Sage Therapeutics, Inc.
Form 10-Q
August 07, 2018

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-Q

(Mark One)

QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the quarterly period ended June 30, 2018

OR

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the transition period from to

Commission file number: 001-36544

Sage Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

Delaware	27-4486580
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)

215 First Street

Cambridge, Massachusetts 02142

(Address of principal executive office) (Zip Code)

Registrant's telephone number, including area code: (617) 299-8380

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 and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes No

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

Large accelerated filer		Accelerated filer
Non-accelerated filer	(Do not check if a smaller reporting company)	Smaller reporting company
Emerging Growth Company		

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

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

As of August 1, 2018, there were 46,664,296 shares of the registrant's common stock, $0.0001 par value per share, outstanding.

Cautionary Note Regarding Forward-Looking Statements

This Quarterly Report on Form 10-Q, or Quarterly Report, contains forward-looking statements that involve risks and uncertainties. We make such forward-looking statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. All statements other than statements of historical facts contained in this Quarterly Report are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as “may”, “will”, “should”, “expects”, “intends”, “plans”, “anticipates”, “beli “estimates”, “predicts”, “potential”, “continue” or the negative of these terms or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- our plans to develop and commercialize our product candidates in the central nervous system, or CNS, disorders we discuss in this Quarterly Report, and potentially in other indications;
- our expectations as to the sufficiency of the data generated from the clinical trials and non-clinical studies of our proprietary intravenous, or IV, formulation of brexanolone to support approval by the U.S. Food and Drug Administration, or FDA, of our new drug application, or NDA, for brexanolone IV in the treatment of postpartum depression, or PPD, and the potential timing of such a decision;
- our expectations as to the timing of a potential launch of brexanolone IV in the U.S. as a treatment for PPD, if our NDA is approved by the FDA; our views as to our future readiness for such a launch; and our plans with respect to the size, readiness and focus of our field force and possible sites of care for administration of brexanolone IV, including supervised home infusion;
- our expectations as to the sufficiency of our planned development program for SAGE-217 in major depressive disorder and PPD, if successful, to expedite our development of SAGE-217, and to support filing of an NDA with the FDA and potential approval in such indications;
- our expectations with respect to the anticipated development pathway and regulatory approval requirements for our product candidates outside the United States, including the potential for filing of a marketing authorization application in the European Union, or EU, and our related plans and expectations, including plans for continuing to build our organization in the EU, and the potential for entering into future collaborations and other types of contractual relationships, if appropriate, for accomplishing our strategic objectives;
- our views as to the anticipated rate and degree of market acceptance, and expectations regarding pricing and the potential scope, level and availability of reimbursement, of brexanolone IV and our other product candidates in any indication and country, if approved
- our ability, within the expected time-frames, to initiate clinical trials and non-clinical studies of existing or future product candidates, including pivotal clinical trials, and to successfully complete and announce the results of ongoing or future clinical trials;
- our estimates regarding expenses, use of cash, timing of future cash needs, and capital requirements;
- our expectations as to the potential to achieve future revenues;
- our expectations with respect to the availability of supplies of our product candidates, and the expected performance of our third-party manufacturers;
- our ability to obtain and maintain intellectual property protection for our proprietary assets and other forms of exclusivity relevant to our business;
- the estimated number of patients in indications of interest to us; the size of the potential markets for our product candidates; the potential for our product candidates in those markets, if approved; and our ability to serve those markets;
- the level of costs we may incur in connection with our activities, the possible timing and sources of future financings, and our ability to obtain additional financing when needed to fund future operations;

- the potential for success of competing products that are or become available for the indications that we are pursuing or may pursue in the future;
- the potential risk of loss of key scientific or management personnel; and
- other risks and uncertainties, including those listed under Part II, Item 1A, Risk Factors.

Any forward-looking statements in this Quarterly Report reflect our current views with respect to future events and with respect to our future financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things, those described under Part II, Item 1A, Risk Factors and elsewhere in this Quarterly Report. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

We may from time to time provide estimates, projections and other information concerning our industry, the general business environment, and the markets for certain diseases, including estimates regarding the potential size of those markets and the estimated incidence and prevalence of certain medical conditions. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties, and actual events, circumstances or numbers, including actual disease prevalence rates and market size, may differ materially from the information reflected in this Quarterly Report. Unless otherwise expressly stated, we obtained this industry, business information, market data, prevalence information and other data from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data, and similar sources, in some cases applying our own assumptions and analysis that may, in the future, prove not to have been accurate.

Sage Therapeutics, Inc.

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PART I — FINANCIAL INFORMATION

Item 1. Financial Statements
Sage Therapeutics, Inc. and Subsidiaries

Condensed Consolidated Balance Sheets

(in thousands, except share and per share data)

(Unaudited)

	June 30, 2018	December 31, 2017
Assets		
Current assets:		
Cash and cash equivalents	$325,830	$306,235
Marketable securities	766,603	212,613
Prepaid expenses and other current assets	12,958	6,227
Receivable from collaborator	18,378	—
Total current assets	1,123,769	525,075
Property and equipment, net	4,445	4,013
Restricted cash	1,269	849
Total assets	$1,129,483	$529,937
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$8,338	$9,350
Accrued expenses	39,581	42,601
Total current liabilities	47,919	51,951
Other liabilities	3,801	2,511
Total liabilities	51,720	54,462
Commitments and contingencies (Note 5)		
Stockholders' equity:		
Preferred stock, $0.0001 par value per share; 5,000,000 shares authorized at June 30, 2018 and December 31, 2017; no shares issued or outstanding at June 30, 2018 and December 31, 2017	—	—
Common stock, $0.0001 par value per share; 120,000,000 shares authorized at June 30, 2018 and December 31, 2017; 46,605,353 and 42,003,894 shares issued at June 30, 2018 and December 31, 2017, respectively; 46,603,839 and 42,002,934 shares outstanding at June 30, 2018 and	5	5

December 31, 2017, respectively		
Treasury stock, at cost, 1,514 and 960 shares		
at June 30, 2018 and December 31, 2017, respectively	(211)	(113)
Additional paid-in capital	1,760,137	1,066,059
Accumulated deficit	(682,023)	(590,447)
Accumulated other comprehensive loss	(145)	(29)
Total stockholders' equity	1,077,763	475,475
Total liabilities and stockholders' equity	$1,129,483	$529,937

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

Sage Therapeutics, Inc. and Subsidiaries

Condensed Consolidated Statements of Operations and Comprehensive Loss

(in thousands, except share and per share data)

(Unaudited)

	Three months ended June 30,		Six months ended June 30,	
	2018	2017	2018	2017
Collaboration revenue	$90,000	$—	$90,000	$—
Operating expenses:				
Research and development	68,980	55,900	118,250	101,100
General and administrative	43,167	14,954	72,016	27,234
Total operating expenses	112,147	70,854	190,266	128,334
Loss from operations	(22,147)	(70,854)	(100,266)	(128,334)
Interest income, net	5,137	672	8,666	1,379
Other expense, net	32	(20)	24	(24)
Net loss	$(16,978)	$(70,202)	$(91,576)	$(126,979)
Net loss per share—basic and diluted	$(0.36)	$(1.88)	$(2.02)	$(3.40)
Weighted average number of common shares outstanding—basic and diluted	46,541,716	37,361,129	45,439,666	37,315,393
Comprehensive loss:				
Net loss	$(16,978)	$(70,202)	$(91,576)	$(126,979)
Other comprehensive items:				
Unrealized gain (loss) on marketable securities	40	14	(116)	35
Total other comprehensive gain (loss)	40	14	(116)	35
Total comprehensive loss	$(16,938)	$(70,188)	$(91,692)	$(126,944)

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

Sage Therapeutics, Inc. and Subsidiaries

Condensed Consolidated Statements of Cash Flows

(in thousands)

(Unaudited)

	Six months ended June 30,	
	2018	2017
Cash flows from operating activities		
Net loss	$(91,576)	$(126,979)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation expense	44,845	15,558
Premium on marketable securities	(75)	—
Amortization of premium (discount) on marketable securities	(4,154)	5
Depreciation	493	260
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(25,091)	(93)
Accounts payable	(903)	(6,768)
Accrued expenses and other liabilities	(2,245)	3,731
Net cash used in operating activities	(78,706)	(114,286)
Cash flows from investing activities		
Proceeds from sales and maturities of marketable securities	263,460	110,436
Purchases of marketable securities	(813,337)	(33,922)
Purchases of property and equipment	(1,054)	(321)
Net cash provided by (used in) investing activities	(550,931)	76,193
Cash flows from financing activities		
Proceeds from stock option exercises and employee stock purchase plan issuances	19,402	3,311
Payment of employee tax obligations related to vesting of restricted stock units	(904)	—
Payments of offering costs	(340)	—
Proceeds from public offerings of common stock, net of commissions and underwriting discounts	631,494	—
Net cash provided by financing activities	649,652	3,311
Net increase (decrease) in cash, cash equivalents and restricted cash	20,015	(34,782)
Cash, cash equivalents and restricted cash at beginning of period	307,084	169,081
Cash, cash equivalents and restricted cash at end of period	$327,099	$134,299
Supplemental disclosure of non-cash investing and financing activities		
Purchases of property and equipment included in accounts payable	$10	$—

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

SAGE THERAPEUTICS, INC. AND SUBSIDIARIES

Notes to Condensed Consolidated Financial Statements

(Unaudited)

1. Nature of the Business

Sage Therapeutics, Inc. ("Sage" or the "Company") is a clinical-stage biopharmaceutical company committed to developing and commercializing novel medicines to treat life-altering central nervous system ("CNS") disorders, where there are no approved therapies or existing therapies are inadequate. The Company has a portfolio of product candidates with a current focus on modulating two critical CNS receptor systems, GABA and NMDA. The GABA receptor family, which is recognized as the major inhibitory neurotransmitter in the CNS, mediates downstream neurologic and bodily function via activation of $GABA_A$ receptors. The NMDA-type receptors of the glutamate receptor system are a major excitatory receptor system in the CNS. Dysfunction in these systems is implicated in a broad range of CNS disorders. The Company is targeting CNS indications where patient populations are easily identified, clinical endpoints are well-defined, and development pathways are feasible.

The Company was incorporated under the laws of the State of Delaware on April 16, 2010, and commenced operations on January 19, 2011 as Sterogen Biopharma, Inc. On September 13, 2011, the Company changed its name to Sage Therapeutics, Inc.

The Company is subject to risks and uncertainties common to companies in the biotech industry, including, but not limited to, the risks associated with developing product candidates at each stage of non-clinical and clinical development; the challenges associated with gaining regulatory approval of such product candidates; the risks associated with commercializing pharmaceutical products, if approved for marketing and sale; the potential for development by third parties of new technological innovations that may compete with the Company's products; the dependence on key personnel; the challenges of protecting proprietary technology; the need to comply with government regulations; the high costs of drug development; and the uncertainty of being able to secure additional capital when needed to fund operations.

Under Accounting Standards Update, or ASU, 2014-15, Presentation of Financial Statements—Going Concern (Subtopic 205-40), or ASC 205-40, the Company has the responsibility to evaluate whether conditions and/or events raise substantial doubt about its ability to meet its future financial obligations as they become due within one year after the date that the financial statements are issued. The Company has incurred losses and negative cash flows from operations since its inception. As of June 30, 2018, the Company had an accumulated deficit of $682.0 million. From its inception through June 30, 2018, the Company received net proceeds of $1.6 billion from the sales of redeemable convertible preferred stock, the issuance of convertible notes, and the sales of common stock in its initial public offering ("IPO") in July 2014 and follow-on public offerings in April 2015, January 2016, September 2016, November 2017 and February 2018. Until such time, if ever, as the Company can generate substantial product revenue and achieve profitability, the Company expects to finance its cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements and other sources of funding. If the Company is unable to raise additional funds through equity or debt financings when needed, the Company may be required to delay, limit, reduce or terminate product development or future commercialization efforts or grant rights to develop and market products or product candidates that the Company would otherwise prefer to develop and market itself. The Company expects that, based on its current operating plans, the Company's existing cash, cash equivalents and marketable securities will be sufficient to fund its current planned operations for at least the next twelve months from the issuance of these unaudited interim condensed consolidated financial statements.

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2. Summary of Significant Accounting Policies

The following is a summary of significant accounting policies followed in the preparation of these unaudited condensed consolidated financial statements.

Basis of Presentation

The unaudited interim condensed consolidated financial statements of the Company included herein have been prepared pursuant to the rules and regulations of the Securities and Exchange Commission (the "SEC"). Certain information and footnote disclosures normally included in financial statements prepared in accordance with accounting principles generally accepted in the United States of America ("GAAP") have been condensed or omitted from this report, as is permitted by such rules and regulations. Accordingly, these unaudited condensed consolidated financial statements should be read in conjunction with the audited consolidated financial statements as of and for the year ended December 31, 2017, included in the Company's Annual Report on Form 10-K for the year ended December 31, 2017.

The unaudited interim condensed consolidated financial statements have been prepared on the same basis as the audited consolidated financial statements. In the opinion of the Company's management, the accompanying unaudited condensed consolidated financial statements contain all adjustments, consisting of only normal recurring adjustments, necessary for a fair statement of its financial position as of June 30, 2018, its results of operations and comprehensive loss for the three and six months ended June 30, 2018 and 2017, and its cash flows for the three and six months ended June 30, 2018 and 2017. The consolidated balance sheet at December 31, 2017 was derived from audited financial statements, but does not include all disclosures required by GAAP. The results for the three and six months ended June 30, 2018 are not necessarily indicative of the results for the year ending December 31, 2018, or for any future period.

Principles of Consolidation

The unaudited interim condensed consolidated financial statements include the accounts of the Company and its wholly-owned subsidiaries as disclosed in Note 2, Summary of Significant Accounting Policies, within the "Notes to Consolidated Financial Statements" accompanying its Annual Report on Form 10-K for the fiscal year ended December 31, 2017. Intercompany accounts and transactions have been eliminated.

Use of Estimates

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

Research and Development

Research and development expenses are comprised of costs incurred in performing research and development activities, including salaries and benefits, overhead costs, depreciation, contract services and other related costs. Research and development costs are expensed to operations as the related obligation is incurred.

The Company has entered into various research and development contracts with research institutions and other companies both inside and outside of the United States. These agreements are generally cancelable, and related costs

are recorded as research and development expenses as incurred. The Company records accruals for estimated ongoing research and development costs. When evaluating the adequacy of the accrued liabilities, the Company analyzes progress of the studies, including the phase or completion of events, invoices received and contracted costs. Significant judgments and estimates may be made in determining the accrued balances at the end of any reporting period. Actual results could differ from the estimates made by the Company. The historical accrual estimates made by the Company have not been materially different from the actual costs.

Stock-Based Compensation

The Company recognizes compensation expense for stock-based awards, including grants of stock options and restricted stock, made to employees and non-employee directors based on the estimated fair value on the date of grant, over the requisite service period.

The Company recognizes compensation expense for stock-based awards granted to non-employee consultants based on the fair value of the award on each date on which the awards vest. Compensation expense is recognized over the vesting period, provided that services are rendered by such non-employee consultants during that time. At the end of each financial reporting period, the fair value of unvested options is re-measured using the then-current fair value of the Company's common stock and updated assumptions in the Black-Scholes option-pricing model; and the fair value of restricted stock awards is re-measured using the then-current fair value of the Company's common stock.

For awards that vest upon achievement of a performance condition, the Company recognizes compensation expense when achievement of the performance condition is met or during the period from which meeting the condition is deemed probable until the expected date of meeting the performance condition.

The fair value of each option grant is estimated using the Black-Scholes option-pricing model. Through December 31, 2015, the Company lacked sufficient Company-specific historical and implied volatility information, and as a result, the Company used the volatility of a group of publicly-traded peer companies in the Black-Scholes calculations. Beginning in 2016, the Company estimated its expected volatility using a weighted average of the historical volatility of publicly-traded peer companies and the volatility of its common stock and expects to continue to do so until such time as it has adequate historical data regarding the volatility of its traded stock price for the duration of the expected term. The expected term of the Company's options has been determined utilizing the "simplified" method for awards that qualify as "plain-vanilla" options, while the expected term of its options granted to consultants and non-employee directors has been determined based on the contractual term of the options. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. The 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.

The Company also applies a forfeiture rate in order to calculate stock-based compensation expense. Expected forfeitures are based on the historical experience of the Company and management's expectations of future forfeitures. To the extent actual forfeitures differ from the estimates, the difference is recorded as a cumulative adjustment in the period in which the estimates are revised. The Company recognizes stock-based compensation expense for only the portion of awards that are expected to vest.

Cash and Cash Equivalents

The Company considers all highly liquid investments with an original maturity of three months or less at the date of purchase to be cash equivalents. As of June 30, 2018, cash equivalents were comprised of cash equivalents and money market funds. As of December 31, 2017, cash equivalents were comprised of cash equivalents, money market funds and overnight reverse repurchase agreements.

Marketable securities

Marketable securities consist of investments with original maturities greater than 90 days. The Company considers its investment portfolio of investments to be available-for-sale. Accordingly, these investments are recorded at fair value, which is based on quoted market prices. Unrealized gains and losses are reported as a component of accumulated

other comprehensive items in stockholders' equity. Realized gains and losses and declines in value judged to be other than temporary are included as a component of other expense, net, based on the specific identification method. When determining whether a decline in value is other than temporary, the Company considers several factors, including whether the Company has the intent to sell the security, and whether it is more likely than not that the Company will be required to sell the security prior to recovery of its amortized cost basis. Marketable securities that have remaining contractual

maturities of one year or less are classified as short term. No declines in value were deemed to be other than temporary during the three and six months ended June 30, 2018 and 2017.

Fair Value Measurements

Fair value is the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. Financial assets and liabilities carried at fair value are classified and disclosed in one of the following three categories:

Level 1 —Quoted market prices in active markets for identical assets or liabilities.

Level 2 —Observable inputs other than Level 1 prices, such as quoted prices for similar assets or liabilities; quoted prices in markets that are not active; or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.

Level 3 —Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

The Company's cash equivalents and marketable securities at June 30, 2018 and December 31, 2017 were carried at fair value, determined according to the fair value hierarchy; see Footnote 3, Fair Value Measurements herein.

The carrying amounts reflected in the unaudited condensed consolidated balance sheets for accounts payable and accrued expenses approximate their fair values due to their short-term maturities at June 30, 2018 and December 31, 2017, respectively.

Revenue Recognition

Effective January 1, 2017, the Company adopted Accounting Standards Codification ("ASC"), Topic 606, Revenue from Contracts with Customers ("Topic 606"). This standard applies to all contracts with customers, except for contracts that are within the scope of other standards, such as collaboration arrangements and leases. Prior to the three months ended June 30, 2018, the Company did not have any revenue-generating arrangements and therefore there was no transition impact from the adoption of Topic 606.

Under Topic 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration that the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of Topic 606, the entity performs the following five steps: (i) identify the contract with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price, including variable consideration, if any; (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 contracts when it is probable that the Company will collect the consideration to which it is entitled in exchange for the goods or services it transfers to a customer.

Once a contract is determined to be within the scope of Topic 606, the Company assesses the goods or services promised within each contract and determines those that are performance obligations. Arrangements that include rights to additional goods or services that are exercisable at a customer's discretion are generally considered options. The Company assesses if these options provide a material right to the customer and if so, they are considered performance obligations. The exercise of a material right may be accounted for as a contract modification or as a continuation of the contract for accounting purposes.

The Company assesses whether each promised good or service is distinct for the purpose of identifying the performance obligations in the contract. This assessment involves subjective determinations and requires management to make judgments about the individual promised goods or services and whether such are separable from the other aspects of the contractual relationship. Promised goods and services are considered distinct provided that: (i) the customer can benefit from the good or service either on its own or together with other resources that are readily available to the

customer (that is, the good or service is capable of being distinct) and (ii) the entity's promise to transfer the good or service to the customer is separately identifiable from other promises in the contract (that is, the promise to transfer the good or service is distinct within the context of the contract). In assessing whether a promised good or service is distinct in the evaluation of a collaboration arrangement subject to Topic 606, the Company considers factors such as the research, manufacturing and commercialization capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. The Company also considers the intended benefit of the contract in assessing whether a promised good or service is separately identifiable from other promises in the contract. If a promised good or service is not distinct, the Company is required to combine that good or service with other promised goods or services until it identifies a bundle of goods or services that is distinct.

The transaction price is then determined and allocated to the identified performance obligations in proportion to their standalone selling prices ("SSP") on a relative SSP basis. SSP is determined at contract inception and is not updated to reflect changes between contract inception and when the performance obligations are satisfied. Determining the SSP for performance obligations requires significant judgment. In developing the SSP for a performance obligation, the Company considers applicable market conditions and relevant entity-specific factors, including factors that were contemplated in negotiating the agreement with the customer and estimated costs. In certain circumstances, the Company may apply the residual method to determine the SSP of a good or service if the standalone selling price is considered highly variable or uncertain. The Company validates the SSP for performance obligations by evaluating whether changes in the key assumptions used to determine the SSP will have a significant effect on the allocation of arrangement consideration between multiple performance obligations.

If the consideration promised in a contract includes a variable amount, the Company estimates the amount of consideration to which it will be entitled in exchange for transferring the promised goods or services to a customer. The Company determines the amount of variable consideration by using the expected value method or the most likely amount method. The Company includes the unconstrained amount of estimated variable consideration in the transaction price. The amount included in the transaction price is constrained to the amount for which it is probable that a significant reversal of cumulative revenue recognized will not occur. At the end of each subsequent reporting period, the Company re-evaluates the estimated variable consideration included in the transaction price and any related constraint, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis in the period of adjustment.

If an arrangement includes development and regulatory milestone payments, the Company evaluates whether the milestones are considered probable of being reached and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the Company's control or the licensee's control, such as regulatory approvals, are generally not considered probable of being achieved until those approvals are received.

In determining the transaction price, the Company adjusts consideration for the effects of the time value of money if the timing of payments provides the Company with a significant benefit of financing. The Company does not assess whether a contract has a significant financing component if the expectation at contract inception is such that the period

between payment by the licensees and the transfer of the promised goods or services to the licensees will be one year or less. The Company assessed its revenue-generating arrangement in order to determine whether a significant financing component exists and concluded that a significant financing component does not exist in the arrangement. For arrangements with licenses of intellectual property that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, the Company recognizes royalty revenue and sales-based milestones at the later of (i) when the related sales occur, or (ii) when the performance obligation to which the royalty has been allocated has been satisfied.

The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) each performance obligation is satisfied at a point in time or over time, and if over time this is based on the use of an output or input method.

Recently Issued Accounting Pronouncements

In February 2016, the Financial Accounting Standards Board (“FASB”) issued ASU No. 2016-02, Leases, which will replace the existing guidance in ASC 840, “Leases.” The updated standard aims to increase transparency and comparability among organizations by requiring lessees to recognize leased assets and leased liabilities on the consolidated balance sheets and requiring disclosure of key information about leasing arrangements. The standard will be effective on January 1, 2019, with early adoption permitted. The Company is in the process of evaluating the impact that this new guidance will have on its consolidated financial statements.

In June 2016, the FASB issued ASU No. 2016-13, Financial Instruments - Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments, which introduces a new methodology for accounting for credit losses on financial instruments, including available-for-sale debt securities. The guidance establishes a new "expected loss model" that requires entities to estimate current expected credit losses on financial instruments by using all practical and relevant information. Any expected credit losses are to be reflected as allowances rather than reductions in the amortized cost of available-for-sale debt securities. Early adoption is permitted for annual periods beginning after December 15, 2018, and interim periods therein. The Company is in the process of evaluating the impact that this new guidance will have on its consolidated financial statements.

In August 2016, the FASB issued ASU No. 2016-15, Statement of Cash Flows (Topic 230): Classification of Certain Cash Receipts and Cash Payments. The standard reduces the diversity in practice in how certain cash receipts and cash payments are presented and classified in the statements of cash flows. The Company adopted the standard on the required effective date of January 1, 2018. This guidance did not have a significant impact on the Company’s consolidated financial statements and related disclosures.

In November 2016, the FASB issued ASU No. 2016-18, Statement of Cash Flows (Topic 230): Restricted Cash that changes the presentation of restricted cash and cash equivalents in the statements of cash flows. Restricted cash and restricted cash equivalents will be included with cash and cash equivalents when reconciling the beginning-of-period and end-of-period total amounts shown on the statements of cash flows. The Company adopted this standard during the first quarter of 2018. Restricted cash is now included as a component of cash, cash equivalents, and restricted cash on the Company’s unaudited condensed consolidated statements of cash flows. Restricted cash balances are classified as non-current unless, under the terms of the applicable agreements, the funds will be released from restrictions within one year from the balance sheet date. The inclusion of restricted cash increased the beginning balances of the unaudited condensed consolidated statements of cash flows by $0.8 million and $0.6 million, respectively, and the ending balances by $1.3 million and $0.8 million, respectively, for the six months ended June 30, 2018 and 2017.

In May 2017, the FASB issued ASU No. 2017-09, Compensation—Stock Compensation (Topic 718) — Scope of Modification Accounting, which applies to entities that change the terms or conditions of a share-based payment award. The amendments in this standard include guidance on determining whether changes to the terms and conditions of share-based payment awards require an entity to apply modification accounting under Topic 718 unless all of the following conditions are met: (1) the fair value of the modified award is the same as the fair value of the original award immediately before the original award is modified, and if the modification does not affect any of the inputs to the valuation technique that the entity uses to value the award, then the entity is not required to estimate the value immediately before and after the modification; (2) the vesting conditions of the modified award are the same as the vesting conditions of the original award immediately before the original award is modified; and (3) the classification of the modified award as an equity instrument or a liability instrument is the same as the classification of the original award immediately before the original award is modified. The Company adopted the standard on the required effective date of January 1, 2018. This guidance did not have a significant impact on the Company’s

consolidated financial statements and related disclosures.

In June 2018, the FASB issued ASU 2018-07, Compensation—Stock Compensation (Topic 718) – Improvements to Nonemployee Share-Based Payment Accounting ("ASU 2018-07"), which aligns the accounting for share-based payment awards issued to employees and non-employees. Under the new guidance, the existing guidance regarding employees will apply to share-based transactions with non-employees, as long as the transaction is not effectively a form of financing, with the exception of specific guidance related to the attribution of compensation cost. The cost of non-employee awards will continue to be recorded as if the grantor had paid cash for the goods or services. In addition, the contractual term will be able to be used in lieu of an expected term in the option-pricing model for non-employee awards. The amendments in

the new guidance are effective for public entities for fiscal years beginning after December 15, 2018, including interim periods within that fiscal year. Early adoption is permitted, including in interim periods, but no earlier than an entity's adoption of Accounting Standards Codification 606. The Company is in the process of evaluating the impact that this new guidance will have on its consolidated financial statements.

Other accounting standards that have been issued or proposed by the FASB or other standards-setting bodies that do not require adoption until a future date are not expected to have a material impact on the Company's consolidated financial statements upon adoption.

3. Fair Value Measurements

The Company's cash equivalents are classified within Level 1 of the fair value hierarchy. The Company's investments in marketable securities are classified within Level 2 of the fair value hierarchy.

The fair values of the Company's marketable securities are based on prices obtained from independent pricing sources. Consistent with the fair value hierarchy described above, securities with validated quotes from pricing services are reflected within Level 2, as they are primarily based on observable pricing for similar assets or other market observable inputs. Typical inputs used by these pricing services include, but are not limited to, reported trades, benchmark yields, issuer spreads, bids, offers or estimates of cash flow, prepayment spreads and default rates.

The following tables summarize the Company's money market funds and marketable securities as of June 30, 2018 and December 31, 2017.

	June 30, 2018			
	Total	Quoted Prices in Active Markets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
	(in thousands)			
Cash equivalents:				
Cash equivalents	$325,830	$325,830	$ —	$ —
Total cash equivalents	325,830	325,830	—	—
Marketable securities:				
U.S. government securities	225,335	—	225,335	—
U.S. corporate bonds	110,363	—	110,363	—
International corporate bonds	26,503	—	26,503	—
U.S. commercial paper	211,144	—	211,144	—
International commercial paper	193,258	—	193,258	—
Total marketable securities	766,603	—	766,603	—
Total cash equivalents and marketable securities	$1,092,433	$325,830	$ 766,603	$ —

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	December 31, 2017			
	Total	Quoted Prices in Active Markets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
	(in thousands)			
Cash equivalents:				
Cash equivalents	$306,235	$306,235	$—	$—
Total cash equivalents	306,235	306,235	—	—
Marketable securities:				
U.S. government securities	49,606	—	49,606	—
U.S. corporate bonds	48,959	—	48,959	—
U.S. commercial paper	65,583	—	65,583	—
International commercial paper	48,465	—	48,465	—
Total marketable securities	212,613	—	212,613	—
Total cash equivalents and marketable securities	$518,848	$306,235	$212,613	$—

During the six months ended June 30, 2018 and 2017, there were no transfers among the Level 1, Level 2 and Level 3 categories.

Marketable Securities

The following tables summarize the gross unrealized gains and losses of the Company's marketable securities as of June 30, 2018 and December 31, 2017:

	June 30, 2018			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
	(in thousands)			
Assets:				
U.S. government securities	$225,363	$ 5	$ (33)	$225,335
U.S. corporate bonds	110,454	1	(92)	110,363
International corporate bonds	26,518	—	(15)	26,503
U.S. commercial paper	211,150	—	(6)	211,144
International commercial paper	193,263	—	(5)	193,258
	$766,748	$ 6	$ (151)	$766,603

	December 31, 2017		
		Gross Unrealized	Gross Unrealized

	Amortized Cost	Gains	Losses	Fair Value
	(in thousands)			
Assets:				
U.S. government securities	$49,612	$ —	$ (6)	$49,606
U.S. corporate bonds	48,982	2	(25)	48,959
U.S. commercial paper	65,583	—	—	65,583
International commercial paper	48,465	—	—	48,465
	$212,642	$ 2	$ (31)	$212,613

As of June 30, 2018, all marketable securities held by the Company had remaining contractual maturities of one year or less.

There have been no impairments of the Company’s assets measured and carried at fair value during the six months ended June 30, 2018 and the year ended December 31, 2017.

4. Balance Sheet Components
Property and Equipment, net

Property and equipment, net, consists of the following:

	June 30, 2018	December 31, 2017
	(in thousands)	
Computer hardware and software	$1,476	$ 1,090
Furniture and equipment	936	1,029
Leasehold improvements	3,599	2,967
	6,011	5,086
Less: Accumulated depreciation	(1,566)	(1,073)
	$4,445	$ 4,013

Depreciation expense for the three months ended June 30, 2018 and 2017 was $0.2 million and $0.1 million, respectively. Depreciation expense for the six months ended June 30, 2018 and 2017 was $0.5 million and $0.3 million, respectively.

The useful life for computer hardware and software is 3 years, furniture and equipment is 5 years and leasehold improvements is the lesser of the useful life or the term of the respective lease.

Accrued Expenses

Accrued expenses consist of the following:

	June 30, 2018	December 31, 2017
	(in thousands)	
Development costs	$23,679	$ 23,473
Employee-related expenses	9,250	15,838
Professional services	6,195	3,166
Other accrued expenses	457	124
	$39,581	$ 42,601

5. Commitments and Contingencies
Operating Leases

The Company leases office space in two multi-tenant buildings in Cambridge, Massachusetts, consisting, as of March 31, 2018, of 54,943 square feet in one building under an operating lease that expires on August 15, 2024 and 19,805 square feet in the second building under an operating lease that will expire on February 28, 2022.

In April 2018, the Company entered into the First Amendment to the lease for office space in the second building. The Company increased the amount of square feet of office space from 19,805 square feet to 40,419 square feet, an increase of 20,614 square feet, consisting of (i) 13,481 square feet beginning on August 1, 2018, and (ii) 7,133 square feet beginning on October 1, 2018. The term for this additional space will expire on August 31, 2024. Additionally, the term of the existing lease will be extended from February 28, 2022 until August 31, 2024.

In May 2018, the Company entered into a lease for office space in a multi-tenant building in Raleigh, North Carolina. The amount of square feet of office space is 15,525 square feet and the lease period will begin on September 1, 2018. The term for this space will expire on November 30, 2024.

Future minimum lease payments under non-cancelable operating leases are as follows at June 30, 2018:

Years Ending December 31,	(in thousands)
2018	$ 2,867
2019	6,657
2020	6,784
2021	6,913
2022	7,106
Thereafter	12,189
	$ 42,516

License Agreements

CyDex License Agreement

In September 2015, the Company and CyDex Pharmaceuticals, Inc. (“CyDex”) amended and restated their existing commercial license agreement. Under the terms of the commercial license agreement as amended and restated, CyDex has granted to the Company an exclusive license to CyDex’s Captisol drug formulation technology and related intellectual property for the manufacture of pharmaceutical products incorporating brexanolone and the Company’s compound known as SAGE-689, and the development and commercialization of the resulting products in the treatment, prevention or diagnosis of any disease or symptom in humans or animals other than (i) the ocular treatment of any disease or condition with a formulation, including a hormone; (ii) topical ocular treatment of inflammatory conditions; (iii) treatment and prophylaxis of fungal infections in humans; and (iv) any ocular treatment for retinal degeneration. As of June 30, 2018, the Company paid to CyDex $1.0 million for licensing fees, which was recorded as research and development expense.

The Company is obligated to make milestone payments under the amended and restated license agreement with CyDex based on the achievement of clinical development and regulatory milestones in the amount of up to $0.8 million in clinical milestones and up to $3.8 million in regulatory milestones for each of the first two fields with respect to brexanolone; up to $1.3 million in clinical milestones and up to $8.5 million in regulatory milestones for each of the third and fourth fields with respect to brexanolone; and up to $0.8 million in clinical milestones and up to $1.8 million in regulatory milestones for one field with respect to SAGE-689. As of June 30, 2018, the Company recorded research and development expense and made cash payments of $2.3 million related to these clinical development and regulatory milestones.

For the three and six months ended June 30, 2018, the Company recorded research and development expense and made cash payments of $0.8 million related to regulatory milestones for the brexanolone program under the license agreement with CyDex. For the three and six months ended June 30, 2017, the Company did not record any expense or make any milestone payments related to clinical development or regulatory milestones for the brexanolone program under the license agreement with CyDex.

University of California License Agreements

In October 2013, the Company entered into a non-exclusive license agreement with The Regents of the University of California under which the Company was granted a non-exclusive license to certain clinical data and clinical material

for use in the development and commercialization of biopharmaceutical products in the licensed field, including status epilepticus and postpartum depression. In May 2014, the license agreement was amended to add the treatment of essential tremor to the licensed field of use, materials and milestone fee provisions of the agreement. As of December 31, 2015, the Company paid to The Regents of the University of California clinical development milestones of $0.1 million and will be required to pay royalties of less than 1% on net sales for a period of fifteen years following the sale of the first product developed using the data and materials. The license will terminate on the earlier to occur of (i) 27 years after the effective date or (ii) 15 years after the last-derived product is first commercially sold.

In June 2015, the Company entered into an exclusive license agreement with The Regents of the University of California whereby the Company was granted an exclusive license to certain patent rights related to the use of allopregnanolone to treat various diseases. In exchange for such license, the Company paid an upfront payment of $50,000 and will make payments of $15,000 for annual maintenance fees until the calendar year following the first sale, if any, of a licensed product. The Company is obligated to make milestone payments following the achievement of specified regulatory and sales milestones of up to $0.7 million and $2.0 million in the aggregate, respectively, of which none have been paid to date. Following the first sale, if any, of a licensed product, the Company is obligated to pay royalties at a low single digit percentage of net sales, if any, of licensed products, subject to specified minimum annual royalty amounts. Unless terminated by operation of law or by acts of the parties under the terms of the agreement, the license agreement will terminate when the last-to-expire patents or last-to-be abandoned patent applications expire, whichever is later. As of June 30, 2018, the Company recorded research and development expense and made cash payments of $0.3 million related to these regulatory and sales milestones.

For the three and six months ended June 30, 2018, the Company recorded research and development expense and made cash payments of $0.2 million related to regulatory milestones under the license agreements with The Regents of the University of California. For the three and six months ended June 30, 2017, the Company did not record any expense or make any milestone or royalty payments under either license agreement with The Regents of the University of California.

Washington University License Agreement

In November 2013, the Company entered into a license agreement with Washington University whereby the Company was granted exclusive, worldwide rights to develop and commercialize a novel set of neuroactive steroids developed by Washington University. In exchange for development and commercialization rights, the Company paid an upfront, non-refundable payment of $50,000 and is required to pay an annual license maintenance fee of $15,000 on each subsequent anniversary date, until the first Phase 2 clinical trial for a licensed product is initiated. The Company is obligated to make milestone payments to Washington University based on achievement of clinical development and regulatory milestones of up to $0.7 million and $0.5 million, respectively. Additionally, the Company fulfilled its obligation to issue to Washington University 47,619 shares of common stock on December 13, 2013. The fair value of these shares of $0.1 million was recorded as research and development expense in 2013. As of June 30, 2018, the Company recorded research and development expense and made a cash payment of $50,000 related to these clinical and development milestones.

The Company is obligated to pay royalties to Washington University at rates in the low single digits on net sales of licensed products covered under patent rights and royalties at rates in the low single digits on net sales of licensed products not covered under patent rights. Additionally, the Company has the right to sublicense and is required to make payments at varying percentages of sublicensing revenue received, initially in the mid-teens and descending to the mid-single digits over time.

For the three and six months ended June 30, 2018 and 2017, the Company did not record any expense or make any milestone payments under the license agreement with Washington University.

Consulting Agreement

In January 2014, the Company entered into a consulting agreement with a non-employee advisor whereby the Company is obligated to make cash payments of up to $2.0 million and to issue up to 126,984 shares of common stock upon attainment of certain clinical development and regulatory milestones. As of June 30, 2018, the Company

recorded research and development expense of $1.8 million, comprised of $0.5 million in cash and $1.3 million related to the issuance of 39,681 shares of the Company's common stock, related to the achievement of these milestones.

For the three and six months ended June 30, 2018 and 2017, the Company did not record any expense or make any milestone payments under the consulting agreement with the non-employee advisor.

6. Collaboration Agreement

Effective June 12, 2018, the Company entered into a strategic collaboration with Shionogi & Co., Ltd., (“Shionogi”) for the clinical development and commercialization of SAGE-217 for the treatment of major depressive disorder (“MDD”) and other indications in Japan, Taiwan and South Korea.

Under the terms of the agreement, Shionogi will be responsible for all clinical development, regulatory filings and commercialization of SAGE-217 for MDD, and potentially other indications, in Japan, Taiwan and South Korea. Shionogi is required to make an upfront payment to the Company of $90.0 million, and the Company will be eligible to receive additional payments of up to $485.0 million if certain regulatory and commercial milestones are achieved by Shionogi. The potential future milestone payments include up to $70.0 million for the achievement of specified regulatory milestones, up to $30.0 million for the achievement of specified commercialization milestones, and up to $385.0 million for the achievement of specified net sales milestones. Due to the uncertainty of pharmaceutical development and the high historical failure rates generally associated with drug development, we may not receive any additional milestone payments or any royalty payments from Shionogi. The Company will receive tiered royalties on sales of SAGE-217 in Japan, Taiwan and South Korea, if development efforts are successful, with tiers averaging in the low to mid-twenty percent range, subject to other terms of the agreement. Shionogi has also granted to the Company certain rights to co-promote SAGE-217 in Japan across all indications. The Company maintains exclusive rights to develop and commercialize SAGE-217 outside of Japan, Taiwan and South Korea. The upfront cash payment and any payments for milestones and royalties are non-refundable, non-creditable and not subject to set-off.

The Company concluded that Shionogi meets the definition to be accounted for as a customer since the Company is delivering intellectual property and know-how rights for the SAGE-217 program in support of territories in which the parties are not jointly sharing the risks and rewards. In addition, the Company determined that the Shionogi collaboration met the requirements to be accounted for as a contract, including that it is probable that the Company will collect the consideration related to the up-front payment to which the Company is entitled in exchange for the goods or services that will be delivered to Shionogi.

In determining the appropriate amount of revenue to be recognized under ASC 606, the Company performed the following steps: (i) identified the promised goods or services in the contract; (ii) determined whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measured the transaction price, including the constraint on variable consideration; (iv) allocated the transaction price to the performance obligations; and (v) recognized revenue when (or as) the Company satisfies each performance obligation.

The Company determined that, pursuant to the new revenue standard, the performance obligations included the license to SAGE-217, supply of certain clinical materials and manufacturing supply of the active pharmaceutical ingredient (“API”). The performance obligation related to the license to SAGE-217 was determined to be distinct from other

performance obligations and therefore was a standalone performance obligation for which control was transferred upon signing. The obligation to provide certain clinical materials was determined to be a separate performance obligation. The agreement related to supplying API was determined to be an option for Shionogi to purchase, rather than a firm obligation since no minimum amount or quantities are specified and, therefore, was not considered a performance obligation within the main agreement. Given this fact pattern, the Company has concluded the agreement has two performance obligations.

The Company completed the evaluation of the standalone selling prices of each of the performance obligations and determined that the standalone selling price of the license performance obligation was $90.0 million. The Company recognized the transaction price allocated to the license performance obligation of $90.0 million as revenue during the quarter upon delivery of the license to the customer and resulting ability of the customer to use and benefit from the license. The remaining transaction price related to the performance obligation for the supply of certain clinical material is not significant. The potential milestone payments that the Company is eligible to receive were excluded from the transaction price, as all milestone amounts were fully constrained based on the probability of achievement. The Company

will reevaluate the transaction price at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur, and, if necessary, adjust its estimate of the transaction price. As of June 30, 2018, the Company received $71.6 million of the $90.0 million upfront license payment and had a receivable from collaborator on the balance sheet for the remaining $18.4 million.

7. Sale of Equity Securities

On November 17, 2017, the Company completed the sale of 4,058,822 shares of its common stock in an underwritten public offering at a price to the public of $85.00 per share, resulting in net proceeds of $325.8 million after deducting commissions and underwriting discounts and offering costs paid by the Company.

On February 13, 2018, the Company completed the sale of 4,032,012 shares of its common stock in an underwritten public offering at a price to the public of $164.00 per share, resulting in net proceeds of $631.2 million after deducting commissions and underwriting discounts and offering costs both paid and payable by the Company.

8. Stock-Based Compensation

Restricted Stock Units

During the six months ended June 30, 2017, the Company granted 32,500 restricted stock units to certain employees of the Company. The Company did not grant restricted stock units prior to January 1, 2017. These restricted stock units vest ratably over two years, with cliff vesting of 50% at both the one-year and two-year anniversary of the grant, which was in February 2018 and will be in February 2019, respectively.

During the three months ended March 31, 2018, the Company granted 33,600 performance restricted stock units to certain employees of the Company. These performance restricted stock units will vest upon the achievement of a certain regulatory milestone, in some cases upon meeting the milestone and, in other cases, on the first anniversary of meeting the milestone.

During the three months ended June 30, 2018, the Company granted 37,800 performance restricted stock units to certain employees of the Company. These performance restricted stock units will vest upon the achievement of a certain commercial milestone.

The fair value of restricted stock units that vested during the six months ended June 30, 2018 was $2.6 million. No restricted stock units vested during the six months ended June 30, 2017 and during the three months ended June 30, 2018.

The table below summarizes activity relating to restricted stock:

	Shares
Outstanding as of December 31, 2017	29,100
Granted	71,400
Vested	(14,550)
Forfeited	(900)
Outstanding as of June 30, 2018	85,050

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Stock Option Plans

On July 2, 2014, the stockholders of the Company approved the 2014 Stock Option and Incentive Plan (the "2014 Stock Option Plan"), which became effective immediately prior to the completion of the Company's IPO. The 2014 Stock Option Plan provides for the grant of restricted stock awards, restricted stock units, incentive stock options and non-statutory stock options. The 2014 Stock Option Plan replaced the Company's 2011 Stock Option and Grant Plan (the "2011 Stock Option Plan"). The Company no longer grants stock options or other awards under the 2011 Stock Option Plan. Any options or awards outstanding under the 2011 Stock Option Plan remained outstanding and effective.

On December 15, 2016, the Board of Directors of the Company approved the 2016 Inducement Equity Plan (the "2016 Stock Option Plan"). The 2016 Stock Option Plan provides for the grant of equity awards to individuals who have not previously been an employee or a non-employee director of the Company to induce them to accept employment and to provide them with a proprietary interest in the Company.

As of June 30, 2018, the total number of shares reserved under all equity plans is 9,030,623, and 1,589,715 shares were available for future issuance under such plans.

The 2014 Stock Option Plan provides for an annual increase, to be added on the first day of each fiscal year, by up to 4% of the Company's outstanding shares of common stock as of the last day of the prior year. On January 1, 2018, 1,680,117 shares of common stock, representing 4% of the Company's outstanding shares of common stock as of December 31, 2017, were added to the 2014 Stock Option Plan.

During the three months ended March 31, 2018 and 2017, the Company granted 323,753 and 449,208 options, respectively, to employees to purchase shares of common stock that contain performance-based vesting criteria, primarily related to the achievement of certain clinical and regulatory development milestones related to product candidates. Recognition of stock-based compensation expense associated with these performance-based stock options commences when the performance condition is considered probable of achievement, using management's best estimates, which consider the inherent risk and uncertainty regarding the future outcomes of the milestones.

During the three months ended June 30, 2018 and 2017, the Company granted 200,250 and no options, respectively, to employees to purchase shares of common stock that contain performance-based vesting criteria, related to the achievement of certain clinical development, regulatory development and commercial milestones related to product candidates. Recognition of stock-based compensation expense associated with these performance-based stock options commences when the performance condition is considered probable of achievement, using management's best estimates, which consider the inherent risk and uncertainty regarding the future outcomes of the milestones.

During the three months ended June 30, 2018, a performance milestone was achieved under a stock option granted to a consultant. The milestone was related to the consummation of a licensing or corporate partnering arrangement. During the three months ended June 30, 2018, the Company recognized stock-based compensation expense related to this milestone of $6.9 million.

During the six months ended June 30, 2018 and 2017, the achievement of the milestones that had not been met that are the criteria for vesting of performance-based stock options was considered not probable, and therefore no expense has been recognized related to these awards for the six months ended June 30, 2018 and 2017.

Stock-based compensation expense for stock options, restricted stock units and the employee stock purchase plan recognized during the three and six months ended June 30, 2018 and 2017 was as follows:

	Three months ended June 30,		Six months ended June 30,	
	2018	2017	2018	2017
	(in thousands)			
Research and development	$12,095	$5,245	$20,994	$8,840
General and administrative	16,933	4,105	23,851	6,718
	$29,028	$9,350	$44,845	$15,558

Stock-based compensation expense by award type recognized during the three and six months ended June 30, 2018 and 2017 was as follows:

	Three months ended June 30,		Six months ended June 30,	
	2018	2017	2018	2017
	(in thousands)			
Stock options	$28,627	$9,119	$44,007	$15,152
Restricted stock units	155	167	324	267
Employee stock purchase plan	246	64	514	139
	$29,028	$9,350	$44,845	$15,558

The weighted average grant date fair value per share relating to outstanding stock options granted under the Company's stock option plans during the six months ended June 30, 2018 and 2017 was $114.72 and $39.62, respectively.

The table below summarizes activity related to stock options:

	Shares	Weighted Average Exercise Price	Weighted Average Remaining Life (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding as of December 31, 2017	5,586,593	$ 43.58	8.09	$ 676,717
Granted	2,313,844	171.26		
Exercised	(490,050)	36.37		
Forfeited	(54,529)	74.88		
Outstanding as of June 30, 2018	7,355,858	$ 83.99	8.26	$ 575,909
Exercisable as of June 30, 2018	2,439,246	$ 34.23	6.89	$ 298,310

At June 30, 2018, the Company had unrecognized stock-based compensation expense related to its unvested service-based stock option awards of $274.5 million, which is expected to be recognized over the remaining weighted average vesting period of 3.04 years. The intrinsic value of stock options exercised during the six months ended June 30, 2018 and 2017 was $64.4 million and $10.0 million, respectively.

At June 30, 2018, 1,148,686 performance-based stock options were both outstanding and unvested, and the total unrecognized stock-based compensation expense related to those awards was $58.8 million.

9. Net Loss Per Share

Basic and diluted net loss per share was calculated as follows for the three and six months ended June 30, 2018 and 2017:

	Three months ended June 30,		Six months ended June 30,	
	2018	2017	2018	2017
Basic net loss per share:				
Numerator:				
Net loss (in thousands)	$(16,978)	$(70,202)	$(91,576)	$(126,979)
Denominator:				
Weighted average common stock outstanding—basic	46,541,716	37,361,129	45,439,666	37,315,393
Dilutive effect of shares of common stock equivalents resulting from common stock options and restricted stock units	—	—	—	—
Weighted average common stock outstanding—diluted	46,541,716	37,361,129	45,439,666	37,315,393
Net loss per share—basic and diluted	$(0.36)	$(1.88)	$(2.02)	$(3.40)

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

	Three months ended June 30,		Six months ended June 30,	
	2018	2017	2018	2017
Stock options	6,207,172	5,313,821	6,207,172	5,313,821
Restricted stock units	13,950	30,400	13,950	30,400
Employee stock purchase plan	8,004	8,697	8,004	8,697
	6,229,126	5,352,918	6,229,126	5,352,918

Stock options and restricted stock units that are outstanding and contain performance-based vesting criteria for which the performance conditions have not been met are excluded from the calculation of common stock equivalents outstanding.

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

You should read the following discussion and analysis of our financial condition and results of operations together with our unaudited condensed consolidated financial statements and related notes appearing elsewhere in this Quarterly Report on Form 10-Q, or Quarterly Report, and the audited financial statements and related notes contained in our Annual Report on Form 10-K for the year ended December 31, 2017, or Annual Report. In addition to historical information, this discussion and analysis contains forward-looking statements that involve risks, uncertainties and assumptions. We caution you that forward-looking statements are not guarantees of future performance, and that our actual results of operations, financial condition and liquidity, and the developments in our business and the industry in which we operate, may differ materially from the results discussed or projected in the forward-looking statements contained in this Quarterly Report. We discuss risks and other factors that we believe could cause or contribute to these potential differences elsewhere in this report, including under Item 1A. "Risk Factors" and under "Cautionary Note Regarding Forward-Looking Statements" in this Quarterly Report. In addition, even if our results of operations, financial condition and liquidity, and the developments in our business and the industry in which we operate are consistent with the forward-looking statements contained in this Quarterly Report, they may not be predictive of results or developments in future periods. We caution readers not to place undue reliance on any forward-looking statements made by us, which speak only as of the date they are made. We disclaim any obligation, except as specifically required by law and the rules of the Securities and Exchange Commission, or SEC, to publicly update or revise any such statements to reflect any change in our expectations or in events, conditions or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in the forward-looking statements.

Overview

We are a clinical-stage biopharmaceutical company committed to developing and commercializing novel medicines to treat life-altering central nervous system, or CNS, disorders, where there are no approved therapies or existing therapies are inadequate. We have a portfolio of product candidates with a current focus on modulating two critical CNS receptor systems, GABA and NMDA. The GABA receptor family, which is recognized as the major inhibitory neurotransmitter in the CNS, mediates downstream neurologic and bodily function via activation of $GABA_A$ receptors. The NMDA-type receptors of the glutamate receptor system are a major excitatory receptor system in the CNS. Dysfunction in these systems is implicated in a broad range of CNS disorders. We are targeting CNS indications where patient populations are easily identified, clinical endpoints are well-defined, and development pathways are feasible.

The following table summarizes the status of our development programs as of the date of this Quarterly Report.

Our lead product candidate, brexanolone (USAN) for intravenous, or IV, use, is a proprietary formulation of allopregnanolone, a naturally occurring neuroactive steroid that acts as a positive allosteric modulator of $GABA_A$ receptors. We are developing brexanolone IV as a treatment for postpartum depression, or PPD. PPD is a common biological complication of childbirth, and is characterized by significant depressive symptoms that typically commence during the third trimester of pregnancy or in the months following childbirth. In November 2017, we announced positive results from two blinded, placebo-controlled Phase 3 clinical trials of brexanolone IV in PPD. We submitted a new drug application, or NDA, to the U.S. Food and Drug Administration, or FDA, in April, 2018 seeking approval to market and sell brexanolone IV as a treatment for PPD in the U.S. The NDA is under review by the FDA. The FDA granted the NDA Priority Review status and assigned a Prescription Drug User Fee Act (PDUFA) target date of December 19, 2018. The FDA is currently planning to hold an advisory committee meeting on November 2, 2018 to discuss the brexanolone IV application, and has conditionally accepted the proprietary name ZULRESSO™ for our product. We have also received Breakthrough Therapy designation from the FDA in the U.S. and PRIority MEdicines, or PRIME, designation from the European Medicines Agency, or EMA, in the European Union, or EU, for brexanolone IV as a potential treatment for PPD. We expect to receive scientific advice from the EMA in the second half of 2018 regarding the potential regulatory pathway for a marketing authorization application, or MAA, filing in the EU. We continue to prepare for a potential commercial launch of brexanolone IV for the treatment of PPD in the U.S. in the first half of 2019, if our NDA is approved.

Our most advanced next-generation product candidate is SAGE-217, a novel neuroactive steroid that, like brexanolone, is a positive allosteric modulator of $GABA_A$ receptors, targeting both synaptic and extrasynaptic $GABA_A$ receptors. We are currently developing SAGE-217 as a potential treatment for major depressive disorder, or MDD, PPD, bipolar depression, and sleep disorders. The FDA has granted SAGE-217 breakthrough therapy designation in the treatment of MDD. In June 2018, we announced our expedited development plan for SAGE-217 in depression following a breakthrough therapy meeting with the FDA. This development plan is intended, if successful, to support a potential filing for approval of SAGE-217 in the U.S. for the episodic treatment of MDD and in the treatment of PPD. The planned expedited development program for SAGE-217 includes one additional placebo-controlled Phase 3 clinical trial in patients with MDD in which we plan to study two weeks of 20mg or 30mg SAGE-217 treatment compared to placebo in 450 patients with MDD, with four weeks of additional follow-up. The program also includes the ongoing placebo-controlled clinical trial in PPD, now designated a pivotal trial, in which we expect to enroll 140 women with PPD. The

planned expedited development program for SAGE-217 in MDD and PPD also includes an open-label study in which approximately 300 patients with MDD treated with SAGE-217 will be followed for six months and 100 patients would be followed for a year after initial treatment and episodic retreatment as needed, to evaluate the potential of episodic treatment for recurrent or new major depressive episodes and provide additional safety data. We plan to initiate the placebo-controlled Phase 3 clinical trial of SAGE-217 in MDD and to announce top-line data from the placebo-controlled pivotal trial of SAGE-217 in PPD during the fourth quarter of 2018. As part of the SAGE-217 mood disorder program, we also plan to initiate in the fourth quarter of 2018 a Phase 2 open-label trial evaluating four weeks of SAGE-217 treatment in up to 30 patients with bipolar I/II disorder with a current major depressive episode. The trial is intended to evaluate the safety and tolerability of SAGE-217 as the primary endpoint and to study secondary endpoints, including efficacy in improving depressive symptoms and sleep. If the results of the trial are positive and warrant moving forward, we then plan to conduct a randomized, placebo-controlled trial in this indication.

In addition to our mood disorder program, we also plan to study SAGE-217 in the treatment of sleep disorders. We plan to initiate a placebo-controlled polysomnography trial of SAGE-217 in patients with MDD who have co-morbid insomnia in the fourth quarter of 2018, and also plan to seek feedback from the FDA in the second half of 2018 on a potential development plan for SAGE-217 in the treatment of sleep disorders. We may also explore the development of SAGE-217 in other indications. In addition to SAGE-217, we have a portfolio of other novel compounds that target $GABA_A$ receptors, including SAGE-324 and SAGE-689, which are at earlier stages of development with a focus on both acute and chronic CNS disorders.

Our second area of focus is the development of novel compounds that target the NMDA receptor. The first product candidate selected for development from this program is SAGE-718, an oxysterol-based positive allosteric modulator of the NMDA receptor. Our initial areas of focus for development of SAGE-718 will be indications involving NMDA receptor hypofunction. Examples of these potential areas for future evaluation include certain types, aspects or subpopulations of a number of diseases such as depression, Alzheimer’s disease, attention deficit hyperactivity disorder, schizophrenia, Huntington’s disease, and neuropathic pain. We completed a Phase 1 single ascending dose trial of SAGE-718 in 2017. A Phase 1 multiple ascending dose trial is ongoing.

We expect to continue our focus on allosteric modulation of the $GABA_A$ and NMDA receptor systems in the brain. The $GABA_A$ and NMDA receptor systems are broadly accepted as impacting many psychiatric and neurological disorders, spanning disorders of mood, seizure, cognition, anxiety, sleep, pain, and movement, among others. We believe that we may have the opportunity to develop molecules from our internal portfolio with the goal of addressing a number of these disorders in the future. Our ability to identify and develop such novel CNS therapies is enabled by our proprietary chemistry platform that is centered, as a starting point, on knowledge of the chemical scaffolds of certain endogenous neuroactive steroids. We believe our knowledge of the chemistry and activity of allosteric modulators allows us to efficiently design molecules with different characteristics. This diversity enables us to regulate important properties such as half-life, brain penetration and receptor pharmacology to develop product candidates that may have the potential for better selectivity, increased tolerability, and fewer off-target side effects than either current CNS therapies or previous therapies which have failed in development.

We have not generated any revenue to date from the sale of products. All of our revenue to date has been derived from a strategic collaboration we entered into in the second quarter of 2018 with Shionogi & Co., Ltd., or Shionogi, for the clinical development and commercialization of SAGE-217 in Japan, Taiwan and South Korea. We have incurred net losses in each year since our inception, and we have an accumulated deficit of $682.0 million as of June 30, 2018. Our net losses were $91.6 million for the six months ended June 30, 2018 and $270.1 million for the year ended December 31, 2017. These losses have resulted principally from costs incurred in connection with research and development activities and general and administrative costs associated with our operations. We expect to incur significant expenses and increasing operating losses for the foreseeable future.

We expect that our expenses will increase substantially in connection with our ongoing activities, as we:

- advance regulatory activities focused on the review process with respect to the NDA we submitted to the FDA seeking approval of brexanolone IV in PPD in the U.S.;
- continue preparations for a potential future commercial launch of brexanolone IV in PPD in the U.S., if approved;
- complete the ongoing clinical trial of SAGE-217 in PPD, and advance SAGE-217 further in development in MDD, bipolar depression, and sleep disorders;
- continue to advance SAGE-718, our early-stage novel allosteric modulator for NMDA, including continuing the ongoing Phase 1 clinical program;
- continue Phase 1 clinical studies of SAGE-324 with potential future focus on epileptiform disorders, Parkinson's disease, essential tremor and other indications involving GABA hypofunction;
- continue our research and development efforts to evaluate the potential for our product candidates in the treatment of additional indications or in new formulations, and to identify new drug candidates in the treatment of CNS disorders;
- continue regulatory and other activities focused on potential pathways for advancing our lead product candidates in the EU, subject to feedback from the EMA, including obtaining scientific advice on the potential regulatory pathway for an MAA filing as part of planned discussions with the EMA regarding brexanolone IV;
- seek regulatory approvals for any product candidates that successfully complete clinical development;
- complete validation work and other supply chain activities related to brexanolone IV to be ready for commercial supply if our NDA is approved; refine and scale-up the manufacturing process for SAGE-217 for planned late stage clinical trials; improve the manufacturing process for our other product candidates; and manufacture clinical supplies as development progresses;
- add personnel, including personnel to support our product development and future commercialization efforts and potential expansion of EU activities, and incur increases in stock-based compensation expense related to existing and new personnel with respect to both service-based and performance-based awards;
- evaluate market opportunities for our product candidates, including brexanolone IV in PPD, in other global markets;
- add operational, financial and management information systems; and
- maintain, leverage and expand our intellectual property portfolio.

As a result, we will need additional financing in the future to support our continuing operations. Until such time that we can generate significant revenue from product sales, if ever, we expect to finance our operations through a combination of equity or debt financings or other sources, which may include collaborations with third parties. We may never successfully complete development of any of our product candidates; obtain adequate patent protection or other exclusivity for our product candidates; obtain necessary regulatory approval for our product candidates; or achieve commercial viability for any approved product. Adequate additional financing may not be available to us on acceptable terms, or at all. Our inability to raise capital as and when needed would have a negative impact on our financial condition and on our ability to pursue our business strategy. Arrangements with collaborators or others may require us to relinquish

rights to certain of our technologies or product candidates. We will need to generate significant revenue to achieve profitability, and we may never do so.

We expect that our existing cash, cash equivalents and marketable securities as of June 30, 2018 will enable us to fund our operating expenses and capital expenditure requirements, based on our current operating plan, into 2020. See "—Liquidity and Capital Resources".

Financial Operations Overview

Revenue

We have not generated any revenue from product sales since our inception. We do not know when, or if, we will generate any revenue from product sales. We do not expect to generate significant revenue from product sales unless and until we successfully develop, obtain regulatory approval of and commercialize one of our current or future product candidates. All of our revenue to date has been derived from our collaboration with Shionogi. If we enter into additional collaboration agreements with third parties for our product candidates, we may generate revenue from those product candidates. We expect that revenue, if any, we generate under collaboration agreements will fluctuate from quarter to quarter as a result of the timing and amount of license fees, research and development services and related reimbursements, payments for clinical materials or manufacturing services, and milestone and other payments.

Operating Expenses

Our operating expenses since inception have consisted primarily of costs associated with research and development activities and general and administrative activities.

Research and Development Expenses

Research and development expenses, which consist primarily of costs associated with our product research and development efforts, are expensed as incurred. Research and development expenses consist primarily of:

- personnel costs, including salaries, benefits, stock-based compensation and travel expenses, for employees engaged in research and development functions;
- expenses incurred under agreements with contract research organizations, or CROs, and sites that conduct our non-clinical studies and clinical trials;
- expenses associated with manufacturing materials for use in clinical trials and developing external manufacturing capabilities;
- costs of outside consultants engaged in research and development activities, including their fees, stock-based compensation and travel expenses;
- other expenses related to our non-clinical studies and clinical trials and expenses related to our regulatory activities; and
- payments made under our third-party license agreements.

Costs for certain development activities are recognized based on an evaluation of the progress to completion of specific tasks using information and data provided to us by our vendors and our clinical sites.

We have been developing our product candidates and focusing on other research and development programs, including exploratory efforts to identify new compounds, target validation for identified compounds and lead optimization for our earlier-validated programs. Our direct research and development expenses are tracked on a

program-by-program basis, and consist primarily of external costs, such as fees paid to investigators, central laboratories, CROs and contract manufacturing organizations, or CMOs, in connection with our non-clinical studies and clinical trials; third-party license fees related to our product candidates; and fees paid to outside consultants who perform work on our programs. We do not allocate employee-related costs and other indirect costs to specific research and development programs because these

costs are deployed across multiple product programs under research and development and, as such, are separately classified as unallocated research and development expenses.

Research and development activities are central to our business. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect that our research and development expenses will continue to increase in the foreseeable future as we continue or initiate clinical trials and non-clinical studies for certain product candidates, and pursue later stages of clinical development of our product candidates.

We cannot determine with certainty the duration and costs of the current or future clinical trials of our product candidates or if, when, or to what extent we will generate revenue from the commercialization and sale of any of our product candidates, if approved for marketing and sale. The duration, costs, and timing of clinical trials and development of our product candidates will depend on a variety of factors, including:

- the scope, size, rate of progress, and expense of our ongoing as well as any additional clinical trials, non-clinical studies, and other research and development activities;
- future clinical trial and non-clinical study results;
- decisions by regulatory authorities related to our product candidates;
- uncertainties in clinical trial enrollment rate or design;
- significant and changing government regulation; and
- the receipt and timing of regulatory approvals, if any.

A change in the outcome of any of these variables with respect to the development of a product candidate could mean a significant change in the costs and timing associated with the development of that product candidate. For example, if the FDA or another regulatory authority were to require us to conduct clinical trials beyond those that we currently anticipate will be required for the completion of clinical development of a product candidate or for regulatory approval, or if we experience significant delays in enrollment in any of our clinical trials or need to enroll additional patients, we could be required to expend significant additional financial resources and time on the completion of clinical development.

General and Administrative Expenses

General and administrative expenses consist primarily of personnel costs, including salaries, benefits, stock-based compensation and travel expenses for our executive, finance, business, commercial, corporate development and other administrative functions. General and administrative expenses also include expenses incurred under agreements with third parties relating to evaluation, planning and preparation for a potential commercial launch; facilities and other related expenses, including rent, depreciation, maintenance of facilities, insurance and supplies; and professional fees for audit, tax and legal services, including legal expenses to pursue patent protection of our intellectual property.

We anticipate that our general and administrative expenses, including payroll and related expenses, will increase in the future as we continue to increase our headcount to support the expected growth in our business, expand our operations and organizational capabilities and prepare for the potential commercialization of brexanolone IV, if approved, and our other product candidates, if successfully developed. We also anticipate increased expenses associated with general operations, including costs related to audit, tax and legal services, director and officer insurance premiums, and investor relations costs.

Results of Operations

Comparison of the Three Months Ended June 30, 2018 and 2017

The following table summarizes our results of operations for the three months ended June 30, 2018 and 2017:

	Three Months Ended		
	June 30, 2018	2017	Increase (Decrease)
	(in thousands)		
Collaboration revenue	$90,000	$-	$ 90,000
Operating expenses:			
Research and development	68,980	55,900	13,080
General and administrative	43,167	14,954	28,213
Total operating expenses	112,147	70,854	41,293
Loss from operations	(22,147)	(70,854)	48,707
Interest income, net	5,137	672	4,465
Other expense, net	32	(20)	52
Net loss	$(16,978)	$(70,202)	$ 53,224

Research and development expenses

	Three Months Ended		
	June 30, 2018	2017	Increase (Decrease)
	(in thousands)		
brexanolone (SAGE-547)	$9,643	$22,242	$ (12,599)
SAGE-217	15,600	12,163	3,437
SAGE-718	2,781	1,505	1,276
Other research and development programs	9,251	3,483	5,768
Unallocated expenses	31,705	16,507	15,198
Total research and development expenses	$68,980	$55,900	$ 13,080

Research and development expenses for the three months ended June 30, 2018 were $69.0 million, compared to $55.9 million for the three months ended June 30, 2017. The increase of $13.1 million was primarily due to the following:

- a decrease of $12.6 million in expenses related to our brexanolone program, due to the completion of the Phase 3 clinical trial in super-refractory status epilepticus, or SRSE, and the Phase 3 clinical trials in PPD. Expenses related to payments to licensors upon achievement of certain regulatory milestones were $1.0 million;

- an increase of $3.4 million in expenses due to conduct of our Phase 2 clinical trial of SAGE-217 in PPD, conduct of supporting clinical pharmacology studies and supply chain activities to support this and other clinical trials;

- an increase of $5.8 million in expenses related to research and development programs and discovery efforts focused on identifying new clinical candidates and additional indications of interest, and on our back-up programs; and

- an increase of $15.2 million in unallocated expenses, mainly due to the hiring of additional full-time employees to support the growth of our operations, including an increase of $6.9 million of non-cash stock-based compensation. There was no non-cash stock-based compensation expense recognized related to the achievement of performance-based vesting criteria during the three months ended June 30, 2018 and 2017.

General and administrative expenses

	Three Months Ended June 30,		
	2018	2017	Increase (Decrease)
	(in thousands)		
Personnel-related	$28,365	$8,073	$ 20,292
Professional fees	5,184	2,928	2,256
Commercial planning	5,769	2,525	3,244
Other	3,849	1,428	2,421
Total general and administrative expenses	$43,167	$14,954	$ 28,213

General and administrative expenses for the three months ended June 30, 2018 and 2017 were $43.2 million and $15.0 million, respectively. The increase of $28.2 million was primarily due to the following:

- an increase of $20.3 million in personnel-related costs in connection with the hiring of additional full-time employees to support planned commercial activities, operations, finance, human resources and legal, including an increase of $12.8 million of non-cash stock-based compensation. The amount of non-cash stock-based compensation expense related to the achievement of performance-based vesting criteria was $6.9 million during the three months ended June 30, 2018 for a milestone related to the consummation of a licensing or corporate partnering arrangement;

- an increase of $2.3 million in professional fees associated with expanding operations, including costs related to legal services, including legal expenses to pursue patent protection of our intellectual property, investor relations and public relations;

- an increase of $3.2 million in costs related to preparations for a potential commercial launch, if we are successful in our efforts to obtain regulatory approval of brexanolone IV in the U.S.; and

- an increase of $2.4 million in other expenses due to increased costs associated with facilities, mainly due to the increase in the amount of rented square feet of office space to accommodate our increased number of employees.

Interest income, net and Other expense, net

Interest income, net, and other expense, net, for the three months ended June 30, 2018 and 2017 were $5.2 million and $0.7 million, respectively. The primary reasons for the increase were an increase in the balances of marketable securities and an increase in interest rates.

Comparison of the Six Months Ended June 30, 2018 and 2017

The following table summarizes our results of operations for the six months ended June 30, 2018 and 2017:

	Six Months Ended June 30,		
	2018	2017	Increase (Decrease)
	(in thousands)		
Collaboration revenue	$90,000	$-	$ 90,000
Operating expenses:			
Research and development	118,250	101,100	17,150
General and administrative	72,016	27,234	44,782
Total operating expenses	190,266	128,334	61,932
Loss from operations	(100,266)	(128,334)	28,068
Interest income, net	8,666	1,379	7,287
Other expense, net	24	(24)	48
Net loss	$(91,576)	$(126,979)	$ 35,403

Research and development expenses

	Six Months Ended		
	June 30, 2018	2017	Increase (Decrease)
		(in thousands)	
brexanolone (SAGE-547)	$18,186	$42,167	$(23,981)
SAGE-217	20,987	21,130	(143)
SAGE-718	4,217	2,811	1,406
Other research and development programs	17,480	6,161	11,319
Unallocated expenses	57,380	28,831	28,549
Total research and development expenses	$118,250	$101,100	$17,150

Research and development expenses for the six months ended June 30, 2018 were $118.3 million, compared to $101.1 million for the six months ended June 30, 2017. The increase of $17.2 million was primarily due to the following:

- a decrease of $24.0 million in expenses related to our brexanolone program, due to the completion of the Phase 3 clinical trial in SRSE and the Phase 3 clinical trials in PPD. Expenses related to payments to licensors upon achievement of certain regulatory milestones were $1.0 million;

- an increase of $11.3 million in expenses related to research and development programs and discovery efforts focused on identifying new clinical candidates and additional indications of interest, and on our back-up programs; and

- an increase of $28.5 million in unallocated expenses, mainly due to the hiring of additional full-time employees to support the growth of our operations, including an increase of $12.2 million of non-cash stock-based compensation. There was no non-cash stock-based compensation expense recognized related to the achievement of performance-based vesting criteria during the six months ended June 30, 2018 and 2017.

General and administrative expenses

	Six Months Ended		
	June 30, 2018	2017	Increase (Decrease)
		(in thousands)	
Personnel-related	$43,283	$14,284	$28,999
Professional fees	9,790	5,261	4,529
Commercial planning	12,362	4,910	7,452

Other	6,581	2,779	3,802
Total general and administrative expenses	$72,016	$ 27,234	$ 44,782

General and administrative expenses for the six months ended June 30, 2018 and 2017 were $72.0 million and $27.2 million, respectively. The increase of $44.8 million was primarily due to the following:

- an increase of $29.0 million in personnel-related costs in connection with the hiring of additional full-time employees to support planned commercial activities, operations, finance, human resources and legal, including an increase of $17.1 million of non-cash stock-based compensation. The amount of non-cash stock-based compensation expense related to the achievement of performance-based vesting criteria was $6.9 million during the six months ended June 30, 2018 for a milestone related to the consummation of a licensing or corporate partnering arrangement;

- an increase of $4.5 million in professional fees associated with expanding operations, including costs related to legal services, including legal expenses to pursue patent protection of our intellectual property, investor relations and public relations;

- an increase of $7.5 million in costs related to preparations for a potential commercial launch, if we are successful in our efforts to obtain regulatory approval of brexanolone IV in the U.S.; and

- an increase of $3.8 million in other expenses due to increased costs associated with facilities, mainly due to the increase in the amount of rented square feet of office space to accommodate our increased number of employees.

Interest income, net and Other expense, net

Interest income, net, and other expense, net, for the six months ended June 30, 2018 and 2017 were $8.7 million and $1.4 million, respectively. The primary reasons for the increase were an increase in the balances of marketable securities and an increase in interest rates.

Liquidity and Capital Resources

Since our inception in April 2010, we have not generated any revenue from the sale of products. All of our revenue to date has been derived from our collaboration with Shionogi. To date, we have incurred recurring net losses. As of June 30, 2018, we had an accumulated deficit of $682.0 million. From our inception through June 30, 2018, we received net proceeds of $1.6 billion from the sales of redeemable convertible preferred stock, the issuance of convertible notes and the sales of common stock in our initial public offering in July 2014 and follow-on offerings in April 2015, January 2016, September 2016, November 2017 and February 2018.

On November 17, 2017, we completed the sale of 4,058,822 shares of our common stock in an underwritten public offering at a price to the public of $85.00 per share, resulting in net proceeds of $325.8 million after deducting commissions and underwriting discounts and offering costs paid by us.

On February 13, 2018, we completed the sale of 4,032,012 shares of our common stock in an underwritten public offering at a price to the public of $164.00 per share, resulting in net proceeds of $631.2 million after deducting commissions and underwriting discounts and offering costs paid and payable by us.

As of June 30, 2018, our primary sources of liquidity were our cash, cash equivalents and marketable securities, which totaled $1.1 billion. We invest our cash in money market funds, U.S. government securities, corporate bonds and commercial paper, with the primary objectives to preserve principal, provide liquidity and maximize income without significantly increasing risk.

The following table summarizes the primary sources and uses of cash for the six months ended June 30, 2018 and 2017:

	Six Months Ended	
	June 30,	
	2018	2017
	(in thousands)	
Net cash provided by (used in):		
Operating activities	$(78,706)	$(114,286)
Investing activities	(550,931)	76,193
Financing activities	649,652	3,311
Total	$20,015	$(34,782)

Operating Activities

Cash used in operating activities for the six months ended June 30, 2018 was $78.7 million, compared to $114.3 million for the six months ended June 30, 2017. The decrease of $35.6 million was primarily due to the following:

- A decrease of $35.4 million in cash used related to our net loss, primarily due to $90.0 million of collaboration revenue that was recorded in six months ended June 30, 2018, offset by an increase in general and administrative expenses resulting from increased headcount and other costs to support our expanding

operations and increased research and development activities related to our development programs along with increased headcount in related functions;
- Offset by an increase of $25.3 million in non-cash charges, primarily due to an increase in stock-based compensation expense due to increased hiring; and
- An increase of $25.1 million in cash used in changes in our operating assets and liabilities, primarily due to the receivable from Shionogi of $18.4 million.

Investing Activities

During the six months ended June 30, 2018 and 2017, net cash used in investing activities was $550.9 million and net cash provided by investing activities was $76.2 million, respectively. During the six months ended June 30, 2018 and 2017, we purchased and sold marketable securities as part of managing our cash and investments portfolio, including purchases using proceeds received in our underwritten follow-on public offering during February 2018.

Financing Activities

During the six months ended June 30, 2018 and 2017, net cash provided by financing activities was $649.7 million and $3.3 million, respectively. Net cash provided by financing activities in the six months ended June 30, 2018 primarily consisted of $631.2 million of net proceeds from a follow-on underwritten public offering of our common stock after deducting commissions and underwriting discounts and offering costs.

Operating Capital Requirements

To date, we have not generated any revenue from product sales. We do not know when, or if, we will generate any revenue from product sales. We do not expect to generate significant revenue from product sales unless and until we successfully develop, obtain regulatory approval of and commercialize one of our current or future product candidates. We anticipate that we will continue to generate losses for the foreseeable future, and we expect the losses to increase as we continue the development of, and seek regulatory approvals for, our product candidates; continue preparations for potential future commercialization; begin to commercialize any products, if successfully developed and approved; and continue our efforts to identify and develop new product candidates. We also expect to incur additional costs associated with general operations. In addition, subject to obtaining regulatory approval of any of our product candidates, we expect to incur significant commercialization expenses for product sales, marketing and outsourced manufacturing. Accordingly, we anticipate that we will need substantial additional funding in connection with our continuing operations.

Based on our current operating plans, we expect that our existing cash, cash equivalents and marketable securities as of June 30, 2018, will enable us to fund our operating expenses and capital expenditure requirements into 2020. During that time, we expect that our expenses will increase substantially as we:

- advance regulatory activities focused on the review process with respect to the NDA we submitted to the FDA seeking approval of brexanolone IV in PPD in the U.S.;
- continue preparations for a potential future commercial launch of brexanolone IV, in the U.S., if approved;
- complete the ongoing clinical trial of SAGE-217 in PPD, and further advance development of SAGE-217 in MDD, bipolar depression, and sleep disorders;
- continue to advance SAGE-718, our early-stage novel allosteric modulator for NMDA, including continuing the ongoing Phase 1 clinical program;

- continue Phase 1 clinical studies of SAGE-324 with a potential focus on indications with high frequencies of seizures, Parkinson's disease, essential tremor and other indications involving GABA hypofunction;
- continue our research and development efforts to evaluate the potential for our product candidates in the treatment of additional indications or in new formulations, and the identification of new drug candidates in the treatment of CNS disorders;

- continue regulatory and other activities focused on potential pathways for advancing our lead product candidates in the EU, subject to feedback from the EMA, including as part of planned discussions regarding brexanolone IV;
- seek regulatory approvals for any product candidates that successfully complete clinical development;
- complete validation work and other supply chain activities related to brexanolone IV to be ready for commercial supply if our NDA is approved; refine and scale-up the manufacturing process for SAGE-217 for planned late stage clinical trials; continue to improve the manufacturing process for our other product candidates; and manufacture clinical supplies as development progresses;
- add personnel, including personnel to support our product development and future commercialization efforts, and potential expansion of EU activities, and incur increases in stock compensation expense related to existing and new personnel with respect to both service-based and performance-based awards;
- evaluate market opportunities for brexanolone IV in PPD in other global markets;
- add operational, financial and management information systems; and
- maintain, leverage and expand our intellectual property portfolio.

Our current operating plan does not contemplate other development activities that we may pursue or that all of our currently planned activities will proceed at the same pace, or that all of these activities will be fully initiated or completed during that time. We have based our estimates on assumptions that could change, and we may use our available capital resources sooner than we currently expect. We may also choose to change or increase our development or other efforts. Because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates, we are unable to estimate the amounts of increased capital outlays and operating expenditures necessary to complete the development and commercialization of our product candidates.

Our future capital requirements will depend on many factors, including:

- the level, timing and amount of costs associated with preparing for a potential future commercial launch of brexanolone IV in the near term, and, if we are successful in obtaining regulatory approval, the cost of executing a commercial launch of brexanolone IV;
- the ability of SAGE-217 and our other clinical-stage product candidates to progress through clinical development successfully; and the level, timing and amount of costs associated with preparing for a potential future commercial launch of any such product candidate that is successfully developed;
- the initiation, progress, timing, costs, and results of non-clinical studies and clinical trials for our existing and future product candidates; the number and length of clinical trials required by regulatory authorities to support regulatory approval; and the costs of preparing regulatory filings;
- the timing, scope and outcome of regulatory reviews and approvals of our products, including review of our NDA for brexanolone IV, or for our other product candidates if we are successful in our development efforts; and the scope and cost of any clinical trials or other commitments required post-approval for any approved products;
- at such time, if any, that we have approved products, the size of the indications for which those products are approved; the portion of the population for which those products are actually prescribed; the rate and degree of market acceptance for those products, and the pricing, availability and level of reimbursement for such products;
- the number and characteristics of the product candidates we pursue in development and the nature and scope of our discovery and development programs;
- the scope and timing of potential expansion of our activities outside the U.S.;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;

- the extent to which we acquire or in-license other products and technologies; and
- our ability to establish any future collaboration arrangements on favorable terms, if at all.

Until such time, if ever, as we can generate substantial product revenue and achieve profitability, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements and other sources of funding. Even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital if market conditions are favorable or in light of specific strategic considerations. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt 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 and may require the issuance of warrants, which could potentially dilute the ownership interest of our stockholders. If we raise additional funds through collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams or research programs or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings or other means 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 products or product candidates that we would otherwise prefer to develop and market ourselves.

Contractual Obligations and Commitments

The following table summarizes our contractual obligations at June 30, 2018 and the effect such obligations are expected to have on our liquidity and cash flow in future periods:

	Payments Due by Period				
	Total	Less Than 1 year	1-3 Years	3-5 Years	More Than 5 years
	(in thousands)				
Operating lease commitments[1]	$42,516	$6,183	$13,569	$14,198	$8,566
Total[1][2][3][4]	$42,516	$6,183	$13,569	$14,198	$8,566

Amounts related to contingent milestone payments are not considered contractual obligations as they are contingent on the successful achievement of certain milestones. These contingent milestones may not be achieved. We have not included any of these amounts in the table as we cannot estimate or predict when, or if, these amounts will become due.

(1) We lease office space in two multi-tenant buildings in Cambridge, Massachusetts, consisting, as of June 30, 2018, of 54,943 square feet in one building under an operating lease that expires on August 15, 2024 and 19,805 square feet in the second building under an operating lease that will expire on February 28, 2022. In April 2018, we

entered into the First Amendment to the lease for office space in a multi-tenant building and thereby increased the amount of square feet of office space from 19,805 square feet to 40,419 square feet, an increase of 20,614 square feet, consisting of (i) 13,481 square feet beginning on August 1, 2018, and (ii) 7,133 square feet beginning on October 1, 2018. The term for this additional space will expire on August 31, 2024. Additionally, the term of the existing lease will be extended from February 28, 2022 until August 31, 2024. In May 2018, the Company entered into a lease for office space in a multi-tenant building in Raleigh, North Carolina. The amount of square feet of office space is 15,525 square feet and the lease period will begin on September 1, 2018. The term for this space will expire on November 30, 2024. We expect to lease additional space prior to the expiration of our leases to meet the needs of the business. The minimum lease payments in the table do not include related common area maintenance charges or real estate taxes, because those costs are variable.

(2) We have acquired exclusive and non-exclusive rights to use, research, develop and offer for sale certain products and patents under license agreements with Washington University, CyDex Pharmaceuticals, Inc. and two license agreements with The Regents of the University of California. The license agreements obligate us to make payments to the licensors for license fees, milestones, license maintenance fees and royalties. We are obligated to make future remaining milestone payments under these agreements of up to an aggregate of $32.4 million upon achieving certain

milestones, related to clinical development, regulatory approvals and sales. For the three and six months ended June 30, 2018, we recorded $1.0 million of research and development expense under these license agreements.

(3) We enter into contracts in the normal course of business with CROs for clinical trials, non-clinical research studies and testing, manufacturing and other services and products as part of general operations. These contracts generally provide for termination upon notice, and we believe that our non-cancelable obligations under these agreements are not material.

(4) Under a January 2014 consulting agreement, we are obligated to make remaining milestone payments of up to $1.5 million and to issue up to 87,303 shares of our common stock to a non-employee consultant upon achieving certain clinical development milestones and regulatory approval milestones. For the three and six months ended June 30, 2018, we did not record any expense or make any milestone payments under this consulting agreement.

Off-Balance Sheet Arrangements

We do not currently have, nor did we have during the periods presented, any off-balance sheet arrangements as defined by SEC rules.

Application of Critical Accounting Policies

We have prepared our consolidated financial statements in accordance with accounting principles generally accepted in the United States. Our preparation of these consolidated financial statements requires us to make estimates, assumptions, and judgments that affect the reported amounts of assets, liabilities, expenses, and related disclosures at the date of the consolidated financial statements, as well as revenue and expenses recorded during the reporting periods. We evaluate our estimates and judgments on an ongoing basis. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results could therefore differ materially from these estimates under different assumptions or conditions.

Except for the revenue recognition policy related to licenses and collaborations described below, there have been no material changes to our critical accounting policies from those described in “Management’s Discussion and Analysis of Financial Condition and Results of Operations” included in our Annual Report on Form 10-K filed by us with the SEC on February 22, 2018.

Effective January 1, 2017, we adopted Accounting Standards Codification (“ASC”), Topic 606, Revenue from Contracts with Customers (“Topic 606”). This standard applies to all contracts with customers, except for contracts that are within the scope of other standards, such as collaboration arrangements and leases. Prior to the three months ended June 30, 2018, we did not have any revenue-generating arrangements and therefore there was no transition impact from the adoption of Topic 606.

Under Topic 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration that the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of Topic 606, the entity performs the following five steps: (i) identify the contract with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price, including variable consideration, if any; (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. We only apply the five-step model to contracts when it is probable that we will collect the

consideration to which we are entitled in exchange for the goods or services it transfers to a customer.

Once a contract is determined to be within the scope of Topic 606, we assess the goods or services promised within each contract and determines those that are performance obligations. Arrangements that include rights to additional goods or services that are exercisable at a customer's discretion are generally considered options. We assess if these options provide a material right to the customer and if so, they are considered performance obligations. The exercise of a material right may be accounted for as a contract modification or as a continuation of the contract for accounting purposes.

We assess whether each promised good or service is distinct for the purpose of identifying the performance obligations in the contract. This assessment involves subjective determinations and requires management to make judgments about the individual promised goods or services and whether such are separable from the other aspects of the contractual relationship. Promised goods and services are considered distinct provided that: (i) the customer can benefit from the good or service either on its own or together with other resources that are readily available to the customer (that is, the good or service is capable of being distinct) and (ii) the entity's promise to transfer the good or service to the customer is separately identifiable from other promises in the contract (that is, the promise to transfer the good or service is distinct within the context of the contract). In assessing whether a promised good or service is distinct, in the evaluation of a collaboration agreement subject to Topic 606, we consider factors such as the research, manufacturing and commercialization capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. We also consider the intended benefit of the contract in assessing whether a promised good or service is separately identifiable from other promises in the contract. If a promised good or service is not distinct, we are required to combine that good or service with other promised goods or services until it identifies a bundle of goods or services that is distinct.

The transaction price is then determined and allocated to the identified performance obligations in proportion to their standalone selling prices ("SSP") on a relative SSP basis. SSP is determined at contract inception and is not updated to reflect changes between contract inception and when the performance obligations are satisfied. Determining the SSP for performance obligations requires significant judgment. In developing the SSP for a performance obligation, we consider applicable market conditions and relevant entity-specific factors, including factors that were contemplated in negotiating the agreement with the customer and estimated costs. In certain circumstances, we may apply the residual method to determine the SSP of a good or service if the SSP is considered highly variable or uncertain. We validate the SSP for performance obligations by evaluating whether changes in the key assumptions used to determine the SSP will have a significant effect on the allocation of arrangement consideration between multiple performance obligations.

If the consideration promised in a contract includes a variable amount, we estimate the amount of consideration to which we will be entitled in exchange for transferring the promised goods or services to a customer. We determine the amount of variable consideration by using the expected value method or the most likely amount method. We include the unconstrained amount of estimated variable consideration in the transaction price. The amount included in the transaction price is constrained to the amount for which it is probable that a significant reversal of cumulative revenue recognized will not occur. At the end of each subsequent reporting period, we re-evaluate the estimated variable consideration included in the transaction price and any related constraint, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis in the period of adjustment.

If an arrangement includes development and regulatory milestone payments, we evaluate whether the milestones are considered probable of being reached and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within our control or the licensee's control, such as regulatory approvals, are generally not considered probable of being achieved until those approvals are

received.

In determining the transaction price, we adjust consideration for the effects of the time value of money if the timing of payments provides us with a significant benefit of financing. We do not assess whether a contract has a significant financing component if the expectation at contract inception is such that the period between payment by the licensees and the transfer of the promised goods or services to the licensees will be one year or less. We assessed our revenue-generating arrangement in order to determine whether a significant financing component exists and concluded that a significant financing component does not exist in the arrangement. For arrangements with licenses of intellectual property that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, we recognize royalty revenue and sales-based milestones at the later of (i) when the related sales occur, or (ii) when the performance obligation to which the royalty has been allocated has been satisfied.

We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) each performance obligation is satisfied at a point in time or over time, and if over time this is based on the use of an output or input method.

A description of the agreement with Shionogi is set forth in Note 6, “Collaboration Agreement”, in the accompanying Notes to Condensed Consolidated Financial Statements included in Item 1 of Part I of this Quarterly Report.

Recently Issued Accounting Pronouncements

A description of recently issued accounting pronouncements that may potentially impact our financial position and results of operations is set forth in Note 2, "Summary of Significant Accounting Policies," in the accompanying Notes to Condensed Consolidated Financial Statements included in Item 1 of Part I of this Quarterly Report.

Item 3. Quantitative and Qualitative Disclosures about Market Risk

We had cash, cash equivalents and marketable securities of approximately $1.1 billion as of June 30, 2018. The primary objectives of our investment activities are to preserve principal, provide liquidity and maximize income without significantly increasing risk. Our primary exposure to market risk relates to fluctuations in interest rates, which are affected by changes in the general level of U.S. interest rates. Given the short-term nature of our cash, cash equivalents and marketable securities, we believe that a sudden change in market interest rates would not be expected to have a material impact on our financial condition and/or results of operations. We do not own any foreign currency or other derivatives financial instruments.

We do not believe that our cash, cash equivalents and marketable securities have significant risk of default or illiquidity. While we believe our cash, cash equivalents and marketable securities do not contain excessive risk, we cannot provide absolute assurance that in the future our investments will not be subject to adverse changes in market value. In addition, we maintain significant amounts of cash, cash equivalents and marketable securities at one or more financial institutions that are in excess of federally insured limits.

Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation had a material effect on our results of operations during the six months ended June 30, 2018 and 2017.

Item 4. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

We maintain disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934) that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Securities Exchange Act of 1934 is (1) recorded, processed, summarized, and reported within the time periods specified in the SEC's rules and forms and (2) accumulated and communicated to our management, including our President and Chief Executive Officer, who is our principal executive officer, and our Chief Financial Officer, who is also our principal financial and accounting officer, as appropriate, to allow timely decisions regarding required disclosure.

As of June 30, 2018, our management, with the participation of our principal executive officer and principal financial and accounting officer, evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934). Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives, and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Our principal executive officer and principal financial and accounting officer have concluded, based upon the evaluation described above, that, as of June 30, 2018, our disclosure controls and procedures were effective at the reasonable assurance level.

Changes in Internal Control over Financial Reporting

During the three months ended June 30, 2018, we completed the migration of our legacy accounting system to an Oracle platform. In connection with this implementation, we updated the processes that constitute our internal control over financial reporting, as necessary, to accommodate related changes in our business processes. There were no other material changes to our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Securities Exchange Act of 1934) that occurred during the period covered by this Quarterly Report 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

In the ordinary course of our business we may, from time to time, be involved in lawsuits, claims, and other legal proceedings related to contracts, employment arrangements, operating activities, intellectual property or other matters. While the outcome of any such proceedings cannot be predicted with certainty, as of June 30, 2018, we were not party to any legal proceedings that we would expect to have a material adverse impact on our financial position, results of operations or cash flow.

Item 1A. Risk Factors

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below, as well as the other information in this Quarterly Report and in our other public filings before making an investment decision. Our business, prospects, financial condition, or operating results could be harmed by any of these risks, as well as other risks not currently known to us or that we currently consider immaterial. If any such risks or uncertainties actually occur, our business, financial condition or operating results could differ materially from the plans, projections and other forward-looking statements included in the section titled “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and elsewhere in this Quarterly Report and in our other public filings and public statements. The trading price of our common stock could decline due to any of these risks, and as a result, our stockholders may lose all or part of their investment.

Risks Related to Product Development, Regulatory Approval and Commercialization

We currently do not have any products approved for marketing and sale, and may never be able to successfully gain approval to market and sell any drug product. We depend heavily on the success of our proprietary intravenous, or IV, formulation of brexanolone for which we have submitted a new drug application, or NDA, seeking approval to market brexanolone IV as a treatment for postpartum depression, or PPD. We cannot be certain that the FDA will approve our NDA for brexanolone IV within the expected timeframes, or at all, or that we will file for or receive regulatory approval in any other region or country. Even if brexanolone IV is approved for marketing and sale, there is no assurance that our commercialization efforts will be successful.

We currently do not have any products approved for marketing and sale, and may never be able to successfully gain approval to market and sell any drug product.

Our business currently depends heavily on our ability to gain approval of brexanolone IV in the U.S. as a treatment for PPD. We submitted an NDA to the FDA seeking such approval in April 2018, and the NDA is currently under review. The FDA may not agree that the clinical and non-clinical data we have generated to date are sufficient to gain regulatory approval to commercialize brexanolone IV in PPD in the U.S. There is also no assurance that we will file a Marketing Authorization Application, or MAA, with the European Medicines Agency, or EMA with respect to brexanolone IV as a treatment for PPD in the EU, and even if we make such filing, we may not receive EMA approval. The FDA, EMA or other regulatory authorities may determine that additional trials or data are necessary in order to obtain approval. The Advisory Committee expected to be convened by the FDA to review the NDA for brexanolone IV may recommend against approval or may recommend limitations, conditions or restrictions on use, including on sites of care, and the FDA may agree with some or all of those recommendations or impose its own limitations, conditions and restrictions. Similarly, regulatory authorities may find fault with the data generated at one of our clinical sites or with the activities of our trial monitor or may disagree with how we conducted our trials or our analyses of the trial results. Regulatory authorities may also identify deficiencies or other issues with our manufacturing or quality systems or processes. Any such findings or issues could require additional data or analyses or the need for changes to our systems or processes that could delay or prevent us from gaining approval of brexanolone IV.

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Even if we gain approval of brexanolone IV, we may never be able to successfully commercialize the product or to meet our expectations with respect to revenues or profits. We have never marketed, sold or distributed for commercial use any pharmaceutical product. We are in the process of building the teams, infrastructure, systems, processes, policies, relationships and materials necessary for launch of brexanolone IV in the U.S. in PPD, and to enable appropriate sites of care for administering the product, including the potential for supervised home infusion. In addition to our efforts in the U.S., we are refining our strategy and market assessments with respect to a potential launch in the EU. We also plan to continue to evaluate market opportunities for brexanolone IV in PPD in other global markets. If we receive regulatory approval to market or sell brexanolone IV or any of our other product candidates, if successfully developed and approved, but are unable to establish adequate sales, marketing and distribution capabilities, whether independently or with third parties, or if we are unable to do so on commercially reasonable terms, our business, results of operations, financial condition and prospects will be materially adversely affected. There is no guarantee that we will be successful in our launch or commercialization efforts with respect to brexanolone IV or with respect to any other product candidate that may be approved in the future. We may encounter issues, delays or other challenges in launching or commercializing brexanolone IV or any of our other product candidates, if approved. For example, our results may be negatively impacted if we have not adequately sized our field teams or our physician segmentation and targeting strategy is inadequate or if we encounter deficiencies or inefficiencies in our infrastructure or processes. We may encounter unexpected limitations in the scope, breadth, availability or amount of reimbursement covering brexanolone IV or our other products, if approved, or other limitations or issues related to the price. We may face issues related to market acceptance and use of any of our products, if approved, including, in the case of brexanolone IV, challenges related to the IV mode of administration or competition from lower cost anti-depressants. We may not be successful in our regulatory and other efforts to enable supervised home infusion as an option for site of administration of brexanolone IV. Even if home infusion is permitted by the FDA or other regulatory authorities as an option, supervision requirements or other conditions, limitations or restrictions imposed by the FDA or another regulatory authority may further limit market acceptance of such option. Any of these issues could impair our ability to successfully commercialize the product or to generate substantial revenues or profits or to meet our expectations with respect to revenues or profits.

Our future business prospects also depend heavily on our ability to successfully develop and gain regulatory approval of our other current product candidates beyond brexanolone IV, of which SAGE-217 is in clinical development for major depressive disorder, or MDD, PPD, bipolar depression, and sleep disorders; and other product candidates are at earlier stages. We cannot be certain that we will be able to complete ongoing clinical trials or initiate future planned clinical trials, or to announce results of such trials, with respect to SAGE-217 or any of our other product candidates on the time-lines we expect or at all. We cannot be certain that we will be able to advance our product candidates into additional trials, or to successfully develop, or obtain regulatory approval for, or successfully commercialize, any of our product candidates.

Drug development is a long, expensive and uncertain process, involving a high degree of risk. Our business depends heavily on our ability to complete clinical development and non-clinical studies of SAGE-217 and our other current product candidates, and to obtain regulatory approval of and successfully commercialize those product candidates. Before obtaining regulatory approvals for the commercial sale of any product candidate, we must demonstrate through non-clinical studies and clinical trials that the product candidate is safe and effective for use in each target indication. We may not be able to demonstrate the efficacy and safety of SAGE-217 or any of our other current product candidates or any future product candidate at each stage of clinical development. Success in non-clinical studies or in earlier stage clinical trials may not be repeated or observed in ongoing or future studies involving the same compound or other product candidates. The results of clinical trials or non-clinical studies of our product candidates at any stage may not support further development or may not be sufficient to obtain regulatory approval. Changes in formulation, or the need to refine or scale-up the manufacturing process, for our product candidates could delay development or

require us to conduct additional clinical trials or non-clinical studies or could lead to different results than achieved with the earlier formulation or processes. We may not be able to initiate or complete our clinical trials or announce results from our clinical trials on the time-lines we expect. We may experience slower than expected enrollment and randomization of patients in our clinical trials, particularly in clinical trials where an in-patient stay or frequent site visits are required or where the patient population is small or where there are existing therapies. These types of delays can lead to delays in completion of a trial and announcement of results. There is also the potential for slower than expected clinical site initiation, delays or problems in analyzing data, and the potential need for additional analysis or data or the need to enroll additional patients

in any of our clinical trials. We may also encounter delays arising from unexpected adverse events in a trial or other unexpected hurdles or issues in the conduct of any trial.

The drug development process can take many years, and may include post-marketing studies and surveillance, which will require the expenditure of substantial resources. Of the large number of drugs in development in the U.S., only a small percentage will successfully complete the FDA regulatory approval process and will be commercialized. Clinical trials of our product candidates are, and the manufacturing and marketing of our product candidates will be, subject to extensive and rigorous review and regulation by numerous government authorities in the U.S. and in other countries where we intend to test and, if approved, market any product candidate. Accordingly, even if we have the requisite financial resources, when needed, to continue to fund our development efforts, we cannot assure you that any of our product candidates will be successfully developed or commercialized either in the U.S. or in any country outside the U.S.

Obtaining regulatory approval to market brexanolone IV or any of our other product candidates is a complex, lengthy, expensive and uncertain process, and the FDA and regulatory authorities outside of the U.S. may delay, limit or deny approval of any of our product candidates for many reasons. Any setback or delay in obtaining regulatory approval for our product candidates or in our ability to commence marketing of our products, if approved, may have a material adverse effect on our business and prospects.

We are not permitted to market any of our product candidates in the U.S. until we receive approval of an NDA from the FDA, or in any foreign countries until we receive the requisite marketing approval from such countries. Obtaining approval of an NDA in the U.S. or marketing approval in any country outside the U.S. is a complex, lengthy, expensive and uncertain process, and the FDA and regulatory authorities outside the U.S. may delay, limit or deny approval of any of our product candidates for many reasons, including, among others:

- we may not be able to demonstrate, to the satisfaction of the FDA or other regulatory authorities that our product candidates are safe and effective in any indication and that the benefits outweigh the safety risks;
- the results of our non-clinical studies and clinical trials may be negative, or may not meet the level of statistical or clinical significance required by the FDA or regulatory authorities outside the U.S. for marketing approval;
- the FDA or regulatory authorities outside the U.S. may disagree with our interpretation of data from our non-clinical studies and clinical trials, or may not accept data generated at one or more of our sites conducting non-clinical studies or clinical trials which may cause the study or trial to fail;
- the FDA or regulatory authorities outside the U.S. may determine that the number, design, size, conduct, or implementation of our non-clinical studies or clinical trials are inadequate for regulatory approval or that changes in drug formulation used in our non-clinical studies or clinical trials require additional trials or studies, even if the regulatory authorities have previously reviewed and commented on the design and details of our plans;
- the FDA or regulatory or other government authorities outside the U.S. may require that we conduct additional non-clinical studies and clinical trials prior to approval or post-approval;
- the FDA or applicable foreign regulatory authorities may not approve the formulation, labeling or specifications of any of our product candidates;
- if an NDA for any of our product candidates is reviewed by an advisory committee, including the expected advisory committee to review brexanolone IV, the advisory committee may recommend against approval of our application or may recommend that the FDA require, as a condition of approval, additional non-clinical studies or clinical trials, limitations on approved labeling or distribution and use restrictions, including restrictions, limitations or conditions that impact availability of sites of care, and the FDA may ultimately agree with the recommendations of the advisory committee;
- the FDA or applicable foreign regulatory authorities may approve a product candidate for which we are seeking regulatory approval for a more limited patient population than we expect or with substantial use restrictions;
-

the FDA may require development of a Risk Evaluation and Mitigation Strategy, or REMS, as a condition of approval or post-approval;

- the FDA or applicable foreign regulatory authorities may determine that the manufacturing processes or facilities of third-party contract manufacturers with which we contract do not conform to applicable requirements, including current Good Manufacturing Practices, or cGMPs; or
- the FDA or applicable foreign regulatory agencies may change their approval policies or adopt new regulations.

Any of these factors, many of which are beyond our control, could jeopardize or delay our ability to obtain regulatory approval for and successfully market our product candidates. Even if we receive marketing approval for any of our other product candidates, regulatory or other governmental authorities may still impose significant restrictions, including restrictions on the indicated use or marketing, or may impose ongoing requirements for potentially costly post-approval studies. For example, the FDA may recommend controlled substances scheduling of brexanolone IV or of any of our other product candidates. In such event, prior to a product launch, the U.S. Drug Enforcement Agency, or DEA, will need to determine the controlled substance schedule of the product, taking into account the recommendation of the FDA. The scheduling process may delay our ability to market any such product if it is approved.

Any setback or delay in obtaining regulatory approval for our product candidates or in our ability to commence marketing of our products, if approved, may have a material adverse effect on our business and prospects.

We cannot be certain that the results of our Phase 3 clinical trials of brexanolone IV in PPD will be sufficient to support approval of our NDA by the FDA, or the submission or approval of an MAA to the EMA for this product candidate in PPD.

We submitted an NDA to the FDA in April 2018 seeking marketing approval for brexanolone IV as a treatment for PPD. The NDA is currently under review. The FDA may not agree that the clinical and non-clinical data we have generated to date are sufficient to gain regulatory approval to commercialize brexanolone IV in PPD in the U.S. Similarly, there is no assurance that we will file an MAA with the EMA with respect to brexanolone IV as a treatment for PPD in the EU, and even if we make such filing, we may not receive EMA approval. We anticipate that planned discussions with the EMA will better inform timing and any additional requirements for an MAA submission, the potential for conditional or full marketing approval and potential post-marketing clinical development obligations if we file an MAA and our application is approved. In either case, the FDA or EMA may require that we conduct additional clinical trials or non-clinical studies before the FDA will approve our NDA or before we can submit an MAA for brexanolone IV in PPD or in order to gain approval of the MAA in PPD. Even if we receive approval of our NDA for brexanolone IV in the U.S., we expect to have post-approval obligations. Similarly, if scientific advice we receive from the EMA supports proceeding with an MAA filing seeking approval of brexanolone IV in the treatment of PPD in the EU, and we file the MAA and are successful in our efforts to gain regulatory approval, we expect to have additional post-approval obligations which are likely to include additional clinical trials.

A Breakthrough Therapy designation or Fast Track designation by the FDA or PRIME designation by the EMA may not actually lead to a faster development or regulatory review or approval process.

We have received Breakthrough Therapy designation in the U.S. and PRIME designation in the EU for brexanolone IV in the treatment of PPD. We have received Breakthrough Therapy designation and Fast Track designation for SAGE-217 in the treatment of MDD. In the future, we may seek Fast Track, Breakthrough Therapy or PRIME designations for these product candidates in indications not yet covered or for our other product candidates. These designations do not necessarily lead to a faster development pathway or regulatory review process, and do not increase the likelihood of regulatory approval. The FDA may withdraw Fast Track designation or Breakthrough Therapy designation, and the EMA may withdraw PRIME designation, if the relevant agency believes that the designation is no longer supported by data from our clinical development programs.

The number of patients with the diseases and disorders for which we are developing our product candidates has not been established with precision. If the actual number of patients with the diseases or disorders we elect to pursue with our product candidates is smaller than we anticipate, we may have difficulties in enrolling patients in our clinical trials which may delay or prevent development of our product candidates, and even if such product candidates are successfully developed and approved, the markets for our products may be smaller than we expect and our revenue potential and ability to achieve profitability may be materially adversely affected.

We have filed an NDA in the U.S. seeking approval of our lead product, brexanolone IV, for the treatment of patients with PPD. We are developing our next generation product candidate, SAGE-217, in MDD, PPD, bipolar depression, and sleep disorders. There is no precise method of establishing the actual number of patients with any of these disorders in any geography over any time period. With respect to many of the indications in which we are developing, or plan to develop, our product candidates, we have or will provide estimates of the prevalence of the disease or disorder. Our estimates as to prevalence may not be accurate, and the actual prevalence or addressable patient population for some or all of those indications, or any other indication that we elect to pursue, may be significantly smaller than our estimates. In estimating the potential prevalence of indications we are pursuing, or may in the future pursue, including our estimates as to the prevalence of PPD, MDD, and bipolar depression, we apply assumptions to available information that may not prove to be accurate. In each case, there is a range of estimates in the published literature and in marketing studies which include estimates within the range that are lower than our estimates. For example, our estimates of the prevalence of PPD are higher than estimates reported in some of the published literature and results obtained from certain studies analyzing claims databases. We believe these differences may be the result of variations in analytical methodologies and possibly under-diagnosis of PPD as a result of lack of screening and under-reporting, and patients being reluctant to seek treatment in clinical practice. The actual number of patients with PPD, MDD, bipolar depression, or any other indication in which we elect to pursue development of our product candidates may, however, be significantly lower than we believe. In addition, a prevalence calculation is an estimate of the total number of patients with a disease or disorder or the rate of occurrence of a disease or disorder in a population. Even if our prevalence estimates are correct, our product candidates may be developed for only a subset of patients with the relevant disease or disorder or our products, if approved, may be indicated or used for only a subset. In addition, the IV infusion mode of administration for brexanolone IV may further limit the number of PPD patients who will be treated with the product if it is ultimately approved, particularly if the FDA or any other regulatory authority imposes restrictions that limit or prevent the availability of supervised home infusion as a site-of-care option. Even if home infusion is permitted by the FDA or other regulatory authorities as an option, supervision requirements or other conditions, limitations or restrictions imposed by the FDA or other regulatory authorities may further limit market acceptance. In the event the number of patients with the diseases and disorders we are studying is significantly lower than we expect, we may have difficulties in enrolling patients in our clinical trials which may delay or prevent development of our product candidates. If any of our product candidates are approved and our prevalence estimates with respect to any indication or our other market assumptions are not accurate, the markets for our product candidates for these indications may be smaller than we anticipate, which could limit our revenues and our ability to achieve profitability or to meet our expectations with respect to revenues or profits.

If serious adverse events or other undesirable side effects are identified during the use of brexanolone IV, SAGE-217, SAGE-718 or any of our other product candidates in clinical trials, emergency-use cases, investigator sponsored trials, expanded access programs, or non-clinical studies, it may adversely affect our development of such product candidates or our ability to gain regulatory approval.

Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials, or could make it more difficult for us to enroll patients in our clinical trials. If serious adverse events or other undesirable side effects, or unexpected characteristics of brexanolone IV, SAGE-217, SAGE-718 or of any of our other product candidates are observed in clinical trials, emergency-use cases, investigator sponsored clinical trials, expanded access, or non-clinical studies, further clinical development of such product candidate may be

delayed or we may not be able to continue development of such product candidates at all or we may also need to discontinue development of other product candidates. Undesirable side effects caused by our product candidates could also result in the delay or denial of regulatory approval by the FDA or other regulatory authorities or in a more restrictive label than we expect. The occurrence of any of these events could have a material adverse effect on our business.

Positive results from early non-clinical studies and clinical trials of our product candidates are not necessarily predictive of the results of later non-clinical studies and clinical trials of our product candidates. If we cannot replicate the positive results from our earlier non-clinical studies and clinical trials of our product candidates in our later non-clinical studies and clinical trials, we may be unable to successfully develop, obtain regulatory approval for and commercialize our product candidates.

Positive results from non-clinical studies and clinical trials of our product candidates may not necessarily be predictive of the results we may obtain from subsequent non-clinical studies or clinical trials using the same product candidate or other product candidates. For example, the results from our Phase 3 clinical trials of brexanolone IV in PPD may not be replicated in our ongoing pivotal clinical trial of SAGE-217 in PPD, and the results of our Phase 2 placebo-controlled clinical trial of SAGE-217 in MDD may not be replicated in the planned Phase 3 clinical trial in MDD which will involve a larger number of patients. By way of example, our results in an earlier clinical trial were not replicated in our Phase 3 clinical trial of brexanolone IV in super-refractory status epilepticus. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in later-stage clinical trials after achieving positive results in early-stage development, and we cannot be certain that we will not face similar setbacks. These setbacks have been caused by, among other things, non-clinical findings made while clinical trials were underway or safety or efficacy observations made in non-clinical studies and clinical trials that are different than in earlier trials or studies, including previously unreported or otherwise unexpected adverse events. For example, we may observe safety issues in clinical studies of our product candidates that we did not observe or appreciate in earlier stage clinical studies or in non-clinical studies. The results from non-clinical animal models may not be replicated in clinical trials. Many drug candidates, including many targeting central nervous system, or CNS, disorders, with promising non-clinical profiles have failed to demonstrate similar safety, non-toxicity and efficacy in humans. Moreover, non-clinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that believed their product candidates performed satisfactorily in non-clinical studies and clinical trials nonetheless failed to obtain FDA approval. If we fail to produce positive results in our planned non-clinical studies or clinical trials of any of our product candidates, the development timeline and regulatory approval and commercialization prospects for our product candidates, and, correspondingly, our business and financial prospects, would be materially adversely affected.

Failures or delays in the commencement or completion of our ongoing and planned clinical trials of our product candidates could cause us not to meet our expected timelines or result in increased costs to us, and could delay, prevent or limit our ability to gain regulatory approval of any product candidate and to generate revenue and continue our business.

Successful completion of clinical trials at each applicable stage of development is a prerequisite to submitting an NDA to the FDA and, consequently, the ultimate approval and commercial marketing of any of our product candidates for the indications in which we develop them. We do not know whether any of our clinical trials will begin or be completed, and results announced, as planned or expected, if at all, as the commencement and completion of clinical trials and announcement of results can be delayed or prevented for a number of reasons, including, among others:

- denial by the FDA of permission to proceed with our planned clinical trials or any other clinical trials we may initiate, or placement of a clinical trial on hold;
- delays in filing or receiving approvals of additional investigational new drug applications, or INDs, that may be required;
- negative results from our ongoing non-clinical studies or clinical trials;
- challenges in identifying, recruiting and enrolling patients to participate in clinical trials, including, in some cases, due to: the small size of the patient population being studied; the lack of proximity of some patients to trial sites; challenges in meeting regulatory and material requirements to commence clinical trials in countries outside the U.S.; eligibility criteria for the clinical trial; challenges associated with the nature of the clinical trial protocol; the

availability of existing treatments for the relevant disease; the requirement for in-patient stays with respect to some of our trials; and competition from other clinical trial programs for similar indications, any of which could delay enrollment of patients in existing or future clinical trials of our product candidates;

- delays in reaching or failing to reach agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- inadequate quantity or quality of supplies of a product candidate or other materials necessary to conduct clinical trials, for example as a result of delays in defining and implementing the manufacturing process for materials used in pivotal trials or for the manufacture of larger quantities or other delays or issues arising in the manufacturing of sufficient supply of finished drug product;
- difficulties obtaining Institutional Review Board, or IRB, approval, and equivalent approval for sites outside the U.S., to conduct a clinical trial at a prospective site or sites;
- delays or problems in analyzing data, or the need for additional analysis or data or the need to enroll additional patients;
- the occurrence of serious adverse events or unexpected drug-related side effects experienced by patients in a clinical trial or unexpected results in ongoing non-clinical studies;
- delays in validating endpoints utilized in a clinical trial;
- our inability to satisfy the requirements of the FDA to commence clinical trials, including chemistry, manufacturing and control, or CMC, requirements, or other FDA requirements prior to the initiation of a clinical trial;
- the FDA or applicable regulatory authorities outside the U.S. disagreeing with our clinical trial design and our interpretation of data from clinical trials, or changing the requirements for approval even after the regulatory authority has reviewed and commented on the design for our clinical trials;
- reports from non-clinical or clinical testing of other CNS therapies that raise safety or efficacy concerns; and
- difficulties retaining patients who have enrolled in a clinical trial but may be prone to withdraw due to rigors of the clinical trials, lack of efficacy, side effects, personal issues or loss of interest.

Clinical trials may also be delayed or terminated as a result of ambiguous or negative interim results. For example, in 2015, in response to an IND filed with respect to SAGE-689, the FDA requested additional non-clinical study data prior to commencement of a Phase 1 clinical trial. We are in the process of evaluating possible alternative formulations of SAGE-689, but there is no guarantee that an alternative formulation for SAGE-689 will be sufficient to continue development. In addition, a clinical trial may be suspended or terminated by us, the FDA, the IRBs at the sites where the IRBs are overseeing a clinical trial, a data and safety monitoring board, or DSMB, overseeing the clinical trial at issue or other regulatory authorities due to a number of factors, including, among others:

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

Changes in regulatory requirements or FDA guidance or unanticipated events during our non-clinical studies and clinical trials of our product candidates may occur, which may result in changes to non-clinical studies and clinical trial protocols or the need for additional non-clinical studies and clinical trials, which could result in increased costs to us and could delay our development timeline.

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

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

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

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

These factors may materially adversely affect the willingness or ability of third parties to conduct our clinical trials, and may subject us to unexpected cost increases that are beyond our control. Nevertheless, we are responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable protocol, legal, regulatory and scientific requirements and standards, and our reliance on CROs does not relieve us of our regulatory responsibilities. We and our CROs are required to comply with regulations and guidelines, including current Good Clinical Practices, or cGCPs, for conducting, monitoring, recording and reporting the results of clinical trials to ensure that the data and results are scientifically credible and accurate, and that the trial patients are adequately informed of the potential risks of participating in clinical trials. These regulations are enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area and comparable foreign regulatory authorities for any products in clinical development. The FDA enforces cGCP regulations through periodic inspections of clinical trial sponsors, principal investigators and trial sites. If we or our CROs or clinical sites fail to comply with applicable cGCPs, 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 before approving our marketing applications. We cannot assure you that, upon inspection, the FDA or applicable regulatory authorities outside the U.S. will determine that our

clinical trials and all of our clinical sites comply with cGCPs. In addition, our clinical trials must be conducted with product candidates produced under cGMPs regulations. Our failure or the failure of our CROs or contract manufacturers to comply with these

regulations may require us to repeat clinical trials, which would delay the regulatory approval process, and could also subject us to enforcement action up to and including civil and criminal penalties.

If any of our relationships with third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for other reasons, and we are unable to rely on clinical data collected, we could be required to repeat, extend the duration of, or increase the size of our clinical trials and this could significantly delay commercialization and require significantly greater expenditures. In such an event, we believe that our financial results and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenue could be delayed.

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

We do not currently have, nor do we plan to acquire, the infrastructure or capability internally to manufacture supplies of our proprietary IV formulation of brexanolone for commercial use, if approved for marketing and sale, or of any of our other existing or future product candidates, for use in the conduct of our clinical trials and non-clinical studies or for future commercial use, and we rely completely on third-party suppliers for both active drug substances and finished drug products.

We are currently working with our contract manufacturers to prepare for validation and commercial manufacture of our proprietary IV formulation of brexanolone. We will rely on our contract manufacturers for commercial supplies of active drug substance, finished drug product and packaged and labeled product with respect to brexanolone IV, if approved. We will also rely on our contract manufacturers to manufacture sufficient quantities of SAGE-217, SAGE-718 and our other product candidates for ongoing and future clinical trials and non-clinical studies, and to scale our manufacturing processes for later stage clinical trials, if our development efforts at each stage are successful. We expect our contract manufacturers to comply with cGMPs in the manufacture of our products. The facilities used by our contract manufacturers to manufacture the active pharmaceutical ingredient and final drug product must typically complete a pre-approval inspection by the FDA and other comparable foreign regulatory agencies to assess compliance with applicable requirements, including cGMPs, after we submit the relevant NDA or equivalent foreign regulatory submission to the applicable regulatory agency. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or applicable foreign regulatory agencies, and pass regulatory inspections, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities with respect to our products. In addition, we have no direct control over our contract manufacturers' ability to maintain adequate quality control, quality assurance and qualified personnel. Furthermore, all of our third-party contract manufacturers are engaged with other companies to supply and/or manufacture materials or products for such companies, which exposes our third-party contract manufacturers to regulatory risks for the production of such materials and products. As a result, failure to satisfy the regulatory requirements for the production of those materials and products may affect the regulatory clearance of our contract manufacturers' facilities generally. If the FDA or an applicable foreign regulatory agency determines now or in the future that these facilities for the manufacture of our product candidates are noncompliant, we may need to find alternative manufacturing facilities, which would significantly adversely delay or impact our ability to develop and obtain regulatory approval for our product candidates and to market any approved products in the future. Our reliance on contract manufacturers also exposes us to the possibility that they, or third parties with access to their facilities, will have access to and may appropriate our trade secrets or other proprietary information.

We do not have long-term supply agreements in place with our contract manufacturers with respect to brexanolone IV or any of our other product candidates, and each batch of our product candidates is individually contracted through a purchase order governed by our master service and quality agreements. If our existing contract manufacturers are not willing to enter into long-term supply agreements, or are not willing or are unable to supply drug substance or drug product to us, and we engage new contract manufacturers, such contractor manufacturers must scale up the manufacturing process, complete validation batches, pass an inspection by the FDA and other applicable foreign regulatory agencies, and be approved by regulatory authorities as our manufacturer before we are able to use drug product or drug substance they

manufacture for commercial purposes which could result in significant delays or gaps in product availability. We plan to continue to rely upon contract manufacturers to manufacture commercial quantities of our products, if approved. If we are unable to maintain arrangements for third-party manufacturing, or are unable to do so on commercially reasonable terms, or are unable to obtain timely regulatory approvals in connection with our contract manufacturers, we may not be able to successfully complete development of our product candidates or commercialize our products, if approved.

Even if we receive marketing approval for our product candidates in the U.S., we may never seek or receive regulatory approval to market our product candidates outside of the U.S., or pricing and reimbursement outside the U.S. at acceptable levels.

Even if we receive marketing approval for our product candidates in the U.S., we may not seek, or may seek but never receive, regulatory approval to market our product candidates outside of the U.S. or in any particular country or region. In order to market any product outside of the U.S., we must establish and comply with the numerous and varying safety, efficacy and other regulatory requirements of other countries. Approval procedures vary among countries and can involve additional non-clinical studies or clinical trials, additional work related to manufacturing and analytical testing on controls, and additional administrative review periods. The time required to obtain approvals in other countries might differ from that required to obtain FDA approval. Marketing approval in one country does not ensure marketing approval in another, but a failure or delay in obtaining marketing approval in one country may have a negative effect on the regulatory process in other countries. The marketing approval processes in other countries may implicate all of the risks detailed above regarding FDA approval in the U.S. as well as other risks. In particular, in many countries outside of the U.S., products must receive pricing and reimbursement approval before the product can be commercialized. Obtaining this approval may require additional studies and data, and can result in substantial delays in bringing products to market in such countries and such investment may not be justified from a business standpoint given the market opportunity or level of required investment. Even if we are able to successfully develop our product candidates and obtain marketing approval in a country, we may not be able to obtain pricing and reimbursement approvals in such country at acceptable levels or at all, and any pricing and reimbursement approval we may obtain may be subject to onerous restrictions such as caps or other hurdles or restrictions on reimbursement. Failure to obtain marketing and pricing approval in countries outside the U.S. without onerous restrictions or limitations related to pricing or any delay or other setback in obtaining such approval, would impair our ability to market our product candidates successfully or at all in such foreign markets. Any such impairment would reduce the size of our potential market or revenue potential, which could have a material adverse impact on our business, results of operations and prospects.

If we are unable to establish effective sales and marketing capabilities or enter into agreements with third parties to market and sell our product candidates, we may not be able to generate any revenue.

We have never marketed, sold or distributed for commercial use any pharmaceutical product. We are in the process of building the teams, infrastructure, systems, processes, policies, relationships and materials necessary for launch of brexanolone IV in the U.S. in PPD, and to enable appropriate sites of care for administering the product, including the potential for supervised home infusion. In addition to our efforts in the U.S., we are refining our strategy and market assessments with respect to a potential launch in the EU. We also plan to continue to evaluate market opportunities for brexanolone IV in PPD in other global markets. If we receive regulatory approval to market or sell brexanolone IV or any of our other product candidates, if successfully developed and approved, but are unable to establish adequate sales, marketing and distribution capabilities, whether independently or with third parties, or if we are unable to do so on commercially reasonable terms, our business, results of operations, financial condition and prospects will be materially adversely affected. There is no guarantee that we will be successful in our launch or commercialization efforts with respect to brexanolone IV or with respect to any other product candidate that may be approved in the future. We may encounter issues, delays or other challenges in launching or commercializing brexanolone IV or any

of our other product candidates, if approved. For example, our results may be negatively impacted if we have not adequately sized our field teams or if our physician segmentation and targeting strategy is inadequate or if we encounter deficiencies or inefficiencies in our infrastructure or processes. We may encounter unexpected limitations in the scope, breadth or amount of reimbursement covering brexanolone IV or our products, if approved, or other limitations or issues related to the price. We may face issues related to market acceptance and use of any of our products, if approved, including, in the case of brexanolone IV, challenges related to the IV mode of administration or competition from lower price antidepressants. We may not be successful in our regulatory and other efforts to enable supervised home infusion as an option for site of administration of brexanolone IV. Even if home infusion is permitted by the FDA or other regulatory authorities as an option, supervision requirements or other conditions, limitations or restrictions imposed by the FDA or other regulatory authorities may further limit market acceptance. Any of these issues could impair our ability to

successfully commercialize the product or to generate substantial revenues or profits or to meet our expectations with respect to revenues or profits.

Even if we receive marketing approval for brexanolone IV or any of our other product candidates, our approved products may not achieve broad market acceptance or reimbursement at sufficient levels, which would limit the revenue that we generate from their sales.

The commercial success of our product candidates, if approved by the FDA or other applicable regulatory authorities, will depend upon the awareness and acceptance of our approved products among the medical community, including physicians, patients and healthcare payors, and reimbursement at sufficient levels. Market acceptance of our products, if approved, will depend on a number of factors, including, among others:

- the efficacy of our products as demonstrated in clinical trials, and, if required by any applicable regulatory authority in connection with the approval for the applicable indications, our ability to demonstrate in clinical trials that our products provide patients with incremental health benefits, as compared with other available CNS therapies;
- limitations or warnings contained in the labeling approved for our products by the FDA or other applicable regulatory authorities;
- the clinical indications and size of patient populations for which our products are approved;
- availability of alternative treatments already approved or expected to be commercially launched in the near future;
- the potential and perceived advantages and limitations of our products, including in the case of our proprietary formulation of brexanolone IV, limitations arising from the IV infusion mode of administration, over current treatment options or alternative treatments, including future alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support and timing of market introduction of competitive products;
- publicity concerning our products or competing products and treatments;
- pricing and cost effectiveness;
- the effectiveness of our sales and marketing deployment and strategies;
- our ability to increase awareness of our approved products through marketing efforts;
- our ability to obtain sufficient third-party coverage or reimbursement; or
- the willingness of patients to pay out-of-pocket in the absence of third-party coverage or as co-pay amounts under third party coverage.

If our product candidates are approved, but do not achieve an adequate level of acceptance by patients, physicians and payors, or reimbursement at reasonable levels, or if the patient population for which any such product is approved is smaller than we expect, we may not generate sufficient revenue from our products to become or remain profitable. Before granting reimbursement approval, healthcare payors may require us to demonstrate that our product candidates, in addition to treating these target indications, also provide incremental health benefits to patients or healthcare costs savings. Our efforts to educate the medical community and third-party payors about the benefits of our products, if approved and to the extent permitted, may require significant resources and may never be successful.

Our product candidates may cause undesirable side effects that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any; or regulatory authorities may require labeling statements, such as boxed warnings, as a result of inclusion in a class of drugs for a particular disease.

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

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

- regulatory authorities may withdraw or limit their approval of such products;
- regulatory authorities may require the addition of labeling statements, such as a “boxed” warning or a contraindication, including as a result of inclusion in a class of drugs for a particular disease;
- we may be required to change the way such products are distributed or administered, conduct additional clinical trials or change the labeling of the products;
- we may be subject to regulatory investigations and government enforcement actions;
- we may decide to remove such products from the marketplace;
- we could be sued and held liable for injury caused to individuals exposed to or taking our product candidates; and
- our reputation may suffer.

We believe that any of these events could prevent us from achieving or maintaining market acceptance of the affected products, and could substantially increase the costs of commercializing our products and significantly impact our ability to successfully commercialize our products and generate revenues.

Even if we receive marketing approval for our product candidates, we may still face significant post-marketing obligations and future development and regulatory difficulties.

Even if we receive marketing approval for our product candidates, including brexanolone IV, regulatory authorities may impose significant and potentially costly post-marketing obligations, including post-marketing studies, additional CMC work and additional pediatric studies. In the event we elect, or are required, to proceed with pediatric studies of any of our product candidates in any indication, regulatory authorities may also require additional nonclinical studies or clinical trials be completed prior to commencement of such pediatric studies. Regulatory authorities may also impose significant restrictions on our products, including restrictions on indicated uses or marketing.

If the FDA approves our NDA for brexanolone IV in PPD, but recommends controlled substances scheduling, then prior to product launch, the DEA will need to determine the controlled substance schedule of brexanolone IV, taking into account the recommendation of the FDA. The scheduling process may also apply to other product candidates. The process may delay our ability to market any such product if it is approved. Our products, if approved, will also be subject to ongoing FDA requirements governing the labeling, packaging, storage and promotion of the product and record keeping and submission of safety and other post-market information. The FDA has significant post-marketing authority, including, for example, the authority to require labeling changes based on new safety information and to require post-marketing studies or clinical trials to evaluate serious safety risks related to the use of a drug. The FDA also has the authority to require, as part of an NDA or post-approval, the submission of a REMS. Any REMS required by the FDA may lead to increased costs to assure compliance with additional post-approval regulatory requirements and potential requirements or restrictions on the sale of approved products, all of which could lead to lower sales

volume and revenue.

Manufacturers of drug products and their facilities are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMPs and other regulations. If we or a regulatory agency discover problems with our products, if approved, such as adverse events of unanticipated severity or frequency, or problems with the facility where our products are manufactured or in the manufacturing process, a regulatory agency may impose restrictions on our products, the manufacturer or us, including requiring withdrawal of such products from the market or suspension of manufacturing. If we, our product candidates or approved products, or the manufacturer for our product candidates or products, fail to comply with applicable regulatory requirements, a regulatory agency may, among other things:

- issue warning letters or untitled letters;
- seek an injunction or impose civil or criminal penalties or monetary fines;
- suspend or withdraw marketing approval;
- suspend any ongoing clinical trials;
- refuse to approve pending applications or supplements to applications submitted by us;
- suspend or impose restrictions on operations, including costly new manufacturing requirements; or
- seize or detain products, refuse to permit the import or export of products, or require that we initiate a product recall.

Competing therapies could emerge that adversely affect our opportunity to generate revenue from the sale of our product candidates, if approved.

The biopharmaceuticals industry is highly competitive. There are many public and private companies, universities, governmental agencies and other research organizations actively engaged in the research and development of products that may be similar to our product candidates or address similar markets. It is probable that the number of companies seeking to develop products and therapies similar to our products will increase.

Currently, there are no pharmacological therapies specifically approved for the treatment of PPD. Current standard of care for PPD commonly consists of psychotherapy; however, patients with moderate or severe PPD are often prescribed antidepressant medications such as selective serotonin reuptake inhibitors, or SSRIs, and serotonin and norepinephrine reuptake inhibitors, or SNRIs.

MDD patients are typically treated with a variety of antidepressant medications, including SSRIs and SNRIs. A number of companies are developing product candidates intended for the treatment of MDD, including NMDA receptor antagonists or partial antagonists such as esketamine, rapastinel, and apimostinel and the opioid receptor antagonist combination product, buprenorphine/samidorphan.

The treatment plan for bipolar depression commonly consists of a combination of medication and psychotherapy. Medications used to treat bipolar depression include mood stabilizers, atypical antipsychotics and antidepressants.

There are a number of pharmacological treatments and nonpharmacological treatments for sleep disorders, depending on the cause and nature of the sleep disruption.

In the field of neuroactive steroids focused specifically on modulation of $GABA_A$ receptors, our principal competitor is Marinus Pharmaceuticals, Inc., or Marinus. Marinus is developing a form of ganaxolone, a known $GABA_A$ positive allosteric modulator neuroactive steroid.

A number of companies are working to develop products targeted at the NMDA receptor, both antagonists and agonists.

Many of our potential competitors, alone or with their strategic partners, have substantially greater financial, technical and human resources than we do, and significantly greater experience in the discovery and development of product candidates, obtaining FDA and other regulatory approvals of treatments and the commercialization of those treatments. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated among a smaller number of our competitors. If we are successful in developing and gaining approval of any of our product candidates, we expect competition in the indications we are pursuing will focus on efficacy, safety, convenience, availability, and price. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. 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.

We have an existing collaboration, and may seek to establish additional collaborations, related to our development and commercialization of product candidates. If we are not able to establish future collaborations on commercially reasonable terms, we may have to alter our development and commercialization plans or expand our internal efforts and growth. Our existing and future collaborations, if any, may not lead to the successful development or commercialization of product candidates.

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

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

We may also be restricted under existing license agreements from entering into future agreements on certain terms with potential collaborators. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable or unwilling to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization in some or all markets or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense, including potentially increasing our infrastructure and investment outside the U.S. Such efforts may require diversion of a disproportionate amount of our attention away from other day-to-day activities, and require devotion of a substantial amount of our time to managing these expansion activities. If we elect to increase our expenditures to fund development or

commercialization activities on our own that we had planned to develop in collaboration with a third party, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue.

Our existing and future collaborations, if any, may not lead to the successful development and commercialization of any products. Our collaborators face both the same challenges and hurdles that we would face in the development and commercialization of product candidates if we were engaged in the activities ourselves, as well as additional challenges related to operating under a collaboration. In addition, under most collaborations, a certain degree of control in decision-making is transferred to or shared with our collaborators in these efforts which may lead to decisions that hamper our overall development and commercialization activities. In addition, if we depend on collaborators for capabilities and funding for major product development efforts globally or in key territories then our business may be adversely affected if the collaboration terminates or if our collaborator fails to perform its obligations under the agreement. Disputes may also arise with respect to the ownership of rights to technology or products developed with collaborators, which could have an adverse effect on our ability to develop and commercialize any affected product candidate.

We may not be successful in our efforts to identify or discover additional product candidates or 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.

The success of our business depends primarily upon our ability to identify, develop and commercialize products based on our proprietary chemistry platform. Although some of our product candidates are in non-clinical and clinical development, our research programs may fail to identify other potential product candidates for clinical development for a number of reasons. Our research methodology may be unsuccessful in identifying additional potential product candidates or our potential product candidates may be shown to have harmful side effects or may not have a positive risk/benefit profile or may have other characteristics that may make the product candidates unmarketable or unlikely to receive marketing approval.

Because we have limited financial and management resources, we focus on a limited number of clinical and research programs and product candidates and are currently focused on certain CNS disorders. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Research programs to identify new product candidates require substantial technical, financial and human resources. We may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful. Our resource allocation decisions may cause us to fail to capitalize on viable commercial drugs 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 drugs. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through future 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. If any of these events occur, we may be forced to abandon our development efforts for a program or programs, which may have a material adverse effect on our business.

If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate Program or other governmental pricing programs, we could be subject to additional reimbursement requirements, penalties, sanctions and fines, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

The Medicaid Drug Rebate Program and other governmental programs impose obligations to report pricing figures to the federal government. If we are successful in developing and gaining regulatory approval for our product candidates, we intend to participate in the Medicaid Drug Rebate Program, meaning that we will be subject to these price reporting and other compliance obligations. Other programs impose limits on the price we will be permitted to charge certain entities for our products for which we receive regulatory approval. Statutory and regulatory changes or binding guidance regarding these programs and their requirements could negatively affect the coverage and reimbursement by

these programs of products for which we receive regulatory approval and could negatively impact our results of operations.

The Medicaid Drug Rebate Program was established by the Omnibus Budget Reconciliation Act of 1990 and amended by the Veterans Health Care Act of 1992 as well as subsequent legislation. If we participate in the Medicaid Drug Rebate Program, we will be required to pay a rebate to each state Medicaid program for our covered outpatient drugs that are dispensed to Medicaid beneficiaries and paid for by a state Medicaid program as a condition of having federal funds being made available to the state for our drugs under Medicaid and Medicare Part B. Those rebates will be based on pricing data reported by us on a monthly and quarterly basis to the Centers for Medicare and Medicaid Services, or CMS, the federal agency that administers the Medicaid Drug Rebate Program. These data will include the average manufacturer price and, in the case of innovator products, the best price for each drug, which, in general, represents the lowest price available from the manufacturer, subject to exceptions, to any wholesaler, retailer, provider, health maintenance organization, nonprofit entity, or governmental entity in the U.S. in any pricing structure, calculated to include all sales and associated rebates, discounts, and other price concessions. Our failure to comply with these price reporting and rebate payment options could negatively impact our financial results.

Federal law requires that any company that participates in the Medicaid Drug Rebate Program also participate in the Health Resources and Services Administration's, or HRSA, 340B drug pricing discount program in order for federal funds to be available for the manufacturer's drugs under Medicaid and Medicare Part B. The 340B drug pricing program requires participating manufacturers to agree to charge statutorily defined covered entities no more than the 340B "ceiling price" for the manufacturer's covered outpatient drugs. These 340B covered entities include a variety of community health clinics and other entities that receive health services grants from the Department of Health and Human Services, or HHS, as well as hospitals that serve a disproportionate share of low-income patients. The 340B ceiling price is calculated using a statutory formula, which is based on the average manufacturer price and rebate amount for the covered outpatient drug as calculated under the Medicaid Drug Rebate Program. Changes to the definition of average manufacturer price and the Medicaid Drug Rebate amount under the ACA or otherwise also could affect our 340B ceiling price calculations and negatively impact our results of operations.

The Affordable Care Act obligates HHS to update the agreement that manufacturers must sign to participate in the 340B program to obligate a manufacturer to offer the 340B price to covered entities if the manufacturer makes the drug available to any other purchaser at any price and to report to the government the ceiling prices for its drugs. HRSA, the federal agency that administers the 340B program, recently updated the agreement with participating manufacturers. The Affordable Care Act also obligates the Secretary of the HHS to create regulations and processes to improve the integrity of the 340B program. On January 5, 2017, HRSA issued a final regulation regarding the calculation of 340B ceiling price and the imposition of civil monetary penalties on manufacturers that knowingly and intentionally overcharge covered entities. The effective date of the regulation has been delayed until July 1, 2018. Implementation of this final rule and the issuance of any other final regulations and guidance could affect our obligations under the 340B program in ways we cannot anticipate. In addition, legislation may be introduced that, if passed, would further expand the 340B program to additional covered entities or would require participating manufacturers to agree to provide 340B discounted pricing on drugs used in the inpatient setting.

Federal law also requires that a company that participates in the Medicaid Drug Rebate Program report average sales price information each quarter to CMS for certain categories of drugs that are paid under the Medicare Part B program. Manufacturers calculate the average sales price based on a statutorily defined formula as well as regulations and interpretations of the statute by CMS. CMS uses these submissions to determine payment rates for drugs under Medicare Part B. Statutory or regulatory changes or CMS guidance could affect the average sales price calculations for our products and the resulting Medicare payment rate, and could negatively impact our results of operations. Also, the Medicare Part B drug payment methodology is subject to change based on potential demonstration projects undertaken by CMS or potential legislation enacted by Congress.

Pricing and rebate calculations vary among products and programs. The calculations are complex and are often subject to interpretation by us, governmental or regulatory agencies and the courts. The Medicaid rebate amount is computed each quarter based on our submission to CMS of our current average manufacturer prices and best prices for the quarter. If we participate in the Medicaid Drug Rebate Program and become aware that our reporting for a prior quarter was incorrect, or has changed as a result of recalculation of the pricing data, we are obligated to resubmit the corrected data for a period not to exceed 12 quarters from the quarter in which the data originally were due. Such restatements and recalculations would increase our costs for complying with the laws and regulations governing the Medicaid Drug Rebate Program. Any corrections to our rebate calculations could result in an overage or underage in our rebate liability for past quarters, depending on the nature of the correction. Price recalculations also may affect the ceiling price at which we are required to offer our products to certain covered entities, such as safety-net providers, under the 340B drug pricing program.

If we participate in the Medicaid Drug Rebate Program and consequently the 340B drug pricing program, we could be held liable for errors associated with our submission of pricing data. In addition to retroactive rebates and the potential for 340B program refunds, if we are found to have knowingly submitted false average manufacturer price or best price information to the government, we may be liable for civil monetary penalties in the amount of $181,071 per item of false information. Our failure to submit monthly/quarterly average manufacturer price and best price data on a timely basis could result in a civil monetary penalty of $18,107 per day for each day the information is late beyond the due date. Such failure also could be grounds for CMS to terminate our Medicaid drug rebate agreement, pursuant to which we participate in the Medicaid program. In the event that CMS terminates our rebate agreement, no federal payments would be available under Medicaid or Medicare Part B for our covered outpatient drugs.

CMS and the OIG have pursued manufacturers that were alleged to have failed to report these data to the government in a timely manner. Governmental agencies may also make changes in program interpretations, requirements or conditions of participation, some of which may have implications for amounts previously estimated or paid. If we participate in the Medicaid Drug Rebate Program and consequently the 340B drug pricing program, we cannot assure you that our submissions will not be found by CMS to be incomplete or incorrect.

In order to be eligible to have our products paid for with federal funds under the Medicaid and Medicare Part B programs and purchased by the Department of Veterans Affairs, or VA, Department of Defense, or DoD, Public Health Service, and Coast Guard (the “Big Four agencies”) and certain federal grantees, we will be required to participate in the VA Federal Supply Schedule, or FSS pricing program, established under Section 603 of the Veterans Health Care Act of 1992. Under this program, we will be obligated to make our covered outpatient drugs available for procurement on an FSS contract and charge a price to the Big Four agencies that is no higher than the Federal Ceiling Price, or FCP, which is a price calculated pursuant to a statutory formula. The FCP is derived from a calculated price point called the “non-federal average manufacturer price”, or Non-FAMP, which we will be required to calculate and report to the VA on a quarterly and annual basis. Pursuant to applicable law, knowing provision of false information in connection with a Non-FAMP filing can subject a manufacturer to penalties of $181,071 for each item of false information. The FSS contract also contains extensive disclosure and certification requirements.

If we participate in the Medicaid Drug Rebate Program, Section 703 of the National Defense Authorization Act for FY 2008, will require us to pay quarterly rebates to DoD on utilization of innovator products that are dispensed through DoD’s Tricare network pharmacies to Tricare beneficiaries. The rebates are calculated as the difference between the annual Non-FAMP and FCP for the calendar year that the product was dispensed. If we overcharge the government in connection with the FSS contract or Tricare Retail Pharmacy Rebate Program, whether due to a misstated FCP or otherwise, we will be required to refund the difference to the government. Failure to make necessary disclosures and/or to identify contract overcharges can result in allegations against us under the False Claims Act and other laws and regulations. Unexpected refunds to the government, and any response to government investigation or enforcement action, would be expensive and time-consuming, and could have a material adverse effect on our

business, financial condition, results of operations and growth prospects.

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

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

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

Ensuring that our future practices and business arrangements comply with applicable healthcare laws and regulations could be costly. It is possible that governmental authorities will conclude that our business practices and arrangements do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our practices or operations, including anticipated activities to be conducted by our sales team, were found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines and exclusion from government funded healthcare programs, such as Medicare and Medicaid, any of which could substantially disrupt our operations and materially adversely affect our business and financial condition. If any of the physicians or other providers or entities with whom we expect to do business are found not to be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare

programs.

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

The FDA and other regulatory and enforcement agencies strictly regulate the promotional claims that may be made about prescription products, if approved, and enforce laws and regulations prohibiting the promotion of off-label uses. In particular, a product may not be promoted for uses that are not approved by the FDA or such other regulatory agencies as reflected in the approved labeling of the product. If we are found to have promoted off-label uses for any product, we may become subject to significant liability. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off-label promotion. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed. If we cannot successfully manage the promotion of our product candidates, if approved, in compliance with applicable laws, we could become subject to significant liability, which would materially adversely affect our business and financial condition.

Our proprietary IV formulation of brexanolone and our other product candidates may be regulated as controlled substances, the manufacture, use, sale, importation, exportation, prescribing and distribution of which are subject to regulation by the DEA, which may entail additional restrictions and cause delays in commercialization even if a product candidate is approved.

If the FDA determines that brexanolone IV or any of our other product candidates should be regulated as controlled substances, then before we can commercialize any such product candidate, the DEA will need to determine the controlled substance schedule, taking into account the recommendation of the FDA. This could delay our marketing of a product candidate and could potentially shorten the benefit of any regulatory exclusivity periods for which we may be eligible. The DEA has established certain registration, security, recordkeeping, reporting, storage, distribution, importation, exportation, inventory, quota and other requirements administered by the DEA with respect to “controlled substances” as defined in the Controlled Substances Act of 1970, or CSA, and the implementing regulations. These requirements may be applicable to us, to our third-party manufacturers and to distributors, prescribers and dispensers of our product candidates. The DEA regulates the handling of controlled substances through a closed chain of distribution. This control extends to the equipment and raw materials used in their manufacture and packaging, in order to prevent loss and diversion into illicit channels of commerce. A number of states and foreign countries also independently regulate these drugs as controlled substances.

The DEA regulates controlled substances as Schedule I, II, III, IV or V substances. Schedule I substances by definition have no established medicinal use, and may not be marketed or sold in the U.S. A pharmaceutical product may be listed as Schedule II, III, IV or V, with Schedule II substances considered to present the highest risk of abuse and Schedule V substances the lowest relative risk of abuse among such substances. As an example, Schedule IV compounds include sedative hypnotics such as benzodiazepines.

If determined to be controlled substances, the manufacturing, shipping, storing, selling and using of the products will be subject to an additional regulation. Distribution, prescribing and dispensing of these drugs are also regulated.

Annual registration is required for any facility that manufactures, distributes, dispenses, imports or exports any controlled substance. The registration is specific to the particular location, activity and controlled substance schedule.

Because of their restrictive nature, these laws and regulations could limit commercialization of our product candidates containing controlled substances. Failure to comply with these laws and regulations could also result in withdrawal of our DEA registrations, disruption in manufacturing and distribution activities, consent decrees, criminal and civil penalties and state actions, among other consequences.

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

Market acceptance and sales of our product candidates will depend on reimbursement policies and may be affected by healthcare reform measures. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels for those medications. Cost containment is a primary concern in the U.S. healthcare industry and elsewhere. Government authorities and these third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. The pricing and reimbursement environment for our products, if approved, is challenging, and may become even more challenging in the future due to, among other reasons, policies advanced by the current presidential administration or federal agencies, new healthcare legislation passed by Congress or fiscal challenges faced by all levels of government health administration authorities. We cannot be sure that reimbursement will be available for our product candidates and, if reimbursement is available, the level of such reimbursement and whether patients will be required to try other therapies prior to being prescribed our product candidate. Reimbursement may impact the demand for, or the price of, our product candidates. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize our product candidates.

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

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

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

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

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

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Risks Related to Our Intellectual Property Rights

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

We strive to protect and enhance the proprietary technologies that we believe are important to our business, including seeking patents intended to cover our products and compositions, their methods of use and any other inventions that are important to the development of our business. We may also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

Our success will depend significantly on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business; defend and enforce our patents, should they issue; preserve the confidentiality of our trade secrets; and operate without infringing the valid and enforceable patents and proprietary rights of third parties. We also rely on know-how, continuing technological innovation and in-licensing opportunities to develop, strengthen and maintain the proprietary position of our product candidates. Our owned and licensed patent applications relate to formulations and methods of use of brexanolone, and compositions and methods of use of certain other $GABA_A$ receptor modulators, including genus and species claims to SAGE-217, SAGE-105, SAGE-324 and SAGE-689 and NMDA receptor modulators, including SAGE-718.

We currently have one issued patent covering the composition of matter of SAGE-217, one issued patent covering the composition of matter of SAGE-689, and one issued patent covering methods of using SAGE-689. We do not have any other issued patents covering our lead product candidates, brexanolone IV, SAGE-217, SAGE-718, or SAGE-324. We cannot provide any assurances that any of our pending patent applications will mature into issued patents and, if they do, that such patents will be enforceable or include, claims with a scope sufficient to protect our product candidates or otherwise provide any competitive advantage. For example, the patent applications that may provide coverage for brexanolone IV only cover particular formulations and particular methods of using such formulations to treat depressive disorders such as PPD and MDD. As a result, if a patent issues from such patent applications, it would not prevent third-party competitors from creating, making and marketing alternative formulations of brexanolone that fall outside the scope of our patent claims or practicing alternative methods. There can be no assurance that any such alternative formulations will not be equally effective as our formulation of brexanolone. Moreover, other parties have developed technologies that may be related or competitive to our approach, and may have filed or may file patent applications and may have received or may receive patents that may overlap or conflict with our patent applications, either by claiming the same methods or formulations or by claiming subject matter that could dominate our patent position. Such third-party patent positions may limit or even eliminate our ability to obtain patent protection for certain inventions.

The patent positions of biotechnology and pharmaceutical companies, including our patent position, involve complex legal and factual questions, and, therefore, the issuance, scope, validity and enforceability of any patent claims that we may obtain cannot be predicted with certainty. Patents, if issued, may be challenged, deemed unenforceable, invalidated, or circumvented. U.S. patents and patent applications may also be subject to interference proceedings, ex parte reexamination, or inter partes review proceedings, supplemental examination and challenges in district court. Patents may be subjected to opposition, post-grant review, or comparable proceedings lodged in various foreign, both national and regional, patent offices. These proceedings could result in either loss of the patent or denial of the patent application or loss or reduction in the scope of one or more of the claims of the patent or patent application. In addition, such proceedings may be costly. Thus, any patents, should they issue, that we may own or exclusively license may not provide any protection against competitors. Furthermore, an adverse decision in an interference proceeding can result in a third party receiving the patent right sought by us, which in turn could affect our ability to develop, market or otherwise commercialize our product candidates.

Furthermore, though a patent, if it were to issue, is presumed valid and enforceable, its issuance is not conclusive as to its validity or its enforceability, and it may not provide us with adequate proprietary protection or competitive advantages against competitors with similar products. Even if a patent issues, and is held to be valid and enforceable, competitors may be able to design around our patents, such as using pre-existing or newly developed technology. Other parties may develop and obtain patent protection for more effective technologies, designs or methods. We may not be able

to prevent the unauthorized disclosure or use of our technical knowledge or trade secrets by consultants, vendors, former employees and current employees. The laws of some foreign countries do not protect our proprietary rights to the same extent as the laws of the U.S., and we may encounter significant problems in protecting our proprietary rights in these countries. If these developments were to occur, they could have a material adverse effect on our sales if any of our product candidates are approved in those countries.

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

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

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

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

We may rely upon unpatented trade secrets, and depend on unpatented know-how and continuing technological innovation to develop and maintain our competitive position, which we seek to protect, in part, by confidentiality agreements with our employees and our CROs, collaborators and consultants. It is possible that technology relevant to our business will be independently developed by a person that is not a party to such an agreement. Furthermore, if the employees and consultants who are parties to these agreements breach or violate the terms of these agreements, we may not have adequate remedies for any such breach or violation, and we could lose our trade secrets through such breaches or violations. Further, our trade secrets could otherwise become known or be independently discovered by our competitors.

We may infringe the intellectual property rights of others, which may prevent or delay our product development efforts and stop us from commercializing or increase the costs of commercializing our product candidates, if approved.

Our success will depend in part on our ability to operate without infringing the intellectual property and proprietary rights of third parties. We cannot assure you that our business, products and methods do not or will not infringe the patents or other intellectual property rights of third parties.

The pharmaceutical industry is characterized by extensive litigation regarding patents and other intellectual property rights. Other parties may allege that our product candidates or the use of our technologies infringes patent claims or other intellectual property rights held by them or that we are employing their proprietary technology without authorization. As we continue to develop and, if approved, commercialize our current product candidates and future products, competitors may claim that our technology infringes their intellectual property rights as part of business strategies designed to impede our successful commercialization. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. Because patent applications can take many years to issue, third parties may have currently pending patent applications which may later result in issued patents that our product candidates may infringe, or which such third parties claim are infringed by our technologies. The outcome of intellectual property litigation is subject to uncertainties that cannot be adequately quantified in advance. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. If we are sued for patent infringement, we would need to demonstrate that our product candidates, products or methods either do not infringe the patent claims of the relevant patent or that the patent claims are invalid or unenforceable, and we may not be able to do this. Even if we are successful in these proceedings, we may incur substantial costs and the time and attention of our management and scientific personnel could be diverted in pursuing these proceedings, which could have a material adverse effect on us. In addition, we may not have sufficient resources to bring these actions to a successful conclusion.

Patent and other types of intellectual property litigation can involve complex factual and legal questions, and their outcome is uncertain. Patent litigation is costly and time-consuming. Any claim relating to intellectual property infringement that is successfully asserted against us may require us to pay substantial damages, including treble damages and attorney’s fees if we are found to be willfully infringing another party’s patents, for past use of the asserted intellectual property and royalties and other consideration going forward if we are forced to take a license. In addition, if any such claim were successfully asserted against us and we could not obtain such a license, we may be forced to stop or delay developing, manufacturing, selling or otherwise commercializing our product candidates. In the case of trademark claims, if we are found to be infringing, we may be required to redesign, or rename, some or all of our product candidates to avoid infringing the intellectual property rights of third parties, which may not be possible and, even if possible, could be costly and time-consuming. Even if we are successful in these proceedings, we may incur substantial costs and divert management time and attention in pursuing these proceedings, which could have a material adverse effect on us.

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

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

We enter into confidentiality and intellectual property assignment agreements with our employees, consultants, CROs, outside scientific collaborators, and other advisors. These agreements generally provide that inventions conceived by the party in the course of rendering services to us will be our exclusive property. However, these agreements may not be honored and may not effectively assign intellectual property rights to us. For example, even if we have a consulting agreement in place with an academic advisor pursuant to which such academic advisor is required to assign to us any

inventions developed in connection with providing services to us, such academic advisor may not have the right to assign such inventions to us, as it may conflict with his or her obligations to assign all such intellectual property to his or her employing institution or another party.

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

in substantial costs and be a distraction to management and other employees which could have a materially adverse effect on our business.

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

The U.S. Patent and Trademark Office, or U.S. PTO, and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other formalities and provisions during the patent process. There are situations in which noncompliance 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. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case.

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.

Even if the patent applications we own or license are issued, competitors may infringe these patents. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that a patent of ours or our licensors is not valid, is unenforceable and/or is not infringed, or may 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 or defense proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly and could put our patent applications at risk of not issuing.

Interference proceedings provoked by third parties or brought by us may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the U.S.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock.

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

If we or one of our licensing partners initiated legal proceedings against a third party to enforce a patent, if and when issued, covering one of our product candidates, the defendant could counterclaim that the patent covering our product candidate is invalid and/or unenforceable. In patent litigation in the U.S., defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge include alleged failures to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for unenforceability assertions include allegations that someone connected with prosecution of the patent withheld relevant information from the U.S. PTO, or made a misleading statement, during prosecution. Third parties may also raise similar claims before administrative bodies in the U.S. or abroad, even outside the context of litigation. Such

mechanisms include re-examination, post grant review, ex parte reexamination, or inter partes review and equivalent proceedings in foreign jurisdictions, e.g., opposition proceedings. Such proceedings could result in revocation or amendment of our patents in such a way that they no longer cover our product candidates or competitive products. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to validity, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and

perhaps all, of the patent protection on our product candidates. Such a loss of patent protection would have a material adverse impact on our business.

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

Filing patent applications and prosecuting and defending patents on product candidates in all countries and jurisdictions throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the U.S. could be less extensive than those in the U.S., assuming that rights are obtained in the U.S. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the U.S. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the U.S., or from selling or importing products made using our inventions in and into the U.S. or other jurisdictions. The statutory deadlines for pursuing patent protection in individual foreign jurisdictions are based on the priority date of each of our patent applications.

Competitors may use our technologies in jurisdictions where we do not pursue patent protection. They may pursue and obtain their own patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the U.S. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. Even if we pursue and obtain issued patents in particular jurisdictions, our patent claims or other intellectual property rights may not be effective or sufficient to prevent third parties from so competing.

The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the U.S. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property protection, especially those relating to biotechnology and pharmaceuticals. For example, a 2018 report from the Office of the U.S. Trade Representative identified a number of countries, including India and China, where challenges to the procurement and enforcement of patent rights have been reported. Several countries, including India and China, have been listed in the report every year since 1989. This could make it difficult for us to stop the infringement of our patents, if obtained, or the misappropriation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. In addition, many countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit. Patent protection must ultimately be sought on a country-by-country basis, which is an expensive and time-consuming process with uncertain outcomes. Accordingly, we may choose not to seek patent protection in certain countries, and we will not have the benefit of patent protection in such countries.

Furthermore, proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

For certain of our product candidates, we are dependent on licensed intellectual property. If we were to lose our rights to licensed intellectual property, we may not be able to continue developing or commercializing certain of our product candidates, if approved. If we breach any of the agreements under which we license the use, development and

commercialization rights to our product candidates or technology from third parties or, in certain cases, we fail to meet certain development deadlines, we could lose license rights that are important to our business.

We are a party to a number of license agreements under which we are granted rights to intellectual property that are important to our business and we expect that we may need to enter into additional license agreements in the future. Our existing license agreements impose, and we expect that future license agreements will impose on us, various development, regulatory and/or commercial diligence obligations, payment of milestones and/or royalties and other obligations. If we fail to comply with our obligations under these agreements, or we are subject to a bankruptcy, the licensor may have the right to terminate the license, in which event we would not be able to market products covered by the license. Our

business could suffer, for example, if any current or future licenses terminate, if the licensors fail to abide by the terms of the license, if the licensed patents or other rights are found to be invalid or unenforceable, or if we are unable to enter into necessary licenses on acceptable terms.

As we have done previously, we may need to obtain licenses from third parties to advance our research or allow commercialization of our product candidates, and we cannot provide any assurances that third-party patents do not exist that might be enforced against our current product candidates or future products in the absence of such a license. We may fail to obtain any of these licenses on commercially reasonable terms, if at all. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to develop or license replacement technology. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates, which could materially harm our business and the third parties owning such intellectual property rights could seek either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties and/or other forms of compensation.

Licensing of intellectual property is of critical importance to our business and involves complex legal, business and scientific issues. Disputes may arise between us and our licensors regarding intellectual property subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- our right to sublicense patent and other rights to third parties under collaborative development relationships;
- our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of our product candidates, and what activities satisfy those diligence obligations; and
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners.

If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates.

We have entered into several licenses to support our various programs.

With respect to our proprietary formulation of brexanolone, we have entered into an exclusive license agreement with CyDex Pharmaceuticals, Inc., or CyDex, a wholly owned subsidiary of Ligand Pharmaceuticals, Inc., to use its Captisol technology to develop brexanolone for the field of use, which includes all fields for the treatment, prevention or diagnosis of any disease or symptom in humans or animals other than (i) the ocular treatment of any disease or condition with a formulation, including a hormone; (ii) topical ocular treatment of inflammatory conditions; (iii) treatment and prophylaxis of fungal infections in humans; and (iv) any ocular treatment for retinal degeneration. We are obligated to pay CyDex certain clinical/regulatory milestones and, if approved and marketed, single-digit royalties on brexanolone. In addition, we have entered into a supply agreement with CyDex, pursuant to which CyDex supplies us with Captisol to formulate both products. Absent an alternative agreement by the parties, our rights under our exclusive license agreement terminate in the event that the supply agreement terminates. Currently, our proprietary formulation of brexanolone is formulated in Captisol. Termination of our license agreement with CyDex would have a material adverse impact on our ability to develop and commercialize brexanolone in its current formulations.

In June 2015, we entered into an exclusive license agreement with The Regents of the University of California, or the Regents under which we were granted an exclusive license to certain patent rights related to the use of allopregnanolone to treat various diseases. In exchange for such license, we paid an upfront payment and will pay annual maintenance fees until the calendar year following the first sale, if any, of a licensed product. We are obligated to make milestone payments following the achievement of specified regulatory and sales milestones. Following the first sale, if any, of a licensed product, we are obligated to pay royalties at a low single digit percentage of net sales, if any, of licensed products, subject to specified minimum annual royalty amounts.

We are also party to a non-exclusive license with the Regents. Pursuant to this agreement the Regents granted us a non-exclusive, non-transferable license under all personal property rights of the Regents covering the tangible personal property in an IND application package owned by the Regents, or the Data, and a specified quantity of cGMP grade allopregnanolone, or the Material, to (i) use the Data for reference or incorporation in an IND for use of the Material as a treatment of SE, essential tremor and/or postpartum depression and (ii) use the Material or modifications of the Material to develop a pharmaceutical formulation for clinical trials for status epilepticus, essential tremor and/or postpartum depression. This agreement requires us to pay milestone payments in connection with the first derived product, which would include brexanolone IV, that meets the relevant milestones and we must also pay single-digit royalties for each derived product for a period of 15 years following the first commercial sale of such derived product. Termination of our license agreement with the Regents would have a material adverse impact on our ability to develop and commercialize derived products, which would include brexanolone IV.

We may enter into additional licenses to third-party intellectual property that are necessary or useful to our business. Our current licenses and any future licenses that we may enter into impose various royalty payment, milestone, and other obligations on us. For example, the licensor may retain control over patent prosecution and maintenance under a license agreement, in which case, we may not be able to adequately influence patent prosecution or prevent inadvertent lapses of coverage due to failure to pay maintenance fees. If we fail to comply with any of our obligations under a current or future license agreement, the licensor may allege that we have breached our license agreement, and may accordingly seek to terminate our license. In addition, future licensors may decide to terminate their licenses with us at will. Termination of any of our current or future licenses could result in our loss of the right to use the licensed intellectual property, which could materially adversely affect our ability to develop and commercialize a product candidate or product, if approved, as well as harm our competitive business position and our business prospects.

In addition, if our licensors fail to abide by the terms of the license, if the licensors fail to prevent infringement by third parties, if the licensed patents or other rights are found to be invalid or unenforceable, or if we are unable to enter into necessary licenses on acceptable terms, our business could materially suffer.

Some intellectual property which we have licensed may have been discovered through government funded programs and thus may be subject to federal regulations such as “march-in” rights, certain reporting requirements, and a preference for U.S. industry. Compliance with such regulations may limit our exclusive rights, subject us to expenditure of resources with respect to reporting requirements, and limit our ability to contract with non-U.S. manufacturers.

Some of the intellectual property rights we have licensed may have been generated through the use of U.S. government funding and may therefore be subject to certain federal regulations. For example, some of the intellectual property rights licensed to us under the license agreement with the Regents may have been generated using U.S. government funds. As a result, the U.S. government may have certain rights to intellectual property embodied in our current or future product candidates pursuant to the Bayh-Dole Act of 1980, or Bayh-Dole Act. These U.S. government rights in certain inventions developed under a government-funded program include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U.S. government has the right to require us to grant exclusive, partially exclusive, or non-exclusive licenses to any of these

inventions to a third party if the government determines that: (i) adequate steps have not been taken to commercialize the invention; (ii) government action is necessary to meet public health or safety needs; or (iii) government action is necessary to meet requirements for public use under federal regulations (also referred to as “march-in rights”). The U.S. government also has the right to take title to these inventions if we fail, or the applicable licensor fails, to disclose the invention to the government and fail to file an application to register the intellectual property within specified time limits. In addition, the U.S. government may acquire title to these inventions in any country in which a patent application is not filed within

specified time limits. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require us, or the applicable licensor, to expend substantial resources. In addition, the U.S. government requires that any products embodying the subject invention or produced through the use of the subject invention be manufactured substantially in the U.S. The manufacturing preference requirement can be waived if the owner of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the U.S. or that under the circumstances domestic manufacture is not commercially feasible. This preference for U.S. manufacturers may limit our ability to contract with non-U.S. product manufacturers for products covered by such intellectual property.

If we enter into future arrangements involving government funding, and we discover compounds or drug candidates as a result of such funding, intellectual property rights to such discoveries may be subject to the applicable provisions of the Bayh-Dole Act.

If we do not obtain new chemical entity or other types of marketing and data exclusivity for brexanolone IV or our other product candidates and if we do not obtain additional protection under the Hatch-Waxman Amendments and similar foreign legislation by extending the patent terms of our product candidates, our business may be materially harmed.

Marketing exclusivity provisions under the Federal Food, Drug, and Cosmetic Act, or FDCA, can delay the submission or the approval of certain marketing applications by other companies for a product with the same active moiety as a product we may in the future sell. The FDCA provides a five-year period of non-patent marketing exclusivity within the U.S. to the first applicant to obtain approval of an NDA for a new chemical entity, or NCE. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application, or ANDA, or a 505(b)(2) NDA submitted by another company for another drug based on the same active moiety, regardless of whether the drug is intended for the same indication as the original innovator drug or for another indication, where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the innovator NDA holder. The FDCA also provides three years of marketing exclusivity for a full NDA, or supplement to an existing NDA, if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the modification for which the drug received approval on the basis of the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the active agent for the original indication or condition of use. We plan to seek NCE exclusivity for brexanolone, and our other product candidates. There is also no guarantee that brexanolone or any of our other product candidates will qualify for marketing or data exclusivity under these provisions or that such exclusivity will alone be sufficient to for our business. Even if we are able to obtain NCE or data exclusivity under the FDCA, the applicable five-year and three-year exclusivity periods will not delay the submission or approval of a full NDA.

Depending upon the timing, duration and specifics of FDA marketing approval of our product candidates, one or more of the future U.S. patents we own or license may be eligible for limited patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. Even if, at the relevant time, we have a valid issued patent covering our product, we may not be granted an extension if we were, for example, to fail to apply within applicable deadlines, to fail to apply prior to expiration of relevant patents or otherwise to fail to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration or the term of any such extension is

less than we request, and we do not have any other exclusivity, our competitors may obtain approval of competing products following our patent expiration and our ability to generate revenues could be materially adversely affected.

If we do not have adequate patent protection or other exclusivity for our products, our business, financial condition or results of operations could be adversely affected.

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

As is the case with other biotechnology companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology industry involve both technological and legal complexity, and is therefore costly, time-consuming and inherently uncertain. In addition, the U.S. has recently enacted and is currently implementing wide-ranging patent reform legislation: the Leahy-Smith America Invents Act, referred to as the America Invents Act. The America Invents Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. It is not yet clear what, if any, impact the America Invents Act will have on the operation of our business. However, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of any patents that may issue from our patent applications, all of which could have a material adverse effect on our business and financial condition.

In addition, recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. The full impact of these decisions is not yet known. For example, on March 20, 2012 in Mayo Collaborative Services, DBA Mayo Medical Laboratories, et al. v. Prometheus Laboratories, Inc., the Court held that several claims drawn to measuring drug metabolite levels from patient samples and correlating them to drug doses were not patentable subject matter. The decision appears to impact diagnostics patents that merely apply a law of nature via a series of routine steps and it has created uncertainty around the ability to obtain patent protection for certain inventions. Additionally, on June 13, 2013 in Association for Molecular Pathology v. Myriad Genetics, Inc., the Court held that claims to isolated genomic DNA are not patentable, but claims to complementary DNA molecules are patent eligible because they are not a natural product. The effect of the decision on patents for other isolated natural products is uncertain. On June 19, 2014 in Alice Corporation Pty. Ltd. v. CLS Bank International, et al., a case involving patent claims directed to a method for mitigating settlement risk, the Court held that the patent eligibility of claims directed to abstract ideas, products of nature, and laws of nature should be determined using the same framework set forth in Prometheus. The U.S. PTO recently issued a set of guidelines setting forth procedures for determining subject matter eligibility of claims directed to abstract ideas, products of nature, and laws of nature in line with the Prometheus, Myriad, and Alice decisions. The guidance does not limit the application of Myriad to DNA but, rather, applies the decision to other natural products.

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

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

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

Although we are not aware of any claims currently pending against us, we may be subject to claims that we or our employees, advisors or consultants have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of a former employer or other third party. We may be subject to claims that an employee, advisor or consultant performed work for us that conflicts with that person’s obligations to a third party, such as an employer, and thus, that the third party has an ownership interest in the intellectual property arising

out of work performed for us. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management. If we fail in defending such claims, in addition to paying monetary claims, we may lose valuable intellectual property rights or personnel. A loss of key personnel or their work product could hamper or prevent our ability to develop and commercialize our product candidates, which would materially adversely affect our efforts and results.

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

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business, provide a barrier to entry against our competitors or potential competitors, or permit us to maintain our competitive advantage. Moreover, if a third party has intellectual property rights that cover the practice of our technology, we may not be able to fully exercise or extract value from our intellectual property rights. The following examples are illustrative:

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

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

General Company-Related Risks

As we plan for a potential commercial launch of our product candidates, we will need to develop and expand our company, and we may encounter difficulties in managing this development and expansion, which could disrupt our operations.

As we plan for a potential commercial launch of our product candidates, if approved, we expect to continue to increase our number of employees and the scope of our operations. To successfully execute our activities, and to manage our anticipated expansion, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. In addition, our management may need to divert a disproportionate amount of its attention away from its day-to-day activities, and devote a substantial amount of time to managing these expansion activities. Due to our limited resources, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. This may result in weaknesses in our infrastructure, give rise to operational mistakes or delays, loss of business opportunities, loss of employees and reduced productivity among remaining employees. The physical expansion of our operations may lead to significant costs, and may divert financial resources from other projects, such as the development of our product candidates. If our management is unable to effectively manage our expected expansion, our expenses may increase more than expected, and our ability to successfully develop and gain regulatory approval of our product candidates and generate or increase our revenue, if such product candidates are approved, could be reduced and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize our product candidates, if approved, and to compete effectively will depend, in part, on our ability to effectively manage the future expansion of our company.

Our future success depends on our ability to retain our President and Chief Executive Officer and to attract, retain and motivate qualified personnel.

We are highly dependent on Dr. Jeffrey M. Jonas, our Chief Executive Officer, President, and Director. We have entered into an employment agreement with Dr. Jonas, but he may terminate his employment with us at any time. Although we do not have any reason to believe that we will lose the services of Dr. Jonas in the foreseeable future, the loss of his services might impede the achievement of our research, development and commercialization objectives. We do not have any key-man life insurance on Dr. Jonas. We rely on consultants and advisors, including scientific, clinical and regulatory advisors, to assist us in formulating and implementing our development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us, and may not be subject to our standard non-compete agreements. Recruiting and retaining qualified personnel will also be critical to our success. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific personnel from universities and research institutions. Failure to succeed in clinical trials or in obtaining regulatory approval may make it more challenging to recruit and retain qualified scientific personnel.

Our employees may engage in misconduct or other improper activities, including violating applicable regulatory standards and requirements or engaging in insider trading, which could significantly harm our business.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to: comply with the regulations of the FDA and applicable non-U.S. regulators; provide accurate information to the FDA and applicable non-U.S. regulators; comply with healthcare fraud and abuse and anti-kick-back laws and regulations, in the U.S. and abroad; comply with anti-bribery and anti-corruption laws and regulations in the U.S. and abroad; report financial information or data accurately; or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of, including trading on, information obtained in the course of clinical trials or other material information, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a code of conduct, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may be ineffective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws 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, including the imposition of significant fines or other sanctions.

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

The use of our product candidates in clinical trials and the sale of our products, if approved, expose us to the risk of product liability claims. Product liability claims might be brought against us by patients, healthcare providers or others selling or otherwise coming into contact with our product candidates. For example, we may be sued if any product candidate we study or product we develop allegedly causes injury or is found to be otherwise unsuitable during clinical trials, manufacturing, marketing, sale or commercial use. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, including as a result of interactions with alcohol or other drugs, knowledge of risks, negligence, strict liability and a breach of warranties. Claims could also be asserted under state consumer protection acts. If we become subject to product liability claims and cannot successfully defend ourselves against them, we could incur substantial liabilities.

In addition, regardless of merit or eventual outcome, product liability claims may result in, among other things:

- withdrawal of patients from our clinical trials, or difficulty in enrolling clinical trials;
- substantial monetary awards to patients or other claimants;
- decreased demand for our products following marketing approval, if obtained;
- damage to our reputation and exposure to adverse publicity;

- increased FDA warnings on product labels;
- litigation costs;
- distraction of management's attention from our primary business;
- loss of revenue; and
- the inability to successfully gain approval and commercialize our product candidates or any future product candidates, if approved.

We maintain product liability insurance coverage for our clinical trials with a $10.0 million annual aggregate coverage limit. Nevertheless, our insurance coverage may be insufficient to reimburse us for any expenses or losses we may suffer. Moreover, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses, including if insurance coverage becomes increasingly expensive. If and when we obtain marketing approval for our product candidates, we intend to expand our insurance coverage to include the sale of commercial products; however, we may not be able to obtain this product liability insurance on commercially reasonable terms. Large judgments have been awarded in class action lawsuits based on drugs that had unanticipated side effects. The cost of any product liability litigation or other proceedings, even if resolved in our favor, could be substantial, particularly in light of the size of our business and financial resources. A product liability claim or series of claims brought against us could cause our stock price to decline and, if we are unsuccessful in defending such a claim or claims and the resulting judgments exceed our insurance coverage, our financial condition, business and prospects could be materially adversely affected.

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

As a public company, we incur significant legal, accounting and other expenses. In addition, the Sarbanes-Oxley Act of 2002 and rules subsequently implemented by the Securities and Exchange Commission and The NASDAQ Stock Market have imposed various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations cause us to incur significant legal and financial compliance costs, and make some activities more time-consuming and costly.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we are required to furnish a report by our management on our internal control over financial reporting, including an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. We conduct a process each year to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we dedicate internal resources, engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that neither we nor our independent registered public accounting firm will be able to conclude that our internal control over financial reporting is effective as required by Section 404. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our consolidated financial statements.

Comprehensive tax reform legislation could adversely affect our business and financial condition.

On December 22, 2017, President Trump signed into law the "Tax Cuts and Jobs Act", or TCJA, that significantly reforms the Internal Revenue Code of 1986, as amended, or the Code. The TCJA, among other things, includes changes to U.S. federal tax rates, imposes significant additional limitations on the deductibility or interest and net operating loss carryforwards, allows for the expensing of capital expenditures, and puts into effect the migration from a "worldwide" system of taxation to a territorial system. Our net deferred tax assets and liabilities will be revalued at the newly enacted U.S. corporate rate. We do not expect to recognize any tax expense in the year of enactment as our net

deferred tax assets have a full valuation allowance recorded. We continue to examine the impact this tax reform legislation may have on our business. The impact of this tax reform is uncertain and could be adverse.

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

As of December 31, 2017, we had federal and state net operating loss carryforwards of $482.9 million and $479.9 million, respectively, which begin to expire in 2031. As of December 31, 2017, we also had federal and state research and development tax credit carryforwards of $12.7 million and $2.3 million, respectively, which begin to expire in 2031 and 2027, respectively. As of December 31, 2017, we had federal orphan drug tax credit carryforwards of $40.0 million, which begin to expire in 2034. Under Section 382 of the Internal Revenue Code of 1986, as amended, or the Code, and similar state tax law, changes in our ownership may limit the amount of our net operating loss carryforwards and tax credit carryforwards that could be utilized annually to offset our future taxable income, if any. This limitation would generally apply in the event of a cumulative change in ownership of our company of more than 50% within a three-year period. Any such limitation, whether as the result of our initial public offering, follow-on offerings, prior private placements, sales of our common stock by certain of our existing stockholders or additional sales of our common stock by us, may significantly reduce our ability to utilize our net operating loss carryforwards and research and development tax credit carryforwards before they expire and could have a material adverse effect on our results of operations in future years. We have performed an analysis of ownership changes through December 31, 2016 and believe that there have been changes in ownership in accordance with Section 382. However, we do not expect that these changes in ownership will materially impact our ability to utilize our net operating loss carryforwards, research and development credits or orphan drug credits, prior to their expiration, although there can be no assurance in this regard. Subsequent ownership changes, as defined by Section 382, may potentially limit the amount of net operating loss carryforwards that could be utilized to offset future taxable income. The TCJA reduced the corporate income tax rate to 21%, from a prior rate of 35%. This may cause a reduction in the economic benefit of our net operating loss carryforwards and other deferred tax assets available to us. Under the TCJA, net operating losses generated after December 31, 2017 will not be subject to expiration.

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

Our results of operations could be adversely affected by general conditions in the U.S. and global economy and financial markets. A severe or prolonged economic downturn could result in a variety of risks to our business, including, weakened demand for our products, if any, and could adversely impact our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption, or cause our customers to delay making payments for our products if we receive marketing approval. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

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

Natural disasters could severely disrupt our operations, and have a material adverse effect on our business, results of operations, financial condition and prospects. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as the manufacturing facilities of our third-party contract manufacturers, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which could have a material adverse effect on our business.

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

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

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

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

Risks Related to Our Financial Position and Need for Capital

We are a biopharmaceutical company with a limited operating history, and have not generated any revenue from product sales. We have incurred significant operating losses since our inception, and anticipate that we will incur continued losses for the foreseeable future.

We are a biopharmaceutical company with a limited operating history on which investors can base an investment decision. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. We were incorporated in April 2010. Our operations to date have been limited primarily to organizing and staffing our company, raising capital and conducting research and development activities and clinical trials of our product candidates. We have never generated any revenue from product sales. We have not obtained regulatory approvals for any of our product candidates.

We have funded our operations to date through proceeds from sales of common stock, redeemable convertible preferred stock and, to a lesser extent, the issuance of convertible notes. From our inception through June 30, 2018, we had received net proceeds of $1.6 billion from such transactions. As of June 30, 2018, our cash, cash equivalents and marketable securities were $1.1 billion. We have incurred significant net losses in each year since our inception, including net losses of $91.6 million for the six months ended June 30, 2018 and $270.1 million for the year ended December 31, 2017. Substantially all of our operating losses have resulted from costs incurred in connection with our research and development programs and from general and administrative costs associated with our operations. We expect to incur increasing levels of operating losses over the next several years and for the foreseeable future. Our prior losses, combined with expected future losses, have had, and will continue to have, an adverse effect on our stockholders' deficit and working capital. We expect our research and development expenses to significantly increase in connection with clinical trials of our product candidates and efforts to seek regulatory approval for any product

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

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

- initiate and successfully complete all efficacy and safety clinical trials and non-clinical studies required to file for, and obtain, U.S. and foreign marketing approval for our product candidates;
- file for and receive marketing approval to commercialize our product candidates, if successfully developed;
- commercialize our product candidates, if approved, by developing a sales force or entering into collaborations with third parties; and
- achieve market acceptance of our product candidates in the medical community and with third-party payors.

We expect to incur significant sales and marketing costs as we prepare to commercialize our product candidates, if and when approved. Even if we successfully complete clinical development of our product candidates, and our product candidates are approved for commercial sale, and despite expending these costs, our product candidates may not be commercially successful. We may not achieve profitability soon after generating product sales, if ever. If we are unable to generate product revenue, we will not become profitable, and may be unable to continue operations without continued funding.

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

We are currently advancing our product candidates through non-clinical and clinical development, and preparing for a potential commercial launch of brexanolone IV, if approved, and potentially other product candidates if successfully developed and approved. Developing small molecule products and preparing for a potential launch are expensive. We expect our research and development and general and administrative expenses to increase substantially in connection with our ongoing activities, particularly as we continue to advance our product candidates in clinical trials, continue our discovery efforts, continue to seek regulatory approval of brexanolone IV and potentially other product candidates, if we generate positive data in our other clinical programs, and commercialize brexanolone IV and other products, if successfully developed and approved. Depending on the status of development efforts, regulatory approval or, if approved, commercialization of our product candidates, as well as the progress we make in selling our products, if approved, we will also require additional capital to fund operating needs. We may also need to raise additional funds if we choose to pursue additional indications and/or geographies for our product candidates, identify new potential opportunities or otherwise expand our activities more rapidly than we presently anticipate.

As of June 30, 2018, our cash, cash equivalents and marketable securities were $1.1 billion. Based on our current operating plans, we expect that our existing cash, cash equivalents and marketable securities, will be sufficient to fund our anticipated level of operations into 2020. Our current operating plan does not contemplate other development activities we may pursue or that all of the currently planned activities will proceed at the same pace, or that all of the activities will be fully initiated or completed during that time. We may use available capital resources sooner than we expect under our current operating plan. In addition, our operating plan may change. We may need or choose to seek additional funds sooner than planned, through equity or debt financings, government or other third-party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements or a combination of these approaches. In any event, we expect to require additional capital to expand future development efforts, obtain regulatory approval for, and to commercialize, our product candidates. Raising funds in the current

economic environment may present additional challenges. Even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital if market conditions are favorable or in light of specific strategic considerations.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. In the event we receive negative data from our key clinical programs or encounter other major setbacks in our development or regulatory activities or in our commercialization efforts, if any of our product candidates are approved, our stock price is likely to decline which would make a future financing more difficult. Moreover, the terms of any financing may adversely affect the holdings or the rights of our stockholders. The issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our shares to decline. The sale of additional equity or convertible securities would dilute all of our stockholders. The incurrence of indebtedness would result in increased fixed payment obligations and we may be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. We could also be required to seek funds through arrangements with collaborative partners or otherwise at an earlier stage than otherwise would be desirable and we may be required to relinquish rights to some of our technologies or product candidates or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, operating results and prospects.

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

Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights.

We may seek additional capital through a combination of private and public equity offerings, debt financings, collaborations and strategic and licensing arrangements. To the extent that we raise additional capital through the sale of common stock or securities convertible or exchangeable into common stock, the ownership interest of our stockholders in our company will be diluted. In addition, the terms of any such securities may include liquidation or other preferences that materially adversely affect the rights of our stockholders. Debt financing, if available, would increase our fixed payment obligations and 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 collaboration, strategic partnerships and licensing arrangements with third parties, we may have to relinquish valuable rights to our product candidates, our intellectual property, future revenue streams or grant licenses on terms that are not favorable to us.

Risks Related to Our Common Stock

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

The market price for our common stock, similar to that of other biopharmaceutical companies, is volatile. The market price of our common stock may fluctuate significantly in response to a number of factors, most of which we cannot control, including, among others:

- the failure or delay of the FDA or any other regulatory authority to approve brexanolone IV or any of our other product candidates that are successfully developed, or any unexpected limitations on the approved indication or on use or onerous conditions of approval;
- plans for, progress of, timing of, changes to, delays in or results from, clinical trials or nonclinical studies of our product candidates, including positive or negative key data from such studies or clinical trials, serious adverse events

arising in the course of development, or any delays or major announcements related to such studies or trials;
- announcements of new products, technologies, commercial relationships, acquisitions or other events by us or our competitors;
- the success or failure of our CNS therapies;

- regulatory or legal developments in the U.S. and other countries;
- adverse developments with respect to our intellectual property portfolio or failure to obtain or loss of exclusivity;
- failure of our product candidates, if approved, to achieve commercial success;
- fluctuations in stock market prices and trading volumes of similar companies;
- general market conditions and overall fluctuations in U.S. equity markets;
- changes in healthcare laws affecting pricing, reimbursement or access;
- variations in our quarterly operating results;
- changes in our financial guidance or securities analysts' estimates of our financial performance;
- changes in accounting principles;
- our ability to raise additional capital and the terms on which we can raise it;
- sales of large blocks of our common stock, including sales by our executive officers, directors and significant stockholders;
- additions or departures of key personnel;
- discussion of us or our stock price by the press and by online investor communities; and
- other risks and uncertainties described in these risk factors.

Future sales of our common stock may cause our stock price to decline.

Sales of a substantial number of shares of our common stock in the public market or the perception that these sales might occur could significantly reduce the market price of our common stock, and impair our ability to raise adequate capital through the sale of additional equity securities.

We have broad discretion in how we use the proceeds from our follow-on public offerings, and may not use these proceeds effectively, which could affect our results of operations and cause our stock price to decline.

We have considerable discretion in the application of the net proceeds from our follow-on public offerings. We may use the net proceeds for purposes that do not yield a significant return or any return at all for our stockholders. In addition, pending their use, we may invest the net proceeds from the follow-on offerings in a manner that does not produce income or that loses value.

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

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

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

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

If equity research analysts stop publishing research or reports about our business or if they issue unfavorable commentary or downgrade our common stock, the price of our common stock could decline.

The trading market for our common stock relies in part on the research and reports that equity research analysts publish about us and our business. We do not control these analysts. The price of our common stock could decline if one or more equity research analysts downgrade our common stock or if analysts issue other unfavorable commentary or cease publishing reports about us or our business.

Item 6. Exhibits

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

Exhibit Index

Exhibit No.	Description
10.1	First Amendment to Lease by and between CLPF-Cambridge Science Center LLC and the Registrant, dated April 4, 2018 (Incorporated by reference to Exhibit 10.1 to our Quarterly Report on Form 10-Q (File No. 001-36544) filed with the SEC on May 3, 2018)
31.1*	Certification of Principal Executive Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002 (18 U.S.C. 1350)
31.2*	Certification of Principal Financial Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002 (18 U.S.C. 1350)
32.1+	Certification of Principal Executive Officer and Principal Financial Officer pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 (18 U.S.C. 1350)
101.INS*	XBRL Instance Document
101.SCH*	XBRL Taxonomy Extension Schema Document
101.CAL*	XBRL Taxonomy Extension Calculation Document

101.DEF* XBRL Taxonomy Extension Definition Linkbase Document

101.LAB* XBRL Taxonomy Extension Labels Linkbase Document

101.PRE* XBRL Taxonomy Extension Presentation Link Document

*Filed herewith.

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

SIGNATURES

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

SAGE THERAPEUTICS, INC.

August 7, 2018 By: /s/ Jeffrey M. Jonas
Jeffrey M. Jonas, M.D.
Chief Executive Officer, President and Director

(Principal Executive Officer)

August 7, 2018 By: /s/ Kimi Iguchi
Kimi Iguchi
Chief Financial Officer

(Principal Financial and Accounting Officer)