b) Form D; Blue Sky Filings. The Company agrees to timely file a Form D with respect to the Shares as required under Regulation D and to provide a copy thereof, promptly upon request of the Investor. The Company shall take all such action, if any, as is reasonably necessary in order to obtain an exemption for or to register or qualify (i) the issuance of the Shares to the Investor under this Agreement and (ii) any subsequent resale of all Shares by the Investor, in each case, under applicable securities or "Blue Sky" laws of the states of the United States in such states as is reasonably requested by the Investor from time to time, and shall provide evidence of any such action so taken to the Investor.

(c) Listing/DTC. The Company shall (a) take all actions that are necessary, including providing appropriate notice to Nasdaq of the transactions contemplated by this Agreement, for the Shares to be listed on the Nasdaq Global Market and (b) comply with all listing, reporting, filing, and other obligations under the rules of Nasdaq and of the SEC. The Company shall use commercially reasonable efforts to maintain the listing of the Common Stock on the Principal Market and shall comply in all respects with the Company's reporting, filing and other obligations under the bylaws or rules and regulations of the Principal Market. Neither the Company nor any of its Subsidiaries shall take any action that would reasonably be expected to result in the delisting or suspension of the Common Stock on the Principal Market. The Company shall pay all fees and expenses in connection with satisfying its obligations under this Section 5(c). The Company shall take all action necessary to ensure that its Common Stock can be transferred electronically as DWAC Shares.

(d) Non-Public Information. Except as provided under the Loan Agreement, the Company confirms that neither it nor any other Person acting on its behalf shall provide the Investor or its agents or counsel with any information that constitutes or might constitute material, non-public information, unless a simultaneous public announcement thereof is made by the Company in the manner contemplated by Regulation FD.

(e) Taxes. The Company shall pay any and all transfer, stamp or similar taxes that may be payable with respect to the issuance and delivery of any shares of Common Stock to the Investor made under this Agreement.

(f) Securities Law Compliance. The Company shall comply with all applicable federal, state and foreign securities laws in connection with the offer, issuance and sale by the Company of the Shares contemplated by the Transaction Documents. Without limiting the generality of the foregoing, neither the Company nor any of its officers, directors or affiliates will take, directly or indirectly, any action designed or intended to stabilize or manipulate the price of any security of the Company, or which would reasonably be expected to cause or result in, stabilization or manipulation of the price of any security of the Company.

(g) Integration. From and after the date of this Agreement, neither the Company, nor any of its affiliates will, and the Company shall use its reasonable best efforts to ensure that no Person acting on any of their behalf will, directly or indirectly, make any offers or sales of any security or solicit any offers to buy any security, under circumstances that would cause this offering of the Shares to be integrated with other offerings of securities by the Company in a manner that would

require stockholder approval pursuant to the rules and regulations of the Principal Market on which any of the securities of the Company are listed or designated, unless stockholder approval is obtained before the closing of such subsequent transaction in accordance with the rules of such Principal Market.

(h) Other Transactions. The Company shall not enter into, announce or recommend to its stockholders any agreement, plan, arrangement or transaction in or of which the terms thereof would restrict, materially delay, conflict with or impair the ability or right of the Company to perform its obligations under any of the Transaction Documents to which it is a party, including, without limitation, the obligation of the Company to deliver the Shares to the Investor in accordance with the terms of this Agreement.

6. TRANSFER AGENT INSTRUCTIONS; TRANSFER RESTRICTIONS.

(a) Transfer Agent Instructions. On the Closing Date, the Company shall issue to the Transfer Agent (and any subsequent transfer agent) instructions to issue the Shares in accordance with the terms of this Agreement (the "Irrevocable Transfer Agent Instructions"). All Shares to be issued to or for the benefit of the Investor pursuant to this Agreement shall be issued to the Invest in book-entry form and held in an account at the Transfer Agent. The Company represents and warrants to the Investor that no instruction other than the Irrevocable Transfer Agent Instructions referred to in this Section 6 will be given by the Company to the Transfer Agent with respect to the Shares. Certificates and any other instruments evidencing the Shares shall bear a restrictive legend pursuant to Section 6(c).

(b) Transfer Restrictions. The Shares may only be disposed of in compliance with state and federal securities laws. In connection with any transfer of the Shares other than pursuant to an effective registration statement or Rule 144 or to the Company, the Company may require the Investor to provide to the Company an opinion of counsel selected by the Investor and reasonably acceptable to the Company, the form and substance of which opinion shall be reasonably satisfactory to the Company, to the effect that such transfer does not require registration of such transferred Shares under the Securities Act and, as a condition of such transfer, any such transferee shall agree in writing to be bound by the terms of this Agreement and shall have the rights and obligations of the Investor under this Agreement

(c) Legend. Each book-entry statement representing the Shares shall be stamped or otherwise imprinted with a legend substantially in the following form (in addition to any legend required by applicable state securities or "blue sky" laws):

THE SECURITIES REPRESENTED BY THIS BOOK-ENTRY STATEMENT (THE "SECURITIES") HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "SECURITIES ACT") OR ANY STATE SECURITIES LAWS AND MAY NOT BE SOLD, TRANSFERRED OR OTHERWISE DISPOSED OF UNLESS REGISTERED UNDER THE SECURITIES ACT AND UNDER APPLICABLE STATE SECURITIES LAWS OR AXSOME THERAPEUTICS, INC. SHALL HAVE RECEIVED AN OPINION OF ITS COUNSEL THAT REGISTRATION OF SUCH SECURITIES UNDER THE SECURITIES ACT AND UNDER THE PROVISIONS OF APPLICABLE STATE SECURITIES LAWS IS NOT REQUIRED.

The above legend may only be removed by the Transfer Agent in accordance with Section 3(h) hereof.

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7. CLOSING CONDITIONS

The obligation of the parties on the Closing Date shall be subject to the satisfaction or, where legally permissible, the waiver of each of the following conditions:

(a) The Investor shall have executed each of the applicable Transaction Documents and delivered the same to the Company; and

(b) The representations and warranties of the Investor shall be true and correct in all material respects as of the date hereof and as of the Closing Date as though made at that time.

(c) The Company shall have executed each of the applicable Transaction Documents and delivered the same to the Investor;

(d) The representations and warranties of the Company shall be true and correct in all material respects (except to the extent that any of such representations and warranties is already qualified as to materiality in Section 4 above, in which case, the portion of such representations and warranties so qualified shall be true and correct without further qualification) as of the date hereof and as of the Closing Date as though made at that time (except for representations and warranties that speak as of a specific date, which shall be true and correct as of such date) and the Company shall have performed, satisfied and complied in all material respects with the covenants, agreements and conditions required by the Transaction Documents to be performed, satisfied or complied with by the Company at or prior to the Closing Date.

(e) The Investor shall have received a certificate, executed by the CEO, President or CFO of the Company, dated as of the Closing Date, to the foregoing effect in the form attached hereto as Exhibit B;

(f) The Company shall have delivered to the Investor a secretary's certificate executed by the Secretary of the Company, dated as of the Closing Date, in the form attached hereto as Exhibit C;

(g) The Company shall have issued the Irrevocable Transfer Instructions to the Transfer Agent;

(h) All federal, state and local governmental laws, rules and regulations applicable to the transactions contemplated by the Transaction Documents and necessary for the execution, delivery and performance of the Transaction Documents and the consummation of the transactions contemplated thereby in accordance with the terms thereof shall have been complied with, and all consents, authorizations and orders of, and all filings and registrations with, all federal, state and local courts or governmental agencies and all federal, state and local regulatory or self-regulatory agencies necessary for the execution, delivery and performance of the Transaction Documents and the consummation of the transactions contemplated thereby in accordance with the terms thereof shall have been obtained or made, including, without limitation, in each case those required under the Securities Act, the Exchange Act, applicable state securities or “Blue Sky” laws or applicable rules and regulations of the Principal Market, or otherwise required by the SEC, the Principal Market or any state securities regulators;

(i) No statute, regulation, order, decree, writ, ruling or injunction shall have been enacted, entered, promulgated, threatened or endorsed by any federal, state, local or foreign court or governmental authority of competent jurisdiction which prohibits the consummation of or which would materially modify or delay any of the transactions contemplated by the Transaction Documents;

(j) No action, suit or proceeding before any federal, state, local or foreign arbitrator or any court or governmental authority of competent jurisdiction shall have been commenced or threatened, and no inquiry or investigation by any federal, state, local or foreign governmental authority of competent jurisdiction shall have been commenced or threatened, against the Company, or any of the officers, directors or affiliates of the Company, seeking to restrain, prevent or change the transactions contemplated by the Transaction Documents, or seeking material damages in connection with such transactions;

(k) No Person shall have commenced a proceeding against the Company pursuant to or within the meaning of any Bankruptcy Law;

(l) The Company, pursuant to or within the meaning of any Bankruptcy Law, shall not have (i) commenced a voluntary case, (ii) consented to the entry of an order for relief against it in an involuntary case, (iii) consented to the appointment of a Custodian of it or for all or substantially all of its property, or (iv) made a general assignment for the benefit of its creditors or is generally unable to pay its debts as the same become due; and

(m) A court of competent jurisdiction shall not have entered an order or decree under any Bankruptcy Law that (i) is for relief against the Company in an involuntary case, (ii) appoints a Custodian of the Company or for all or substantially all of its property, or (iii) orders the liquidation of the Company or any Subsidiary.

8. MISCELLANEOUS.

(a) Governing Law; Jurisdiction; Jury Trial. The corporate laws of the State of Delaware shall govern all issues concerning the relative rights of the Company and its stockholders. All other questions concerning the construction, validity, enforcement and interpretation of this Agreement and the other Transaction Documents shall be governed by the internal laws of the State of New York, without giving effect to any choice of law or conflict of law provision or rule (whether of the State of New York or any other jurisdictions) that would cause the application of the laws of any jurisdictions other than the State of Illinois. Each party hereby irrevocably submits to the exclusive jurisdiction of the state court located in the State of New York in the Borough of Manhattan and federal court located in the Southern District of the State of New York for the adjudication of any dispute hereunder or under the other Transaction Documents or in connection herewith or therewith, or with any transaction contemplated hereby or discussed herein, and hereby irrevocably waives, and agrees not to assert in any suit, action or proceeding, any claim that it is not personally subject to the jurisdiction of any such court, that such suit, action or proceeding is brought in an inconvenient forum or that the venue of such suit, action or proceeding is improper. Each party hereby irrevocably waives personal service of process and consents to process being served in any such suit, action or proceeding by mailing a copy thereof to such party at the address for such notices to it under this Agreement and the other Transaction Documents and agrees that such service shall constitute good and sufficient service of process and notice thereof. Nothing contained herein shall be deemed to limit in any way any right to serve process in any manner permitted by law. **EACH PARTY**

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HEREBY IRREVOCABLY WAIVES ANY RIGHT IT MAY HAVE, AND AGREES NOT TO REQUEST, A JURY TRIAL FOR THE ADJUDICATION OF ANY DISPUTE HEREUNDER OR IN CONNECTION HEREWITH OR ARISING OUT OF THIS AGREEMENT OR ANY OF THE OTHER TRANSACTION DOCUMENTS OR ANY TRANSACTION CONTEMPLATED HEREBY OR THEREBY.

(b) Counterparts. This Agreement may be executed in two or more identical counterparts, all of which shall be considered one and the same agreement and shall become effective when counterparts have been signed by each party and delivered to the other party; provided that a facsimile signature or signature delivered by e-mail in a ".pdf" format data file shall be considered due execution and shall be binding upon the signatory thereto with the same force and effect as if the signature were an original signature.

(c) Headings. The headings of this Agreement are for convenience of reference and shall not form part of, or affect the interpretation of, this Agreement.

(d) Severability. If any provision of this Agreement shall be invalid or unenforceable in any jurisdiction, such invalidity or unenforceability shall not affect the validity or enforceability of the remainder of this Agreement in that jurisdiction or the validity or enforceability of any provision of this Agreement in any other jurisdiction.

(e) Entire Agreement; Amendment. This Agreement and the other Transaction Documents supersede all other prior oral or written agreements among the Investor, the Company, their respective affiliates and Persons acting on their behalf with respect to the subject matter hereof, and this Agreement, the other Transaction Documents and the instruments referenced herein contain the entire understanding of the parties with respect to the matters covered herein and therein and, except as specifically set forth herein or therein, neither the Company nor the Investor makes any representation, warranty, covenant or undertaking with respect to such matters. The Company acknowledges and agrees that is has not relied on, in any manner whatsoever, any representations or statements, written or oral, other than as expressly set forth in the Transaction Documents. No provision of this Agreement or the other Transaction Documents may be amended other than by a written instrument signed by both parties hereto.

(f) Notices. Any notices, consents, waivers or other communications required or permitted to be given under the terms of this Agreement must be in writing and will be deemed to have been delivered: (i) upon receipt when delivered personally; (ii) upon receipt when sent by facsimile or email (provided confirmation of transmission is mechanically or electronically generated and kept on file by the sending party); or (iii) one Business Day after deposit with a nationally recognized overnight delivery service, in each case properly addressed to the party to receive the same. The addresses for such communications shall be:

If to the Company:

Axsome Therapeutics, Inc.
22 Cortlandt St., 16th Floor
New York, New York 10007
Telephone: (212) 332-3241
Facsimile: (212) 320-6270
E-mail: npizzie@axsome.com
Attention: Nick Pizzie, Chief Financial Officer

With a copy to (which shall not constitute notice or service of process):

DLA Piper LLP (US)
51 John F. Kennedy Parkway, Suite 120
Short Hills, New Jersey 07078
Telephone: (973) 307-3004
Facsimile: (973) 520-2551
E-mail: emilio.ragosa@dlapiper.com
Attention: Emilio Ragosa, Esq.

If to the Investors:

Hercules Capital, Inc.
400 Hamilton Avenue, Suite 310
Palo Alto, CA 94301
Telephone: 650-289-3060
E-mail: legal@htgc.com and mdutra@htgc.com
Attention: Legal Department
Chief Legal Officer and Michael Dutra

With a copy to (which shall not constitute notice or service of process):

LATHAM & WATKINS LLP
505 Montgomery Street, Suite 2000
San Francisco, CA 94111
Attn: Haim Zaltzman
Telephone: (415) 395-8095
E-mail: haim.zaltzman@lw.com
Attention: Haim Zaltzman

If to the Transfer Agent:

American Stock Transfer & Trust Company, LLC
6201 15th Avenue
Brooklyn, NY 11219

or at such other address and/or facsimile number and/or to the attention of such other Person as the recipient party has specified by written notice given to each other party three (3) Business Days prior to the effectiveness of such change. Written confirmation of receipt (A) given by the recipient of such notice, consent, waiver or other communication, (B) mechanically or electronically generated by the sender's facsimile machine or email account containing the time, date, and recipient facsimile number or email address, as applicable, and an image of the first page of such transmission or (C) provided by a nationally recognized overnight delivery service, shall be rebuttable evidence

of personal service, receipt by facsimile or email or receipt from a nationally recognized overnight delivery service in accordance with clause (i), (ii) or (iii) above, respectively.

(g) Successors and Assigns. This Agreement shall be binding upon and inure to the benefit of the parties and any permitted successors and assigns of the Company. The Company shall not assign this Agreement or any rights or obligations hereunder without the prior written consent of the Investor, including by merger or consolidation. The Investor may not assign its rights or obligations under this Agreement.

(h) No Third Party Beneficiaries. This Agreement is intended for the benefit of the parties hereto and any permitted successors and assigns of the Company and is not for the benefit of, nor may any provision hereof be enforced by, any other Person.

(i) Publicity. The Company shall afford the Investor and its counsel with the opportunity to review and comment upon the form and substance of, and shall give reasonable consideration to all such comments from the Investor or its counsel on, the Current Report and the Company's initial press release disclosing the Transaction Documents, if any, not less than one (1) business day prior to the issuance, filing or public disclosure thereof. The Company agrees and acknowledges that its failure to fully comply with this provision constitutes a Material Adverse Effect. Investor shall not issue a press release or any other public disclosure regarding this Agreement or the substance hereof without the prior written consent of the Company, which consent shall not be unreasonably withheld, conditioned or delayed.

(j) Further Assurances. Each party shall do and perform, or cause to be done and performed, all such further acts and things, and shall execute and deliver all such other agreements, certificates, instruments and documents, as the other party may reasonably request in order to carry out the intent and accomplish the purposes of this Agreement and the consummation of the transactions contemplated hereby.

(k) No Financial Advisor, Placement Agent, Broker or Finder. The Company represents and warrants to the Investor that it has not engaged any financial advisor, placement agent, broker or finder in connection with the transactions contemplated hereby. The Investor represents and warrants to the Company that it has not engaged any financial advisor, placement agent, broker or finder in connection with the transactions contemplated hereby. The Company shall be responsible for the payment of any fees or commissions, if any, of any financial advisor, placement agent, broker or finder relating to or arising out of the transactions contemplated hereby. The Company shall pay, and hold the Investor harmless against, any liability, loss or expense (including, without limitation, reasonable attorneys' fees and out of pocket expenses) arising in connection with any such claim.

(l) No Strict Construction. The language used in this Agreement will be deemed to be the language chosen by the parties to express their mutual intent, and no rules of strict construction will be applied against any party.

(m) Remedies, Other Obligations, Breaches and Injunctive Relief. The Investor's remedies provided in this Agreement shall be cumulative and in addition to all other remedies available to the Investor under this Agreement, at law or in equity (including a decree of specific performance and/or other injunctive relief), no remedy of the Investor contained herein shall be deemed a waiver of compliance with the provisions giving rise to such remedy and nothing herein shall limit the Investor's right to pursue actual damages for any failure by the Company to comply

with the terms of this Agreement. The Company acknowledges that a breach by it of its obligations hereunder will cause irreparable harm to the Investor and that the remedy at law for any such breach may be inadequate. The Company therefore agrees that, in the event of any such breach or threatened breach, the Investor shall be entitled, in addition to all other available remedies, to an injunction restraining any breach, without the necessity of showing economic loss and without any bond or other security being required.

(n) Enforcement Costs. If: (i) this Agreement is placed by the Investor in the hands of an attorney for enforcement or is enforced by the Investor through any legal proceeding; (ii) an attorney is retained to represent the Investor in any bankruptcy, reorganization, receivership or other proceedings affecting creditors' rights and involving a claim under this Agreement; or (iii) an attorney is retained to represent the Investor in any other proceedings whatsoever in connection with this Agreement, then the Company shall pay to the Investor, as incurred by the Investor, all reasonable costs and expenses including reasonable attorneys' fees incurred in connection therewith, in addition to all other amounts due hereunder. If this Agreement is placed by the Company in the hands of an attorney for enforcement or is enforced by the Company through any legal proceeding, then the Investor shall pay to the Company, as incurred by the Company, all reasonable costs and expenses including reasonable attorneys' fees incurred in connection therewith, in addition to all other amounts due hereunder.

(o) Waivers. No provision of this Agreement may be waived other than in a written instrument signed by the party against whom enforcement of such waiver is sought. No failure or delay in the exercise of any power, right or privilege hereunder shall operate as a waiver thereof, nor shall any single or partial exercise of any such power, right or privilege preclude other or further exercise thereof or of any other right, power or privilege.

[SIGNATURE PAGE FOLLOWS]

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IN WITNESS WHEREOF, the Investor and the Company have caused this Agreement to be duly executed as of the date first written above.

THE COMPANY:

AXSOME THERAPEUTICS, INC.

By:_____
Name:

Title:

INVESTORS:

HERCULES CAPITAL, INC.

By:_____
Name:
Title:

HERCULES PRIVATE GLOBAL VENTURE GROWTH FUND I L.P.

By:_____
Name:
Title:

HERCULES PRIVATE CREDIT FUND I L.P.

By:_____
Name:
Title:

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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, 2022

/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, 2022

/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, 2022 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, 2022

/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, 2022 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, 2022

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