Sage Therapeutics, Inc.
Form 10-Q
November 03, 2016

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-Q

QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the quarterly period ended September 30, 2016

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, or a smaller reporting company. See the definitions of "large accelerated filer", "accelerated filer" and "smaller reporting 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

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

As of November 1, 2016, there were 37,167,174 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 ability, within the expected timeframes, to complete our ongoing non-clinical studies and clinical trials; to announce the results of such studies and trials; to advance our product candidates into additional clinical trials, including pivotal clinical trials; and to successfully complete such clinical trials;
- our expectations as to the sufficiency of the planned clinical development programs for our product candidates, if successful, to support regulatory approval; our plans with respect to filing for regulatory approval for our product candidates, if clinical development is successful; and the potential to obtain such approval and to commercialize any product, if approved;
- our estimates regarding expenses; use of cash; timing of future cash needs; and capital requirements;
- the potential for 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 expectations with respect to the performance of our contract research organizations and other third parties whose activities are important to our development and future commercialization efforts;
- 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 potential for our product candidates in those indications; the size of the potential markets for our product candidates; and our ability to serve those markets;
- the anticipated rate and degree of market acceptance of our product candidates for any indication once approved;
- 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;
- the potential for success of competing products that are or become available for the indications that we are pursuing or may in the future pursue;
- 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.

This Quarterly Report contains 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, not prove to have been accurate.

Sage Therapeutics, Inc.

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PART I — FINANCIAL INFORMATION

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

Consolidated Balance Sheets

(in thousands, except share and per share data)

(Unaudited)

| | September 30, 2016 | December 31, 2015 |
|---|---|---|
| Assets | | |
| Current assets: | | |
| Cash and cash equivalents | $320,078 | $186,753 |
| Marketable securities | 111,192 | — |
| Prepaid expenses and other current assets | 3,418 | 1,738 |
| Total current assets | 434,688 | 188,491 |
| Property and equipment, net | 1,049 | 286 |
| Restricted cash | 564 | 39 |
| Deferred offering costs | — | 200 |
| Total assets | $436,301 | $189,016 |
| Liabilities and Stockholders' Equity | | |
| Current liabilities: | | |
| Accounts payable | $5,237 | $5,159 |
| Accrued expenses | 17,093 | 10,148 |
| Total current liabilities | 22,330 | 15,307 |
| Other liabilities | 234 | 14 |
| Total liabilities | 22,564 | 15,321 |
| Commitments and contingencies (Note 5) | | |
| Stockholders' equity: | | |
| Preferred stock, $0.0001 par value per share; 5,000,000 shares authorized at September 30, 2016 and December 31, 2015, respectively; no shares issued or outstanding at September 30, 2016 and December 31, 2015, respectively | — | — |
| Common stock, $0.0001 par value per share; 120,000,000 shares authorized at September 30, 2016 and December 31, 2015, respectively; 37,165,124 and 28,823,549 shares issued and outstanding at September 30, 2016 and December 31, 2015, respectively | 4 | 3 |
| Additional paid-in capital | 678,194 | 335,032 |
| Accumulated deficit | (264,426) | (161,340) |

| | | |
|---|---|---|
| Accumulated other comprehensive items | (35) | — |
| Total stockholders' equity | 413,737 | 173,695 |
| Total liabilities and stockholders' equity | $436,301 | $189,016 |

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

Sage Therapeutics, Inc. and Subsidiaries

Consolidated Statements of Operations and Comprehensive Loss

(in thousands, except share and per share data)

(Unaudited)

| | Three Months Ended September 30, | | Nine Months Ended September 30, | |
|---|---|---|---|---|
| | 2016 | 2015 | 2016 | 2015 |
| Operating expenses: | | | | |
| Research and development | $29,075 | $17,478 | $78,752 | $48,981 |
| General and administrative | 8,989 | 6,604 | 25,033 | 17,057 |
| Total operating expenses | 38,064 | 24,082 | 103,785 | 66,038 |
| Loss from operations | (38,064) | (24,082) | (103,785) | (66,038) |
| Interest income, net | 275 | 53 | 717 | 115 |
| Other expense, net | (7) | (6) | (18) | (10) |
| Net loss | $(37,796) | $(24,035) | $(103,086) | $(65,933) |
| Net loss per share—basic and diluted | $(1.15) | $(0.84) | $(3.20) | $(2.40) |
| Weighted average common shares outstanding—basic and diluted | 32,975,897 | 28,737,743 | 32,218,204 | 27,430,275 |
| Comprehensive loss: | | | | |
| Net loss | $(37,796) | $(24,035) | $(103,086) | $(65,933) |
| Other comprehensive items: | | | | |
| Unrealized loss on marketable securities | (74) | — | (35) | — |
| Total other comprehensive loss | (74) | — | (35) | — |
| Total comprehensive loss | $(37,870) | $(24,035) | $(103,121) | $(65,933) |

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

Sage Therapeutics, Inc. and Subsidiaries

Consolidated Statements of Cash Flows

(in thousands)

(Unaudited)

| | Nine Months Ended September 30, | |
|---|---|---|
| | 2016 | 2015 |
| Cash flows from operating activities | | |
| Net loss | $(103,086) | $(65,933) |
| Adjustments to reconcile net loss to net cash used in operating activities: | | |
| Stock-based compensation expense | 12,927 | 11,154 |
| Non-cash licensing and consulting fees | — | 1,211 |
| Premium on marketable securities | (663) | — |
| Amortization of premium on marketable securities | 87 | — |
| Depreciation | 199 | 83 |
| Changes in operating assets and liabilities: | | |
| Prepaid expenses and other current assets | (1,680) | (1,548) |
| Accounts payable | 116 | 808 |
| Accrued expenses and other liabilities | 7,198 | 1,661 |
| Net cash used in operating activities | (84,902) | (52,564) |
| Cash flows from investing activities | | |
| Proceeds from sales of marketable securities | 7,999 | — |
| Purchases of marketable securities | (118,650) | — |
| Purchases of property and equipment | (901) | (160) |
| Increase in restricted cash | (525) | — |
| Net cash used in investing activities | (112,077) | (160) |
| Cash flows from financing activities | | |
| Proceeds from stock option exercises and employee stock purchase plan issuances | 728 | 663 |
| Payments of offering costs | (599) | (548) |
| Proceeds from public offerings of common stock, net of commissions and underwriting discounts | 330,175 | 129,720 |
| Net cash provided by financing activities | 330,304 | 129,835 |
| Net increase in cash and cash equivalents | 133,325 | 77,111 |
| Cash and cash equivalents at beginning of period | 186,753 | 127,766 |
| Cash and cash equivalents at end of period | $320,078 | $204,877 |
| Supplemental disclosure of non-cash financing activities | | |
| Public offering costs included in accounts payable or accrued expenses | $— | $4 |
| Purchases of property and equipment included in accounts payable or accrued expenses | $106 | $— |

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

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SAGE THERAPEUTICS, INC. AND SUBSIDIARIES

Notes to Consolidated Financial Statements

(Unaudited)

1. Nature of Operations

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 inadequate or no approved existing therapies. 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. under its Second Amended and Restated Certificate of Incorporation.

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 it is able to obtain regulatory approval; 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.

The Company has incurred losses and negative cash flows from operations since its inception. As of September 30, 2016, the Company had an accumulated deficit of $264.4 million. From its inception through September 30, 2016, the Company received net proceeds of $643.3 million from the sales of redeemable convertible preferred stock, the issuance of convertible notes, and the proceeds from its initial public offering (“IPO”) in July 2014 and follow-on underwritten public offerings in April 2015, January 2016 and September 2016. Based on its current operating plans, the Company believes its cash, cash equivalents and marketable securities of $431.3 million as of September 30, 2016 will be sufficient to fund its anticipated level of operations and capital expenditures into the second quarter of 2018.

2. Summary of Significant Accounting Policies

Basis of Presentation

The unaudited interim 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 have been condensed or omitted from this report, as is permitted by such rules and regulations. Accordingly, these consolidated financial statements should be read in conjunction with the

audited consolidated financial statements as of and for the year ended December 31, 2015.

The unaudited interim 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 September 30, 2016, its results of operations and comprehensive loss for the three and nine months ended September 30, 2016 and 2015, and its cash flows for the nine months ended September 30, 2016 and 2015. The condensed consolidated balance sheet at December 31, 2015 was derived from audited financial statements, but does not contain all of the footnote disclosures from the annual financial statements. The results for the three and nine months ended September 30, 2016 are not necessarily indicative of the results for the year ending December 31, 2016, or for any future period.

Principles of Consolidation

The unaudited interim 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, 2015. Intercompany accounts and transactions have been eliminated.

Use of Estimates

The preparation of consolidated financial statements in conformity with accounting principles generally accepted in the United States of America 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.

Marketable securities

Marketable securities consist of investments with original maturities greater than ninety 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 various 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.

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 September 30, 2016 and December 31, 2015 were carried at fair value, determined according to the fair value hierarchy; see Footnote 3, Fair Value Measurements.

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 September 30, 2016 and December 31, 2015, respectively.

Deferred Offering Costs

The Company capitalizes certain legal, accounting and other third-party fees that are directly associated with in-process equity financings as deferred offering costs until such financings are consummated. After consummation of the follow-on public offerings of common stock in January 2016 and April 2015, $0.6 million and $0.6 million,

respectively, of these costs were recorded in stockholders' equity as a reduction of additional paid-in capital generated as a result of the offering.

Restricted Cash

A deposit of $0.5 million was restricted from withdrawal as of September 30, 2016. The restriction is related to securing the facility lease in May 2016, under which the Company rented 19,805 square feet of additional office space in a separate multi-tenant building beginning in September 2016. The lease for the additional space will expire in February 2022. The restriction expires in 2022, in accordance with the operating lease agreement. This balance is included in restricted cash on the accompanying unaudited condensed consolidated balance sheets.

Recently Issued Accounting Pronouncements

In May 2014, the Financial Accounting Standards Board ("FASB") issued guidance that outlines a single comprehensive model for entities to use in accounting for revenue arising from contracts with customers and supersedes most current revenue recognition guidance, including industry specific guidance. The guidance is based on the principle that an entity should recognize revenue to depict the transfer of goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. The guidance also requires additional disclosure about the nature, amount, timing and

uncertainty of revenue and cash flows arising from customer contracts, including significant judgments and changes in judgments and assets recognized from costs incurred to fulfill a contract. Entities have the option of using either a full retrospective or a modified retrospective approach for the adoption of the new standard. The guidance becomes effective for the Company in the year ending December 31, 2018, and the Company could early adopt the standard for the year ending December 31, 2017. The Company is currently assessing the method of adoption and is in the process of evaluating the impact that this new accounting guidance will have on its consolidated financial statements and footnote disclosures, although it does not currently have any revenue.

In August 2014, the FASB issued Accounting Standards Update, or ASU, 2014-15, Presentation of Financial Statements—Going Concern (Subtopic 205-40). The guidance addresses management's responsibility to evaluate whether there is substantial doubt about an entity's ability to continue as a going concern and to provide related footnote disclosures. Management's evaluation should be based on relevant conditions and events that are known and reasonably knowable at the date that the financial statements are issued. The standard will be effective for the year ending December 31, 2016. Early adoption is permitted. The Company does not expect that the adoption of this new guidance will have a material impact on its footnote disclosures.

In February 2016, the FASB issued ASU 2016-02, Leases (ASC 842), which sets out the principles for the recognition, measurement, presentation and disclosure of leases for both parties to a contract (i.e., lessees and lessors). The standard requires lessees to apply a dual approach, classifying leases as either finance or operating leases based on the principle of whether or not the lease is effectively a financed purchase by the lessee. This classification will determine whether lease expense is recognized based on an effective interest method or on a straight line basis over the term of the lease, respectively. A lessee is also required to record a right-of-use asset and a lease liability for all leases with a term of greater than 12 months regardless of their classification. Leases with a term of 12 months or less will be accounted for similarly to existing guidance for operating leases today. ASC 842 supersedes the previous leases standard, ASC 840 Leases. 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 March 2016, the FASB issued ASU No. 2016-09, Compensation-Stock Compensation (Topic 718): Improvements to Employee Share-Based Payment Accounting. The standard involves several aspects of the accounting for share-based payment transactions, including the income tax consequences, classification of awards as either equity or liabilities and classification on the statement of cash flows. The standard will be effective on January 1, 2017. 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. The standard changes the impairment model for most financial assets and certain other instruments. Under the standard, entities holding financial assets and net investment in leases that are not accounted for at fair value through net income are to be presented at the net amount expected to be collected. An allowance for credit losses will be a valuation account that will be deducted from the amortized cost basis of the financial asset to present the net carrying value at the amount expected to be collected on the financial asset. The standard will be effective on January 1, 2020. 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 statement of cash flows. The standard will be effective on January 1, 2018. The Company is in the process of evaluating the impact that this new guidance will have on its consolidated financial statements.

3. Fair Value Measurements

The Company’s cash equivalents are generally 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 generally based on prices obtained from independent pricing sources. Consistent with the fair value hierarchy described above, securities with validated quotes from pricing services are generally 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 September 30, 2016 and December 31, 2015:

| | September 30, 2016 | | | |
|---|---|---|---|---|
| | Total | Quoted Prices in Active Markets (Level 1) | Significant Other Observable Inputs (Level 2) | Significant Unobservable Inputs (Level 3) |
| | (in thousands) | | | |
| Money market funds: | | | | |
| Money market funds | $320,078 | $320,078 | $ — | $ — |
| Total money market funds | 320,078 | 320,078 | — | — |
| Marketable securities: | | | | |
| U.S. government securities | 24,050 | — | 24,050 | — |
| Corporate bonds | 64,672 | — | 64,672 | — |
| Commercial paper | 22,470 | — | 22,470 | — |
| Total marketable securities | 111,192 | — | 111,192 | — |
| Total money market funds and marketable securities | $431,270 | $320,078 | $ 111,192 | $ — |

| | December 31, 2015 | | | |
|---|---|---|---|---|
| | Total | Quoted Prices in Active Markets (Level 1) | Significant Other Observable Inputs (Level 2) | Significant Unobservable Inputs (Level 3) |
| | (in thousands) | | | |
| Cash and cash equivalents: | | | | |
| Money market funds | $186,753 | $186,753 | $ — | $ — |
| Total cash and cash equivalents | $186,753 | $186,753 | $ — | $ — |

During the three and nine months ended September 30, 2016 and 2015, there were no transfers among the Level 1, Level 2 and Level 3 categories.

Marketable Securities

The following table summarizes the Company's marketable securities as of September 30, 2016:

| | September 30, 2016 | | |
|---|---|---|---|
| | Amortized Cost | Gross Unrealized Gains | Gross Unrealized Losses | Fair Value |
| | (in thousands) | | | |
| Assets: | | | | |
| U.S. government securities (due within 1 year) | $24,037 | $ 13 | $ — | $24,050 |
| Corporate bonds (due within 1 year) | 64,720 | 4 | (52) | 64,672 |
| Commercial paper (due within 1 year) | 22,470 | — | — | 22,470 |
| | $111,227 | $ 17 | $ (52) | $111,192 |

There have been no impairments of the Company's assets measured and carried at fair value during the three and nine months ended September 30, 2016 and 2015. The Company held no marketable securities as of December 31, 2015.

4. Accrued Expenses

Accrued expenses consist of the following:

| | September 30, 2016 | December 31, 2015 |
|---|---|---|
| | (in thousands) | |
| Development costs | $12,840 | $ 6,466 |
| Employee-related expenses | 3,010 | 2,718 |
| Professional services | 1,225 | 935 |
| Other accrued expenses | 18 | 29 |
| | $17,093 | $ 10,148 |

5. Commitments and contingencies

Operating Leases

The Company rents 22,067 square feet of office space in a multi-tenant building under an operating lease that will expire in February 2022.

In May 2016, the Company entered into a separate lease under which, beginning on September 1, 2016, the Company rents 19,805 square feet of additional office space in a separate multi-tenant building. The lease for the additional space will also expire in February 2022.

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 the Company’s compounds known as SAGE-547 and 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 consideration for the inclusion of SAGE-689 in the license granted by CyDex, the Company paid to CyDex $0.1 million, which was recorded as research and development expense for the three months ended September 30, 2015 in connection with the execution of the amended and restated license agreement.

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 SAGE-547; 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 SAGE-547; 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.

In March 2015, a clinical development milestone was met for the SAGE-547 program under the license agreement with CyDex, and accordingly, the Company recorded research and development expense for the three months ended March 31, 2015 of $0.3 million.

In April 2015, an additional clinical development milestone was met for the SAGE-547 program under the license agreement with CyDex, and accordingly, the Company recorded research and development expense for the three months ended June 30, 2015 of $0.5 million.

In August 2016, an additional clinical development milestone was met for the SAGE-547 program under the license agreement with CyDex, and accordingly, the Company recorded research and development expense for the three and nine months ended September 30, 2016 of $0.3 million.

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.

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.

In September 2015, a regulatory milestone was met for one of the programs. Accordingly, the Company recorded research and development expenses and made a cash payment of $50,000.

For the three and nine months ended September 30, 2016, the Company did not record any expense or make any milestone payments under the license agreement with Washington University.

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 whereby 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 post-partum 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. The Company paid to The Regents of the University of California clinical development milestones of up to $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. 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.

During the three months ended March 31, 2015, one clinical development milestone was met. Accordingly, the Company recorded research and development expenses and made a cash payment totaling $0.1 million.

During the three months ended June 30, 2015, an additional clinical development milestone was met. Accordingly, the Company recorded research and development expenses for the three months ended June 30, 2015 totaling $25,000. 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. 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.

For the three and nine months ended September 30, 2016, 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.

Consulting Agreement

In January 2014, the Company entered into a consulting agreement with a nonemployee 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.

In March 2015, the second clinical development milestone for one of the programs included in the consulting agreement was met. Accordingly, the Company recorded research and development expense for the three months ended March 31, 2015 of $0.6 million, comprised of $0.2 million in cash and $0.4 million related to the issuance of 7,936 shares of the Company's common stock, related to the achievement of this milestone.

In April 2015, the third clinical development milestone for one of the programs included in the consulting agreement was met. Accordingly, the Company recorded research and development expense for the three months ended June 30, 2015 of $1.1 million, comprised of $0.3 million in cash and $0.8 million related to the issuance of 15,873 shares of the Company's common stock, related to the achievement of this milestone.

For the three and nine months ended September 30, 2016, the Company did not record any expense or make any milestone payments under the consulting agreement with the nonemployee advisor.

6. Sale of Equity Securities

On January 12, 2016, the Company completed the sale of 3,157,894 shares of its common stock at a price to the public of $47.50 per share, resulting in net proceeds to the Company of $140.4 million after deducting underwriting discounts and commissions and offering expenses paid by the Company.

On September 14, 2016, the Company completed the sale of 5,062,892 shares of its common stock at a price to the public of $39.75 per share, resulting in net proceeds to the Company of $189.2 million after deducting underwriting discounts and commissions paid by the Company.

7. Stock-Based Compensation

Stock Option Plans

On July 2, 2014, the Company's stockholders approved the 2014 Stock Option and Incentive Plan (the "2014 Stock Option Plan"), which became effective upon the completion of the IPO. The 2014 Stock Option Plan provides for the grant of restricted stock awards, 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 will no longer grant 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. As of September 30, 2016, the total number of shares reserved under all equity plans for outstanding grants was 4,061,280, and the Company had 885,723 shares 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 issued and outstanding shares of common stock on the immediately preceding December 31. On January 1, 2016, 1,154,653 shares of common stock, representing 4% of the Company's issued and outstanding shares of common stock as of December 31, 2015, were added to the 2014 Stock Option Plan.

Terms of restricted stock awards and stock option agreements, including vesting requirements, are determined by the Board of Directors or the Compensation Committee of the Board of Directors, subject to the provisions of the applicable stock option plan. Options and restricted stock awards granted by the Company that are not performance-based, generally vest based on the continued service of the grantee with the Company during a specified period following the grant. These awards, when granted to employees, generally vest ratably over four years, with a 25% cliff vesting at the one year anniversary. All awards expire in ten years.

During the nine months ended September 30, 2016 and 2015, the Company granted 74,039 and 497,100 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. During the three months ended June 30, 2015, the achievement of one milestone was considered probable and that milestone was achieved during the three months ended September 30, 2015. The estimated quantity of awards expected to vest was recognized by determining the cumulative expense as of June 30, 2015 and the remaining expense was recognized over the estimated service period. This milestone represents 35% of the performance-based option grants that were made during 2015. During the three and nine months ended September 30, 2015, the Company recognized stock-based compensation expense related to this milestone of $1.4 million and $4.8 million, respectively.  three and nine months ended September 30, 2016

The achievement of the remaining milestones was deemed to be not probable as of September 30, 2016 and therefore no expense has been recognized related to these awards for the three and nine months ended September 30, 2016.

Stock-based compensation expense recognized during the three and nine months ended September 30, 2016 and 2015 was as follows:

| | Three Months Ended September 30, | | Nine Months Ended September 30, | |
|---|---|---|---|---|
| | 2016 | 2015 | 2016 | 2015 |
| | (in thousands) | | | |
| Research and development | $2,530 | $1,472 | $6,179 | $4,293 |
| General and administrative | $2,218 | 2,935 | $6,748 | 6,861 |
| | $4,748 | $4,407 | $12,927 | $11,154 |

For stock option awards, the fair value is estimated at the grant date using the Black-Scholes option-pricing model, taking into account the terms and conditions upon which options are granted. The fair value of the options is amortized on a straight-line basis for awards to employees and on a graded basis for awards to non-employees over the requisite service period of the awards. The weighted average grant date fair value per share relating to outstanding stock options granted under the Company's stock option plans during the nine months ended September 30, 2016 and 2015 was $23.32 and $33.44, respectively.

The fair value of each option granted to employees and nonemployee directors during the three and nine months ended September 30, 2016 and 2015, under the Company's stock option plans has been calculated on the date of grant using the following weighted average assumptions:

| | Three Months Ended September 30, | | Nine Months Ended September 30, | |
|---|---|---|---|---|
| | 2016 | 2015 | 2016 | 2015 |
| Expected dividend yield | 0 % | 0 % | 0 % | 0 % |
| Expected volatility | 80.19 % | 86.59 % | 80.12 % | 91.03 % |
| Risk free interest rate | 1.25 % | 1.80 % | 1.38 % | 1.57 % |
| Expected term | 6.03 years | 6.08 years | 6.05 years | 6.03 years |

Expected dividend yield: The Company has not paid, and does not anticipate paying, any dividends in the foreseeable future.

Risk-free interest rate: The Company determined the risk-free interest rate by using a weighted average equivalent to the expected term based on the U.S. Treasury yield curve in effect as of the date of grant.

Expected volatility: The Company does not have sufficient history to support a calculation of volatility using only its historical data. The Company uses a weighted-average volatility considering the Company's own volatility since the IPO in July 2014 and the volatilities of a peer group of comparable companies for time periods prior to the IPO.

Expected term (in years): Expected term represents the period that the Company's stock option grants are expected to be outstanding. As the Company has only been publicly traded since July 2014, there is not sufficient historical term data to calculate the expected term of the options. Therefore, the Company elected to utilize the "simplified" method to estimate the expected term of options granted to employees. Under this approach, the weighted average expected life is presumed to be the average of the vesting term and the contractual term of the option.

Forfeitures are estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from estimates. The Company estimates forfeitures based on historical termination behavior. For the nine months ended September 30, 2016 and 2015, forfeiture rates of 11.2% and 10.0%, respectively, were applied.

For options granted to nonemployees, the expected life of the option used is ten years, which is the contractual term of each option. All other assumptions used to calculate the grant date fair value are generally consistent with the assumptions used for options granted to employees.

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, 2015 | 3,002,809 | $ 26.67 | 8.67 | $ 96,479 |
| Granted | 1,213,068 | 33.68 | | |
| Exercised | (69,822) | 4.52 | | |
| Forfeited | (84,775) | 46.47 | | |
| Outstanding as of September 30, 2016 | 4,061,280 | 28.74 | 8.39 | $ 76,947 |
| Vested and expected to vest as of September 30, 2016 | 3,327,569 | 27.53 | 8.33 | $ 67,698 |
| Exercisable as of September 30, 2016 | 1,363,896 | 21.87 | 7.73 | $ 35,845 |

At September 30, 2016, the Company had unrecognized stock-based compensation expense related to its unvested service-based stock option awards of $40.0 million, which is expected to be recognized over the remaining weighted average vesting period of 2.79 years. The total fair value of shares vested for the nine months ended September 30, 2016 and 2015 was $14.9 million and $7.3 million, respectively. In addition, the Company has 429,815 outstanding unvested stock options that vest upon the achievement of certain performance criteria. Total unrecognized stock-based compensation expense related to those awards was $8.5 million at September 30, 2016.

The intrinsic value of stock options exercised during the nine months ended September 30, 2016 and 2015 was $2.6 million and $28.2 million, respectively.

Restricted Stock Awards

During the year ended December 31, 2013, the Company granted restricted stock awards to certain officers, employees, directors, and consultants of the Company. During the three months ended September 30, 2016 and 2015, the Company recorded $4,000 and $0.1 million, respectively, of stock-based compensation expense related to its restricted stock. During the nine months ended September 30, 2016 and 2015, the Company recorded $35,000 and $0.2 million, respectively, of stock-based compensation expense related to its restricted stock. The table below summarizes activity relating to restricted stock:

| | Shares |
|---|---|
| Outstanding as of December 31, 2015 | 42,781 |
| Issued | — |
| Vested | (40,468) |
| Forfeited | — |
| Repurchased | — |
| Outstanding as of September 30, 2016 | 2,313 |

At September 30, 2016, the Company had unrecognized stock-based compensation expense related to its unvested restricted stock awards of $1,000 which is expected to be recognized over the remaining weighted average vesting period of 0.13 years.

During the nine months ended September 30, 2016 and 2015, no shares of restricted stock were issued.

Unvested shares are subject to repurchase by the Company, at the issuance price, upon the termination of the employee at the sole discretion of the Company. No shares were repurchased during the nine months ended September 30, 2016 and 2015.

2014 Employee Stock Purchase Plan

On July 2, 2014, the Company’s stockholders approved the 2014 Employee Stock Purchase Plan, which had been previously approved by the Board of Directors. A total of 282,000 shares of common stock were initially authorized for issuance under this plan. The 2014 Employee Stock Purchase Plan became effective upon the completion of the IPO. As of September 30, 2016, 14,351 shares have been issued under this plan.

8. Net Loss Per Share

Basic and diluted net loss per share was calculated as follows for the three and nine months ended September 30, 2016 and 2015:

| | Three Months Ended September 30, | | Nine Months Ended September 30, | |
|---|---|---|---|---|
| | 2016 | 2015 | 2016 | 2015 |
| Basic net loss per share: | | | | |
| Numerator: | | | | |
| Net loss (in thousands) | $(37,796) | $(24,035) | $(103,086) | $(65,933) |
| Denominator: | | | | |
| Weighted average common stock outstanding—basic | 32,975,897 | 28,737,743 | 32,218,204 | 27,430,275 |
| Dilutive effect of shares of common stock equivalents resulting from common stock options | — | — | — | — |
| Weighted average common stock outstanding—diluted | 32,975,897 | 28,737,743 | 32,218,204 | 27,430,275 |
| Net loss per share—basic and diluted | $(1.15) | $(0.84) | $(3.20) | $(2.40) |

The following common stock equivalents outstanding as of September 30, 2016 and 2015 were excluded from the computation of diluted net loss per share for the periods presented because including them would have been anti-dilutive:

| | Three and Nine Months Ended September 30, | |
|---|---|---|
| | 2016 | 2015 |
| Stock options | 3,631,465 | 2,510,900 |
| Employee stock purchase plan | 4,368 | 2,803 |
| Restricted stock | 2,313 | 71,319 |
| | 3,638,146 | 2,585,022 |

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

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our unaudited consolidated financial statements and related notes appearing elsewhere in this Quarterly Report on Form 10-Q, or Quarterly Report, and the Annual Report on Form 10-K for the year ended December 31, 2015, or Annual Report, and the audited financial information and the notes thereto.

Our actual results and timing of certain events may differ materially from the results discussed, projected, anticipated, or indicated in any forward-looking statements. 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 forward-looking statements contained 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.

The following information and any forward-looking statements should be considered in light of factors discussed elsewhere in this Quarterly Report, including those risks identified under Part II, Item 1A, Risk Factors, and in the Annual Report.

We disclaim any obligation, except as specifically required by law and the rules of the SEC, to publicly update or revise any such forward-looking statements to reflect any change in our expectations or in events, conditions or circumstances under 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 inadequate or no approved existing therapies. 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 report.

Our lead product candidate is SAGE-547, a proprietary intravenous, or IV, formulation of allopregnanolone, a naturally occurring neurosteroid that acts as a synaptic and extrasynaptic modulator of the $GABA_A$ receptor. GABA is the major inhibitory neurotransmitter in the CNS, and mediates downstream neurologic and bodily function via activation of $GABA_A$ receptors. We believe that allosteric modulation of the $GABA_A$ receptor has the potential to be well-suited for the treatment of a variety of CNS disorders because it allows for the fine-tuning of neuronal signals rather than complete activation or complete inhibition. SAGE-547 is in Phase 3 clinical development as an adjunctive therapy for the treatment of super-refractory status epilepticus, or SRSE. SRSE is a rare and life-altering condition in which a patient is in a state of continuous seizure called status epilepticus, or SE, and all of the standard treatment regimens normally sufficient to stop the seizure activity have failed. We expect to report top-line results from the global, randomized, double-blind, placebo-controlled Phase 3 trial of SAGE-547 in SRSE in the first half of 2017. If successful, we believe the results of the Phase 3 clinical trial, together with other clinical data obtained from the SAGE-547 clinical program, and results of ongoing non-clinical studies, could form the basis of a New Drug Application, or NDA, submission, for SAGE-547. Based on scientific advice we recently received from the European Medicines Agency, or EMA, we also believe our current Phase 3 program, if successful, will be sufficient to support a marketing authorization application to the EMA seeking approval of SAGE-547 for SRSE in the EU.

We are also developing SAGE-547 for the treatment of post-partum depression, or PPD. PPD is a distinct and readily identified major depressive disorder affecting a small percentage of women after childbirth, and is characterized by sadness and depressed mood, loss of interest in daily activities, changes in eating and sleeping habits, fatigue and decreased energy, inability to concentrate, and feelings of worthlessness, shame or guilt, which can lead to significant functional impairment. Without sufficient treatment, PPD may inhibit the mother’s ability to perform daily activities and to bond with the baby and other members of the family. PPD also carries an increased risk for suicide in some women. Onset of moderate-severe symptoms is typically 2-4 weeks after birth. Current standard of care for severe PPD comprises the cautious use of pharmacological therapies. Women with severe PPD may be hospitalized to provide a safe and stable environment for recovery if they have suicidal ideation or attempt, are unable to function and care for themselves, or require monitoring during a change in or trial of a new medication. There are no current approved therapies specifically for PPD.

Naturally occurring allopregnanolone is found at its highest levels in women during the third trimester of pregnancy, returning to normal level generally within 24 hours of giving birth. Data suggest that women with PPD may be unusually sensitive to this rapid decline in allopregnanolone, potentially causing $GABA_A$ -system mediated mood disruption. Given these data, we believe that allosteric modulators of the $GABA_A$ receptor may have potential in the treatment of PPD. In July 2016, we announced positive top-

line results from our multi-center, placebo-controlled, double-blind Phase 2 clinical trial of SAGE-547 for the treatment of severe PPD. Twenty-one patients were enrolled in the trial. Patients were required to have had a major depressive episode that began no earlier than the third trimester and no later than the first four weeks following delivery, and also to be less than six months postpartum at the time of enrollment. Trial participants were also required to have a Hamilton Rating Scale for Depression, or HAM-D, score of 26 or above prior to treatment. In the trial, SAGE-547 achieved the primary endpoint of a significant reduction in the HAM-D compared to placebo at 60 hours (p=0.008). In the trial, there was a greater than 20 point mean reduction in the depression scores of the SAGE-547 group at 60 hours through completion of the trial with a greater than 12 point difference from placebo. The statistically significant difference in treatment effect began at 24 hours (p=0.006) with an effect that was maintained at similar magnitude through to the 30-day follow-up period (p=0.01). Remission from depression, as determined by a HAM-D <7, measured at 60 hours, was seen in 7 of 10 of the SAGE-547 group compared with 1 of 11 in the placebo group. Similarly, at 30 days, 7 of 10 of the SAGE-547 group and 2 of 11 in the placebo group were in remission. SAGE-547 was found to be generally well-tolerated with no serious adverse events reported during the treatment and follow-up periods. The results of this Phase 2 trial replicate and extend the findings of an earlier open-label probe study of SAGE-547 in severe PPD reported in 2015. We have initiated an expansion of this Phase 2 clinical program to study efficacy of SAGE-547 in patients with moderate PPD, and to further study dosing of SAGE-547 in the treatment of severe PPD. We expect to announce data from these trials in the second half of 2017. On September 6, 2016, we announced that the U.S. Food and Drug Administration, or FDA, granted Breakthrough Therapy designation to SAGE-547 for the treatment of PPD. Breakthrough Therapy designation is intended to expedite the development and review of a drug candidate that is planned for use, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition when preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. The benefits of Breakthrough Therapy designation include more intensive FDA guidance on an efficient drug development program, an organizational commitment involving senior FDA managers, and eligibility for rolling review and priority review. We are in discussions with the FDA on the development pathway for SAGE-547 in PPD.

Our most advanced next-generation product candidate is SAGE-217, a novel neuroactive steroid that is a positive allosteric modulator of $GABA_A$ receptors. Like SAGE-547, SAGE-217 targets synaptic and extrasynaptic $GABA_A$ receptors. In the second quarter of 2016, we announced positive top-line results of a Phase 1 clinical program of SAGE-217. In the trial, SAGE-217 was found to be generally well-tolerated with no serious adverse events reported during the treatment and follow-up periods. Assessment of electrical activity in the brain using an electroencephalogram, or EEG, showed clear evidence of target engagement ($GABA_A$ receptor modulation) starting at the lowest dose tested (15 mg). The observed EEG effect was sustained throughout the 7-day dosing period without diminution. Rates of moderate to deep sedation defined by a structured rating scale (MOAA/S < 3) were comparable to placebo until the maximum tolerated dose (MTD) was reached, in both the single and multiple ascending dose phases of the trial. The presence of sedation was associated with maximum drug exposure. In July 2016, Sage announced that safety, tolerability and pharmacokinetics of SAGE-217 were also studied in a small open-label Phase 1 cohort of essential tremor patients (n=6). While not designed to demonstrate efficacy, preliminary data show that single doses of SAGE-217 resulted in a similar reduction in tremor symptoms as achieved with a single 12 hour infusion of SAGE-547 in our previous placebo-controlled probe study (n=25). Given the results of the Phase 1 trial and the results of the proof-of-concept Phase 2 clinical trials of SAGE-547 in PPD and essential tremor, we plan to commence Phase 2 clinical trials of SAGE-217, initially in essential tremor and PPD prior to the end of 2016. Given the potential role of $GABA_A$ receptor modulation in reducing tremors, we are also planning to initiate a proof-of-concept Phase 2 clinical trial of SAGE-217 in the treatment of Parkinson's disease prior to the end of 2016. We also plan to initiate a proof-of-concept Phase 2 clinical trial using SAGE-217 in major depressive disorder, or MDD, prior to the end of 2016. In 2017, we plan to evaluate the data read-outs from various SAGE-217 clinical trials to determine which indications to pursue in further development. While SAGE-547 is an IV infusion intended for acute administration, SAGE-217 is currently being studied as an oral solution. We are in the process of developing a solid dosage formulation of SAGE-217 intended for chronic use.

We also have a portfolio of other novel compounds that target the $GABA_A$ receptors, including SAGE-105, SAGE-324 and SAGE-689. We plan to prioritize advancement of an oral novel GABA candidate, such as SAGE-105 or SAGE-324, into investigational new drug application, or IND-enabling studies for development in GABA-related indications, such as orphan epilepsies. SAGE-689, a novel positive allosteric modulator of $GABA_A$ receptors, is in non-clinical development. Phase 1 clinical development of SAGE-689 remains delayed given requests from the FDA for additional non-clinical study data. We continue to evaluate next steps in the development of SAGE-689. There is no guarantee that we will be able to successfully address the FDA's questions.

We are also studying novel compounds that target the NMDA receptor, a critical excitatory receptor system in the brain implicated in a broad range of CNS disorders. The first product candidate selected for development from this program is SAGE-718, an oxysterol-based NMDA positive allosteric modulator. We have begun non-clinical studies of SAGE-718, with an initial development focus on two rare conditions, Smith-Lemli-Opitz Syndrome and Anti-NMDA Receptor Encephalitis. Beyond these conditions, we believe measuring levels of anti-NMDA antibodies or decreased levels of cerebrosterol, a naturally occurring oxysterol, may represent biomarkers to identify, for future study, broader patient populations characterized by cognitive dysfunction

and neuropsychiatric symptoms resulting from NMDA receptor dysfunction or 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 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, epilepsy, and movement disorders, among others. We believe that we will 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 on a scaffold of chemically-modified endogenous neuroactive steroid compounds. We believe our know-how around the chemistry and activity of allosteric modulators allows us to efficiently design molecules with different characteristics by enabling us to control important properties such as half-life, brain penetration and the types of receptors with which our compounds interact with the goal of developing product candidates that have the potential to bind with targets in the brain with more precision, increased tolerability, and fewer off-target side effects than either current CNS therapies or previous therapies which have failed in development.

Sage was founded in 2010, based on leading research in the areas of brain function and neuroactive steroids, to explore novel approaches to treatment of CNS disorders. Since our inception, we have continued to expand our know-how related to CNS therapeutics through our research and development programs, and to pursue intellectual property protection with respect to our proprietary chemistry platform. In addition, we have assembled a strong management team that together has been a part of the successful discovery, development and commercialization of more than 20 marketed CNS therapies.

We have not generated any revenue to date. We have incurred net losses in each year since our inception, and we have an accumulated deficit of $264.4 million as of September 30, 2016. Our net losses were $103.1 million for the nine months ended September 30, 2016 and $94.5 million for the year ended December 31, 2015. 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 clinical development of SAGE-547, including completing the Phase 3 clinical trial for SAGE-547 in SRSE, expanding the Phase 2 clinical program for SAGE-547 in PPD, and conducting additional clinical trials and non-clinical studies of SAGE-547 required for regulatory approval in SRSE and PPD;
- advance clinical development of SAGE-217, including initiating and conducting planned Phase 2 clinical trials of SAGE-217 in essential tremor and PPD, a proof-of-concept Phase 2 clinical trial in Parkinson's disease, and a proof-of-concept Phase 2 trial of SAGE-217 in MDD;
- conduct further non-clinical studies of SAGE-689;
- continue to advance SAGE-718, our early-stage novel allosteric modulator for NMDA, in non-clinical studies; and prioritize advancement of a novel GABA candidate, such as SAGE-105 or SAGE-324, into IND-enabling studies for development in other GABA-related indications, such as orphan epilepsies;
- continue our research and development efforts to evaluate the potential for our existing product candidates in the treatment of additional indications, and the identification of new drug candidates in the treatment of CNS disorders;
- advancing regulatory activities focused on a potential filing of an NDA and MAA for SAGE-547 in SRSE; advancing regulatory activities with respect to SAGE-547 in PPD; and initial preparations for a potential future commercial launch;

- seek regulatory approvals for our product candidates that successfully complete clinical development;
- add personnel, including personnel to support our product development and future commercialization efforts, and incur increases in stock compensation expense related to existing and new personnel with respect to both time-based and performance-based awards;
- add operational, financial and management information systems; and
- maintain, leverage and expand our intellectual property portfolio.

As a result, we will, in the future, need additional financing 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 public or private equity or debt financings or other sources, which may include collaborations with third parties. Arrangements with collaborators or others may require us to relinquish rights to certain of our technologies or product candidates. In addition, 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. 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 September 30, 2016 will enable us to fund our operating expenses and capital expenditure requirements, based on our current operating plan, into the second quarter of 2018. See "—Liquidity and Capital Resources".

Financial Operations Overview

Revenue

We have not generated any revenue from product sales since our inception, and do not expect to generate any revenue from the sale of products in the near future. If our developmental efforts result in clinical success and regulatory approval or collaboration agreements with third parties for our product candidates, we may generate revenue from those product candidates.

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 any 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 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, consisting of salaries, benefits, stock-based compensation and travel expenses of 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 will increase in the future as we increase our headcount to support the expected growth in our business and the potential commercialization of our product candidates. 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. Additionally, we anticipate an increase in payroll and related expenses as we continue to build our organizational capabilities, expand our operations, and prepare for possible future commercial operations, including sales and marketing of our product candidates, if approved.

Results of Operations

Comparison of Three Months Ended September 30, 2016 and 2015

The following table summarizes our results of operations for the three months ended September 30, 2016 and 2015:

| | Three Months Ended September 30, | | |
|---|---|---|---|
| | 2016 | 2015 | Increase (Decrease) |

| | (in thousands) | | |
|---|---|---|---|
| Operating expenses: | | | |
| Research and development | $29,075 | $17,478 | $11,597 |
| General and administrative | 8,989 | 6,604 | 2,385 |
| Total operating expenses | $38,064 | $24,082 | $13,982 |
| Loss from operations | (38,064) | (24,082) | (13,982) |
| Interest income, net | 275 | 53 | 222 |
| Other income, net | (7) | (6) | (1) |
| Net loss | $(37,796) | $(24,035) | $(13,761) |

Research and development expenses

| | Three Months Ended September 30, | | Increase (Decrease) |
|---|---|---|---|
| | 2016 | 2015 | |
| | (in thousands) | | |
| SAGE-547 | $13,557 | $9,891 | $ 3,666 |
| SAGE-217 | 3,304 | 1,048 | 2,256 |
| SAGE-689 | 375 | 521 | (146) |
| SAGE-718 | 2,114 | 1,060 | 1,054 |
| Other research and development programs | 2,037 | 1,804 | 233 |
| Unallocated expenses | 7,688 | 3,154 | 4,534 |
| Total research and development expenses | $29,075 | $17,478 | $ 11,597 |

Research and development expenses for the three months ended September 30, 2016 were $29.1 million, compared to $17.5 million for the three months ended September 30, 2015. The increase of $11.6 million was primarily due to the following:

- an increase of $3.7 million in expenses related to our SAGE-547 program, due to the continued advancement of the program in clinical development, including ongoing enrollment in the Phase 3 clinical trial in SRSE; continued conduct of the Phase 2 clinical trial of SAGE-547 in PPD; conduct of supporting clinical pharmacology studies; and an increase in chemistry, manufacturing and controls, or CMC, work in preparation for a potential filing for regulatory approval. Expenses related to payments to consultants and licensors upon achievement of certain clinical development milestones were $0.3 million and $0.2 million for the three months ended September 30, 2016 and 2015, respectively;
- an increase of $2.3 million in expenses related to our SAGE-217 program due to the initiation and conduct of two Phase 1 clinical trials and the initiation of Phase 2-enabling toxicology, formulation and manufacturing activities;
- a decrease of $0.1 million in expenses related to our SAGE-689 program due to the delay in commencement of a Phase 1 clinical trial as a result of a request from the FDA for additional non-clinical study data;
- an increase of $1.1 million in expenses due to the progression of our SAGE-718 program to IND-enabling non-clinical development and CMC activities in preparation for IND filing;
- an increase of $0.2 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 $4.5 million in unallocated expenses, including an increase of $1.1 million of non-cash stock-based compensation expense, mainly due to the hiring of additional full-time employees to support the growth in our operations.

General and administrative expenses

| | Three Months Ended September 30, | | Increase |
|---|---|---|---|

| | 2016 | 2015 | (Decrease) |
|---|---|---|---|
| | (in thousands) | | |
| Personnel-related | $4,770 | $4,235 | $ 535 |
| Professional fees | 1,858 | 894 | 964 |
| Commercial planning | 1,190 | 679 | 511 |
| Other | 1,171 | 796 | 375 |
| Total general and administrative expenses | $8,989 | $6,604 | $ 2,385 |

General and administrative expenses for the three months ended September 30, 2016 and 2015 were $9.0 million and $6.6 million, respectively. The increase of $2.4 million was primarily due to the following:

- an increase of $0.5 million in personnel-related costs due to the effects of hiring additional full-time employees to support operations, finance, human resources, legal and early commercial planning activities, offset by a decrease of $0.7 million in non-cash stock-based compensation expense, primarily because expense related to the achievement of performance-based vesting criteria was zero and $0.8 million for the three months ended September 30, 2016 and 2015, respectively;
- an increase of $1.0 million in professional fees due to increased costs associated with expanding operations, including costs related to audit, legal, and tax-related services, as well as investor relations costs;

- an increase of $0.5 million in commercial planning due to preparations for a potential commercial launch; and
- an increase of $0.4 million in other due to increased costs associated with facilities, due to the increase in the rented square feet of office space to accommodate our increase in employees.

Interest Income, net and Other expense, net

Interest income, net, and other expense, net, for the three months ended September 30, 2016 and 2015 were $0.3 million and $47,000, respectively. The primary reason for the increase was the purchase of marketable securities during the three months ended September 30, 2016.

Comparison of nine months ended September 30, 2016 and 2015

The following table summarizes our results of operations for the nine months ended September 30, 2016 and 2015:

| | Nine Months Ended September 30, | | Increase (Decrease) |
|---|---|---|---|
| | 2016 | 2015 | |
| | (in thousands) | | |
| Operating expenses: | | | |
| Research and development | $78,752 | $48,981 | $ 29,771 |
| General and administrative | 25,033 | 17,057 | 7,976 |
| Total operating expenses | 103,785 | 66,038 | 37,747 |
| Loss from operations | (103,785) | (66,038) | (37,747) |
| Interest income, net | 717 | 115 | 602 |
| Other income, net | (18) | (10) | (8) |
| Net loss | $(103,086) | $(65,933) | $ (37,153) |

Research and development expenses

| | Nine Months Ended September 30, | | Increase (Decrease) |
|---|---|---|---|
| | 2016 | 2015 | |
| | | (in thousands) | |
| SAGE-547 | $35,943 | $ 26,654 | $ 9,289 |
| SAGE-217 | 12,306 | 3,386 | 8,920 |
| SAGE-689 | 1,259 | 2,643 | (1,384) |
| SAGE-718 | 4,716 | 2,949 | 1,767 |
| Other research and development programs | 5,220 | 4,038 | 1,182 |
| Unallocated expenses | 19,308 | 9,311 | 9,997 |
| Total research and development expenses | $78,752 | $ 48,981 | $ 29,771 |

Research and development expenses for the nine months ended September 30, 2016 were $78.8 million, compared to $49.0 million for the nine months ended September 30, 2015. The increase of $29.8 million was primarily due to the following:

- an increase of $9.3 million in expenses related to our SAGE-547 program, due to the continued advancement of the program in clinical development, including ongoing enrollment in the Phase 3 clinical trial in SRSE; continued conduct of the Phase 2 clinical trial of SAGE-547 in PPD; conduct of supporting clinical pharmacology studies; and an increase in CMC work in preparation for a potential filing for regulatory approval. Expenses related to payments to consultants and licensors upon achievement of certain clinical development milestones were $0.3 million and $2.7 million for the nine months ended September 30, 2016 and 2015, respectively;
- an increase of $8.9 million in expenses related to our SAGE-217 program due to the initiation and conduct of the Phase 1 clinical program and the initiation of Phase 2-enabling toxicology, formulation and manufacturing activities;
- a decrease of $1.4 million in expenses related to our SAGE-689 program due to the delay in commencement of a Phase 1 clinical trial as a result of a request from the FDA for additional non-clinical study data;
- an increase of $1.8 million in expenses due to the progression of our SAGE-718 program to IND-enabling non-clinical development and CMC activities in preparation for IND filing;

- an increase of $1.2 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 $10.0 million in unallocated expenses, including an increase of $1.9 million of non-cash stock-based compensation expense, mainly due to the hiring of additional full-time employees to support the growth in our operations.

General and administrative expenses

| | Nine Months Ended September 30, | | Increase (Decrease) |
|---|---|---|---|
| | 2016 | 2015 | |
| | | (in thousands) | |
| Personnel-related | $13,772 | $ 10,530 | $ 3,242 |
| Professional fees | 5,093 | 2,600 | 2,493 |
| Commercial planning | 2,917 | 1,807 | 1,110 |
| Other | 3,251 | 2,120 | 1,131 |
| Total general and administrative expenses | $25,033 | $ 17,057 | $ 7,976 |

General and administrative expenses for the nine months ended September 30, 2016 and 2015 were $25.0 million and $17.1 million, respectively. The increase of $8.0 million was primarily due to the following:

- an increase of $3.2 million in personnel-related costs due to the effects of hiring additional full-time employees to support operations, finance, human resources, legal and early commercial planning activities. Non-cash stock-based compensation expense related to the achievement of performance-based vesting criteria was zero and $2.7 million for the nine months ended September 30, 2016 and 2015, respectively;
- an increase of $2.5 million in professional fees due to increased costs associated with expanding operations, including costs related to audit, legal, and tax-related services, as well as investor relations costs;
- an increase of $1.1 million in commercial planning due to preparations for a potential commercial launch; and
- an increase of $1.1 million in other due to increased costs associated with facilities, due to the increase in the rented square feet of office space to accommodate our increase in employees.

Interest Income, net and Other expense, net

Interest income, net, and other expense, net, for the nine months ended September 30, 2016 and 2015 were $0.7 million and $0.1 million, respectively. The primary reason for the increase was the purchase of marketable securities during the nine months ended September 30, 2016.

Liquidity and Capital Resources

Since our inception in April 2010, we have not generated any revenue, and have incurred recurring net losses. As of September 30, 2016, we had an accumulated deficit of $264.4 million. From our inception through September 30, 2016, we received net proceeds of $643.3 million from the sales of redeemable convertible preferred stock, the issuance of convertible notes and the proceeds from our IPO in July 2014 and follow-on offerings in April 2015, January 2016 and September 2016. On January 12, 2016, we completed the sale of 3,157,894 shares of our common stock in an underwritten public offering at a price to the public of $47.50 per share, resulting in net proceeds of $140.4 million after deducting commissions and underwriting discounts and offering costs paid by us. On September 14,

2016, we completed the sale of 5,062,892 shares of our common stock in an underwritten public offering at a price to the public of $39.75 per share, resulting in net proceeds of $189.2 million after deducting commissions and underwriting discounts paid by us.

As of September 30, 2016, our primary sources of liquidity were our cash, cash equivalents and marketable securities, which totaled $431.3 million. 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 nine months ended September 30, 2016 and 2015:

| | Nine Months Ended September 30, | |
|---|---|---|
| | 2016 | 2015 |
| | (in thousands) | |
| Net cash provided by (used in): | | |
| Operating activities | $(84,902) | $(52,564) |
| Investing activities | (112,077) | (160) |
| Financing activities | 330,304 | 129,835 |
| Net increase in cash and cash equivalents | $133,325 | $77,111 |

Operating activities

Cash used in operating activities for the nine months ended September 30, 2016 was $84.9 million as compared to $52.6 million for the nine months ended September 30, 2015. The increase of $32.3 million was primarily due to the following:

- An increase of $37.2 million in cash used related to our net loss, primarily due to increased research and development activities related to our lead programs in development and increased general and administrative expenses due to increased headcount to support our operations; and
- An increase of $4.7 million in cash provided by changes in our operating assets and liabilities, primarily due to the growth of the business and the timing of vendor invoicing and payments.

Investing activities

During the nine months ended September 30, 2016 and 2015, net cash used by investing activities was $112.1 million and $0.2 million, respectively. During the nine months ended September 30, 2016, we used $118.7 million to purchase marketable securities and received proceeds of $8.0 million from sales of marketable securities. During the nine months ended September 30, 2015, we purchased no marketable securities.

Financing activities

During the nine months ended September 30, 2016 and 2015, net cash provided by financing activities was $330.3 million and $129.8 million, respectively. Net cash provided by financing activities in the nine months ended September 30, 2016 and 2015 primarily consisted of $329.6 million and $129.2 million, respectively, of net proceeds from follow-on underwritten public offerings 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, and begin to commercialize any products, if approved. We 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 September 30, 2016, will enable us to fund our operating expenses and capital expenditure requirements into the second quarter of 2018. During that time, we expect that our expenses will increase substantially as we:

- advance clinical development of SAGE-547, including completing the Phase 3 clinical trial for SAGE-547 in SRSE, expanding the Phase 2 clinical program for SAGE-547 in PPD, and conducting additional clinical trials and non-clinical studies of SAGE-547 required for regulatory approval in SRSE and PPD;
- advance clinical development of SAGE-217, including initiating and conducting planned Phase 2 clinical trials of SAGE-217 in essential tremor and PPD, a proof-of-concept Phase 2 clinical trial in Parkinson's disease, and a proof-of-concept Phase 2 trial of SAGE-217 in MDD;
- conduct further non-clinical studies of SAGE-689;
- continue to advance SAGE-718, our early-stage novel allosteric modulator for NMDA, in non-clinical studies; and prioritize advancement of a novel GABA candidate, such as SAGE-105 or SAGE-324, into IND-enabling studies for development in other GABA-related indications, such as orphan epilepsies;
- continue our research and development efforts to evaluate the potential for our existing product candidates in the treatment of additional indications, and the identification of new drug candidates in the treatment of CNS disorders;
- advancing regulatory activities focused on a potential filing of an NDA and MAA for SAGE-547 in SRSE; advancing regulatory activities with respect to SAGE-547 in PPD; and initial preparations for a potential commercial launch;
- seek regulatory approvals for our product candidates that successfully complete clinical development;
- add personnel, including personnel to support our product development and future commercialization efforts, and incur increases in stock compensation expense related to existing and new personnel with respect to both time-based and performance-based awards;
- 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 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 ability of our product candidates to progress through clinical development successfully;
- 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 cost, timing, and outcome of regulatory reviews and approvals;
- the number and characteristics of the product candidates we pursue and the nature and scope of our discovery and development programs;
- 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;
    - our ability to establish any future collaboration arrangements on favorable terms, if at all; and
- the level and timing of costs associated with preparations for a potential commercial launch, including manufacturing-related costs.

Until such time, if ever, as we can generate substantial product revenue, 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 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 September 30, 2016 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] | $14,838 | $2,513 | $5,480 | $5,647 | $1,198 |
| Total [1][2][3][4] | $14,838 | $2,513 | $5,480 | $5,647 | $1,198 |

[1] We lease 22,067 square feet of office space in Cambridge, Massachusetts, in a multi-tenant building under an operating lease that will expire in February 2022. In May 2016, we entered into a lease under which, beginning in September 2016, we rent 19,805 square feet of additional office space, also in Cambridge, Massachusetts, in a separate multi-tenant building. The lease for the additional space will expire in February 2022. 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 $33.9 million upon achieving certain milestones, related to clinical development, regulatory approvals and sales. For the three and nine months ended September 30, 2016, we recorded $0.3 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 nonemployee consultant upon achieving certain clinical development milestones and regulatory approval milestones. For the three and nine months ended September 30, 2016, 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.

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 29, 2016.

Recently Issued Accounting Pronouncements

For detailed information regarding recently issued accounting pronouncements and the expected impact on our consolidated financial statements, see Note 2, "Summary of Significant Accounting Policies," in the accompanying Notes to Consolidated Financial Statements included in Item 1 of Part I of this Form 10-Q.

Item 3. Quantitative and Qualitative Disclosure about Market Risk

We had cash, cash equivalents and marketable securities of approximately $431.3 million at September 30, 2016. 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 and the conservative nature of our investments, 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 derivative 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 and cash equivalents 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 nine months ended September 30, 2016.

Item 4. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Securities and 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 to our President and Chief Executive Officer, who is our principal executive officer, and to our Chief Financial Officer, who is also our principal financial and accounting officer, as appropriate, to allow timely decisions regarding required disclosure.

As of September 30, 2016, 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 and 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 September 30, 2016, our disclosure controls and procedures were effective at the reasonable assurance level.

Changes in Internal Control Over Financial Reporting

There were no changes to our internal control over financial reporting 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

As of the date of this filing, we are not party to any legal matters or claims. In the future, we may become party to legal matters and claims arising in the ordinary course of business, the resolution of which we do not anticipate would have a material adverse impact on our financial position, results of operations or cash flows.

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 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 depend heavily on the success of our current product candidates, of which SAGE-547 is in Phase 3 clinical development for super-refractory status epilepticus, or SRSE, and in Phase 2 development for post-partum depression, or PPD; SAGE 217 has completed Phase 1 clinical development, and is expected to commence Phase 2 clinical trials for PPD, essential tremor (ET), Parkinson's disease and major depressive disorder (MDD); SAGE-689 and SAGE-718 are in non-clinical development; and other product candidates, including SAGE-105 and SAGE-324, are at earlier stages. We cannot be certain that we will be able to complete, within the expected time-frames, our non-clinical studies or clinical trials, or to announce results on the time-lines we expect. 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.

We currently have no drug products for sale, and may never be able to successfully develop marketable drug products. Our business depends heavily on our ability to successfully complete non-clinical and clinical development of our current product candidates, and to obtain regulatory approval 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. Our lead product candidate, SAGE-547, is currently in Phase 3 clinical development for the treatment of SRSE and in Phase 2 clinical development for PPD. SAGE-217 has recently completed Phase 1 clinical development, and is expected to commence Phase 2 clinical trials. SAGE-689 and SAGE-718 are in non-clinical development and other product candidates are at earlier stages. Drug development involves a high degree of risk.

We may not be able to complete our clinical trials or announce results from our clinical trials on the time-lines we expect. For instance, we have experienced slower than expected enrollment and randomization of patients in our Phase 3 clinical trial in SRSE. These issues may continue, or we may encounter similar difficulties in our other trials. 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. 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.

We may not be able to demonstrate the efficacy and safety of our current product candidates or any other product candidate at each stage of clinical development. Changes in formulations of our product candidates, such as moving

from oral solution to solid dosage form which we are working to do with respect to SAGE-217 for later stage development, could delay development or require us to conduct additional clinical trials or non-clinical studies. 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. 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. Drug development is a long, expensive and uncertain process, and delay or failure can occur at any stage of our clinical trials. 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 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 U.S. Food and Drug Administration, or FDA, regulatory approval process and will be commercialized. Accordingly, even if we are able to obtain the requisite financing,

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.

We are not permitted to market our product candidates in the U.S. until we receive approval of a New Drug Application, or 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;
- 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 the number, design, size, conduct, or implementation of our non-clinical studies or clinical trials or changes in drug formulation used in our non-clinical studies or clinical trials even if the regulatory authorities have previously reviewed and commented on the design and details of our plans;
- the FDA or regulatory 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 the applicable foreign regulatory agency may not approve the formulation, labeling or specifications of any of our product candidates;
- the contract research organizations, or CROs, that we retain to conduct our non-clinical studies and clinical trials may take actions outside of our control that materially adversely impact our non-clinical studies and clinical trials;
- the FDA or regulatory authorities outside the U.S. may find the data from non-clinical studies and clinical trials insufficient to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- the FDA or regulatory authorities outside the U.S. may disagree with our interpretation of data from our non-clinical studies and clinical trials;
- the FDA or regulatory authorities outside the U.S. may not accept data generated at our non-clinical studies and clinical trial sites;
- if our New Drug Application, or NDA, if and when submitted, is reviewed by an advisory committee, the FDA may have difficulties scheduling an advisory committee meeting in a timely manner or 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;
- if an NDA for one of our product candidates is submitted, the FDA may approve the product candidate for a more limited patient population than we expect;
- 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 the applicable foreign regulatory agency 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 agency may change its approval policies or adopt new regulations.

Even if we receive marketing approval for our product candidates, regulatory or other governmental authorities may still impose significant restrictions on our products, including restrictions on indicated uses or marketing, or may impose ongoing requirements for potentially costly post-approval studies. For example, we expect that, prior to product launch, the U.S. Drug Enforcement Agency, or DEA, will need to determine the controlled substance schedule of SAGE-547, taking into account the recommendation of the FDA. The process may be more time consuming than we expect, and may delay our ability to market SAGE-547 if it is approved. 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. Any such setback would have a material adverse effect on our business and prospects.

We cannot be certain that the results of our ongoing Phase 3 clinical trial of SAGE-547 in SRSE will be sufficient to support the submission of an NDA or MAA for this product candidate in SRSE, and in any event we must obtain additional clinical and non-clinical data before an NDA or MAA may be submitted.

In general, the FDA requires two pivotal trials to support approval of an NDA, but in certain circumstances, will approve an NDA based on only one pivotal trial. If successful, we believe the results from our ongoing Phase 3 clinical trial of SAGE-547, together with other safety and efficacy data from the SAGE-547 development program, could form the basis of an NDA submission for SAGE-547 in the treatment of SRSE. However, depending upon the outcome of the Phase 3 clinical trial and the other development activities under the current program, the FDA may require that we conduct additional pivotal trials before we can submit an NDA for SAGE-547.

Furthermore, we will need to complete several other clinical and non-clinical studies prior to submitting an NDA to the FDA, including studies to evaluate the pharmacokinetics and/or pharmacodynamics of SAGE-547 in special populations. If the results of these additional clinical and non-clinical studies are delayed or yield unanticipated results, it may delay or prevent the submission or approval of an NDA for SAGE-547.

Based on scientific advice we recently received from the EMA, we also believe our current Phase 3 program, if successful, will be sufficient to support a marketing authorization application, or MAA, to the EMA seeking approval of SAGE-547 for SRSE in the EU. However, depending upon the outcome of the Phase 3 clinical trial and the other development activities under the current program, the EMA may, despite our current expectations, require that we conduct additional pivotal trials before we can submit an MAA for SAGE-547.

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

We have received Fast Track designation for our investigational new drug application, or IND, for SAGE-547 for the treatment of SRSE, and in the future we may seek Fast Track designation for other product candidates as well. If a product is intended for the treatment of a serious or life-altering condition and the product demonstrates the potential to address unmet medical needs for this condition, the sponsor may apply for the FDA Fast Track designation. We have also received Breakthrough Therapy designation for SAGE-547 in the treatment of PPD. Fast Track designation and Breakthrough Therapy designation 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 if it believes that the designation is no longer supported by data from our clinical development programs.

The number of patients with SRSE, PPD, ET and the other diseases and disorders for which we are developing product candidates has not been established with precision. If the actual number of patients with SRSE, PPD, ET or any other diseases or disorders we elect to pursue with our product candidates is smaller than we anticipate, we may encounter difficulties in enrolling patients in our clinical trials, thereby delaying or preventing development of our product candidates, and even if such product candidates are approved, our revenue and ability to achieve profitability may be materially adversely affected.

Our lead product, SAGE-547, is currently being studied in a Phase 3 clinical trial for the treatment of patients with SRSE and in Phase 2 clinical development for PPD. The number of patients suffering from these disorders is small. We plan to commence Phase 2 clinical trials of our next generation product candidate, SAGE-217 in ET, PPD, Parkinson’s disease and MDD. There is no precise method of establishing the actual number of patients with any of these disorders in any geography over any time period. Moreover, SRSE is an acute episodic condition. If we are not able to identify patients at the time of SRSE onset, we will have difficulty completing our Phase 3 clinical trial. Given the small number of patients, and nature of the disease, it may also be difficult to identify PPD patients for clinical

trials, particularly severe PPD patients. We plan to develop our product candidates in certain other indications, including potentially: orphan epilepsies, Smith-Lemli-Opitz Syndrome and anti-NMDA receptor encephalitis. With respect to many of the indications in which we are conducting trials or plan to conduct clinical trials, 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 SRSE, PPD, ET and Parkinson's disease, 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 which include estimates within the range that are lower than our estimates. For example, there are estimates in the literature on the prevalence of SRSE, particularly from studies outside the U.S., that are significantly lower than our estimates. We believe that differences in prevalence rates for SRSE among studies in the published literature may be the result of: differences from country-to-country in the prevalence or rate of occurrence of the underlying conditions and disorders that cause SRSE; challenges in making an accurate diagnosis of SRSE, particularly in a patient population with multiple complications; limitations and variations in the diagnosis coding

for these conditions; the small size of the populations studied in the literature; and differences and limitations in the analytical plans underlying the various published studies. The actual number of patients with SRSE, PPD, ET, Parkinson's disease or any other indication in which we elect to pursue development of our product candidates may; however, be significantly lower than we believe. If the actual number of patients with SRSE, PPD, ET, Parkinson's disease or any other indication in which we elect to pursue development of our product candidates is lower than our estimates, we may experience difficulty in enrolling patients in our clinical trials, thereby delaying development of our product candidates. A prevalence calculation is an estimate of the total number of patients with a disease or the rate of occurrence of a disease in a population. Even if our prevalence estimates are correct, our products, if approved, may be indicated for only a subset of patients with a particular disease or condition. In addition, the IV infusion mode of administration for SAGE-547 may further limit the number of PPD patients who will be treated with the product if it is ultimately approved. If any of our product candidates are approved and our prevalence estimates with respect to any indication or our 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.

If serious adverse events or other undesirable side effects are identified during the use of SAGE-547, SAGE-217 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.

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 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 SAGE-547, SAGE-217 or any of our other product candidates are observed in clinical trials, emergency-use cases, investigator sponsored clinical trials, 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, and the occurrence of these events could have a material adverse effect on our business. 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.

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, including proof-of-concept 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 positive results from our Phase 1/2 clinical trial of SAGE-547 in SRSE and results from earlier emergency use cases, may not be replicated in our ongoing Phase 3 clinical trial. Our Phase 3 clinical trial of SAGE-547 differs in important ways from the Phase 1/2 clinical trial, which could cause the outcome of the Phase 3 clinical trial to differ from the earlier stage clinical trial. The Phase 3 clinical trial of SAGE-547 is a placebo-controlled trial, while our Phase 1/2 clinical trial was open-label, and in our Phase 3 clinical trial an intent-to-treat statistical analysis, which is a more rigorous statistical analysis, will be employed in evaluating the Phase 3 data. In addition, the formulation of SAGE-547 we are using in our Phase 3 trial is somewhat different than the formulation used in the Phase 1/2 trial. We do not believe the change in formulation will negatively affect trial results, but we cannot be sure. Similarly, the results from our Phase 2 clinical trials of SAGE-547 in severe PPD or our Phase 2 proof-of concept study of SAGE-547 in ET may not be replicated in subsequent clinical trials of SAGE-547 or in clinical trials using a different compound, SAGE-217, in those indications. 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, including previously unreported 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 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 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 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 SAGE-547 for SRSE or PPD and SAGE-217 or any of our other 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:

- the FDA may deny permission to proceed with our planned clinical trials or any other clinical trials we may initiate, or may place 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 the case of SAGE-547, challenges we have faced, and may continue to face, due to: the small size of the patient population and acute nature of SRSE; the lack of proximity of some patients to trial sites; the lack of a pediatric investigation plan which is required to be submitted to enroll pediatric patients in most EU countries; challenges in meeting regulatory and material requirements to commence clinical trials in countries outside the U.S.; eligibility criteria for the clinical trial; and challenges associated with the nature of the clinical trial protocol; the potential for some or all of the same issues with respect to SAGE-547 in PPD or with respect to SAGE-217 or our other product candidates with respect to future clinical trials or other issues with respect to any of our clinical trials, such as the availability of existing treatments for the relevant disease, and competition from other clinical trial programs for similar indications, to delay enrollment of patients in existing or future clinical trials of our other product candidates;
- delays in reaching or failing to reach agreement on acceptable terms with prospective 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 a product candidate or other materials necessary to conduct clinical trials, for example delays 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 any endpoints utilized in a clinical trial;
- our inability to satisfy the requirements of the FDA to commence clinical trials, including CMC requirements, or to file amendments to our IND as requested by the FDA prior to the initiation of a clinical trial;
- the FDA and 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, commencement of a Phase 1 clinical trial of SAGE-689 has been delayed to respond to a request from the FDA for additional non-clinical study data. There is no guarantee that we will be able to generate data that will satisfy the FDA, and enable us to commence the Phase 1 clinical trial. 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 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 or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize 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;
- experience regulatory compliance issues;

- undergo changes in priorities or become financially distressed; or
- form relationships with other entities, some of which may be our competitors.

These factors may materially adversely affect the willingness or ability of third parties to conduct our clinical 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 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 these 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 product candidates, or any future product candidates, for use in the conduct of our non-clinical studies and clinical trials, or for future commercial use, and we rely completely on third-party suppliers for both active drug substances and finished drug products. For example, SAGE-547 used in the emergency-use cases was manufactured at an academic site, the active pharmaceutical ingredient for SAGE-547 for our Phase 1/2 clinical trial was manufactured at an academic site and SAGE-547 as formulated for our Phase 1/2 clinical trial was manufactured at a third-party manufacturer’s site. SAGE-547, as formulated for our Phase 3 clinical trial and our Phase 2 clinical program, is also manufactured at a third-party manufacturer’s site.

We will rely on our contract manufacturers to manufacture registration batches of both active drug substances and finished drug products required for regulatory approval as well as validation batches required for commercial manufacture. 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 our 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. 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 adversely 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, and each batch of our product candidates is individually contracted under a quality agreement, service agreement and purchase order. 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 receive regulatory approval to market our product candidates outside of the U.S.

Even if we receive marketing approval for our product candidates in the U.S., we may never receive regulatory approval to market our product candidates outside of the U.S. 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 product candidate testing and additional administrative review periods. The time required to obtain approvals in other countries might differ from that required to obtain FDA approval. Marketing approval in one country does not ensure marketing approval in another, but a failure or delay in obtaining marketing approval in one country may have a negative effect on the regulatory process in others. 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 can result in substantial delays in bringing products to market in such countries. 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. or any delay or other setback in obtaining such approval would impair our ability to market our product candidates in such foreign markets. Any such impairment would reduce the size of our potential market, which could have a material adverse impact on our business, results of operations and prospects.

If we are unable to establish 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 do not currently have an infrastructure for the sales, marketing and distribution of pharmaceutical products. In order to market our product candidates, if approved by the FDA or any other regulatory body, we must build our sales, marketing, managerial and other non-technical capabilities or make arrangements with third parties to perform these services. If we are unable to establish adequate sales, marketing and distribution capabilities, whether independently or with third parties, or if we are unable to do so on commercially reasonable terms, our business, results of operations, financial condition and prospects will be materially adversely affected.

Even if we receive marketing approval for our product candidates, our approved products may not achieve broad market acceptance, 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. 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 of our products 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 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.

If our product candidates are approved, but do not achieve an adequate level of acceptance by patients, physicians and payors, 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, 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.

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 and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other regulatory authorities.

Further, clinical 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;
- 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 future development and regulatory difficulties.

Even if we receive marketing approval for our product candidates, regulatory authorities may still impose significant restrictions on our products, indicated uses or marketing or impose ongoing requirements for potentially costly post-approval studies. For example, we expect that, prior to product launch, the DEA will need to determine the controlled substance schedule of SAGE-547, taking into account the recommendation of the FDA. The DEA process may be more time consuming than we expect. 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, 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 manufacturing facilities 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 adversely affecting 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 therapies specifically approved for SRSE. However, many products approved for other indications, including general anesthetics, ketamine and anti-seizure drugs, are used off-label for various stages of status epilepticus therapy. Additionally, though not indicated, acupuncture, hypothermia, and electroconvulsive therapy are sometimes used prior to withdrawal of care for patients with SRSE.

There are also no pharmacological therapies specifically currently approved for the treatment of PPD. Patients with PPD may be prescribed anti-depressant medications, and receive psychotherapy.

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

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. 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 may seek to establish collaborations, and, if we are not able to establish them on commercially reasonable terms, we may have to alter our development and commercialization plans.

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 subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be

available to collaborate on and whether such 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 to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue.

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

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 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 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 would have a material adverse effect on our business.

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

SAGE-547 will, and our other product candidates may, contain controlled substances, the manufacture, use, sale, importation, exportation, prescribing and distribution of which are subject to regulation by the DEA.

Before we can commercialize SAGE-547, and potentially our other product candidates, it is expected that 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. If approved, SAGE-547 is expected to be, and our other product candidates may be, regulated as "controlled substances" as defined in the Controlled Substances Act of 1970, or CSA, and the implementing regulations of the DEA, which establish registration, security, recordkeeping, reporting, storage, distribution, importation, exportation, inventory, quota and other requirements administered by the DEA. These requirements are 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.

We expect that SAGE-547 will be, and our other product candidates may be, listed by the DEA as Schedule IV controlled substances under the CSA. Consequently, 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. Other Schedule IV compounds include sedative hypnotics such as benzodiazepines.

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.

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

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

In 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 12 months or longer after the receipt of regulatory approval and product launch. To obtain favorable

reimbursement for the indications sought or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidates with other available therapies. If reimbursement for our product candidates is unavailable in any country in which we seek reimbursement, if it is limited in scope or amount, if it is conditioned upon our completion of additional clinical 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.

Even though we have obtained orphan drug designation for SAGE-547 as a treatment for SE, including SRSE, there may be limits to the regulatory exclusivity afforded by such designation, and such exclusivity will not apply to any non-orphan indications for which SAGE-547 may be approved.

Even though we have obtained orphan drug designation for SAGE-547 for treatment of SE, including SRSE, from the FDA, there are limitations to exclusivity afforded by such designation. In the U.S., the company that first obtains FDA approval for a designated orphan drug for the specified rare disease or condition receives orphan drug marketing exclusivity for that drug for a period

of seven years. This orphan drug exclusivity prevents the FDA from approving another application, including a full NDA to market the same drug for the same orphan indication, except in very limited circumstances, including when the FDA concludes that the later drug is safer, more effective or makes a major contribution to patient care. For purposes of small molecule drugs, the FDA defines "same drug" as a drug that contains the same active moiety and is intended for the same use as the drug in question. To obtain approval for a drug that shares the same active moiety as an already approved orphan-designated drug, it must be demonstrated to the FDA that the drug is safer or more effective than the approved orphan designated drug, or that it makes a major contribution to patient care. In addition, a designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. In addition, orphan drug exclusive marketing rights in the U.S. may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition.

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 collaboration 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.

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 SAGE-547, and compositions and methods of use of certain other $GABA_A$ receptor modulators, including genus and species claims to SAGE-217 and SAGE-689 and NMDA receptor modulators, including SAGE-718.

We currently have no issued patents covering any of our lead product candidates, SAGE-547, SAGE-217, SAGE-689 or SAGE-718. 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 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 SAGE-547 only cover particular formulations and particular methods of using such formulations to treat seizure conditions, such as SE and to treat PPD. 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, 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 SAGE-547. 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 would be materially and adversely impacted. In addition, if a court found that valid, enforceable patents held by third parties covered our product candidates, our financial position and results of operations would also be materially and adversely impacted.

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, 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 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, 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, outside scientific collaborators, sponsored researchers and other advisors. These agreements generally provide that inventions conceived by the party in the course of rendering services to us will be our exclusive property. However, these agreements may not be honored and may not effectively assign intellectual property rights to us. 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.

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

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

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 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, 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 and obtain patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the 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. For example, an April 2014 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.

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 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. We are parties to an exclusive license agreement with Washington University, or WU, under which we have licensed certain patent families that comprise a variety of small molecule allosteric modulators of $GABA_A$ receptors and for which we have the worldwide right to develop and commercialize. A patent family that discloses and claims SAGE-689 is licensed to us under this agreement. We are obligated to pay WU certain clinical/regulatory milestones and single-digit royalties on products developed from this technology. Termination of our license agreement with WU would have a material adverse impact on our ability to develop and commercialize SAGE-689.

We have also 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 SAGE-547 and SAGE-689 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 SAGE-547 and SAGE-689. 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 SAGE-547 and SAGE-689 product candidates are formulated in Captisol. Termination of our license agreement with CyDex would have a material adverse impact on our ability to develop and commercialize SAGE-547 and SAGE-689 in their current formulations.

We also entered into a non-exclusive license with The Regents of the University of California, or 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 SE, essential tremor and/or postpartum depression. This agreement requires us to pay milestone payments in connection with the first derived product, which would include SAGE-547, 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 SAGE-547.

In June 2015, we entered into an exclusive license agreement with 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 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, as is the case for the Washington University license, 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 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 agreements with WU and 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 it 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 additional protection under the Hatch-Waxman Amendments and similar foreign legislation by extending the patent terms and obtaining data exclusivity for our product candidates, our business may be materially harmed.

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. However, we may not be granted an extension because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. For example, we may not be granted an extension if the active ingredient of SAGE-547, allopregnanolone, is used in another drug company’s product candidate

and that product candidate is the first to obtain FDA approval. 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.

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 have and may in the future also be subject to claims that an employee, advisor or consultant performed work for us that conflicts with that person's obligations to a third party, such as an employer, and thus, that the third party has an ownership interest in the intellectual property arising out of work performed for us. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management. If we fail in defending such claims, in addition to paying 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 patents, should such patents issue from our patent applications;
- we might not have been the first to make the inventions covered by a pending patent application that we own;
- we might not have been the first to file patent applications covering an invention;
- others may independently develop similar or alternative technologies without infringing our intellectual property rights;
- pending patent applications that we own or license may not lead to issued patents;
- patents, if issued, that we own or license may not provide us with any competitive advantages, or may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- third parties may compete with us in jurisdictions where we do not pursue and obtain patent protection;
- we may not be able to obtain and/or maintain necessary or useful licenses on reasonable terms or at all;
- third parties may assert an ownership interest in our intellectual property and, if successful, such disputes may preclude us from exercising exclusive rights over that intellectual property;
- we may not develop or in-license additional proprietary technologies that are patentable; and
- the patents of others may have an adverse effect on our business.

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

General Company-Related Risks

As our product candidates reach later stage clinical development, 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 our product candidates reach later stage clinical development and, as we plan for a potential commercial launch of products, 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 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 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 we develop allegedly causes injury or is found to be otherwise unsuitable during clinical trials, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, including as a result of interactions with alcohol or other drugs, negligence, strict liability and a breach of warranties. Claims could also be asserted under state consumer protection acts. If we become subject to product liability claims and cannot successfully defend ourselves against them, we could incur substantial liabilities. In addition, regardless of merit or eventual outcome, product liability claims may result in, among other things:

- withdrawal of 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 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 will be required to devote substantial time to compliance initiatives.

As a public company, we incur significant legal, accounting and other expenses that we did not incur as a private company. 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.

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

As of December 31, 2015, we had federal and state net operating loss carryforwards of $131.5 million and $130.7 million, respectively, which begin to expire in 2031. As of December 31, 2015, we also had federal and state research and development tax credit carryforwards of $1.6 million and $0.7 million, respectively, which begin to expire in 2031 and 2027, respectively. As of December 31, 2015, we had federal orphan drug tax credit carryforwards of $16.4 million, which begin to expire in 2034. Under Section 382 of the Internal Revenue Code of 1986, as amended, or the Code, 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 may significantly reduce our ability to utilize our net operating loss carryforwards and research and development tax credit carryforwards before they expire. The completion of follow-on public offerings in April 2015, January 2016, September 2016 and our initial public offering, or IPO, together with private placements and other transactions that have occurred since our inception, may have triggered such an ownership change pursuant to Section 382. Any such limitation, whether as the result of our IPO, follow-on offerings, prior private placements, sales of our common stock by our existing stockholders or additional sales of our common stock by us, could have a material adverse effect on our results of operations in future years. We have not completed a study to assess whether an ownership change for purposes of Section 382 has occurred, or whether there have been multiple ownership changes since our inception, due to the significant costs and complexities associated with such study.

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 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 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 approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of or damage to our data or applications or other data or applications relating to our technology or product candidates, or inappropriate disclosure of confidential or proprietary information, we could incur liabilities and the further development of our product candidates could be delayed.

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

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

- On July 23, 2014, we completed the sale of 5,750,000 shares of our common stock in our IPO, at a price to the public of $18.00 per share, resulting in net proceeds of $94.0 million after deducting underwriting discounts and commissions and offering expenses paid by us.
- On April 20, 2015, we completed the sale of 2,628,571 shares of our common stock in a public offering, at a price to the public of $52.50 per share, resulting in net proceeds of $129.1 million after deducting underwriting discounts and

commissions and offering expenses paid by us.

- On January 12, 2016, we completed the sale of 3,157,894 shares of our common stock in a public offering at a price to the public of $47.50 per share, resulting in net proceeds of $140.4 million after deducting underwriting discounts and commissions and offering expenses paid by us.
- On September 14, 2016, we completed the sale of 5,062,892 shares of our common stock in a public offering at a price to the public of $39.75 per share, resulting in net proceeds of $189.2 million after deducting underwriting discounts and commissions and offering expenses paid by us.

From our inception through September 30, 2016, we had received net proceeds of $643.3 million from such transactions. As of September 30, 2016, our cash, cash equivalents and marketable securities were $431.3 million. We have incurred significant net losses in each year since our inception, including net losses of $103.1 million for the nine months ended September 30, 2016 and $94.5

million for the year ended December 31, 2015. 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 revenue. To date, we have not generated any 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 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;
- 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.

Absent our entering into a collaboration or partnership agreement, 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. Developing small molecule products is expensive, and we expect our research and development expenses to increase substantially in connection with our ongoing activities, particularly as we continue to advance our product candidates in clinical trials. Depending on the status of regulatory approval or, if approved, commercialization of our product candidates, as well as the progress we make in selling our products, if approved, we may also require additional capital to fund operating needs even after approval. 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 September 30, 2016, our cash, cash equivalents and marketable securities were $431.3 million. 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 the second quarter of 2018. 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 public or private equity or debt financings, government or other third-party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements or a combination of these approaches. In any event, we expect to require additional capital to 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. Moreover, the terms of any financing may adversely affect the holdings or

the rights of our stockholders and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our shares to decline. The sale of additional equity or convertible securities would dilute all of our stockholders. The incurrence of indebtedness would result in increased fixed payment obligations and we may be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. We could also be required to seek funds through arrangements with collaborative partners or otherwise at an earlier stage than otherwise would be desirable and we may be required to relinquish rights to some of our technologies or product 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:

- plans for, progress of, timing of, changes to, delays in or results from, non-clinical studies and clinical trials of our product candidates, including any adverse events, delays or announcements related to such studies or trials;
- any delay in filing for regulatory approval of our product candidates;
- the failure or delay of the FDA or any other regulatory authority to approve our product candidates, or any unexpected limitation on the approved indication or onerous condition of approval;
- 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 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;
- 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.

Our executive officers, directors, principal stockholders and their affiliates will continue to exercise significant control over our company, which will limit the ability of our stockholders to influence corporate matters and could delay or prevent a change in corporate control.

As of September 30, 2016, existing holdings of our executive officers, directors, investment funds affiliated with TRV, and entities affiliated with Fidelity Investment, or Fidelity, represent beneficial ownership, in the aggregate, of approximately 25.5% of our outstanding common stock. As a result, these stockholders, if they act together, will be able to influence significantly our management and affairs and the outcome of matters submitted to our stockholders for approval, including the election of directors and any sale, merger, consolidation, or sale of all or substantially all of our assets. Some of these stockholders acquired some or all of their shares of common stock for substantially less than the price of the shares of common stock acquired in our IPO or any follow-on offering, and these stockholders may have interests, with respect to their common stock, that are different from those of investors in our IPO or any follow-on offering and the concentration of voting power among these stockholders may have an adverse effect on the price of our common stock. In addition, this concentration of ownership might adversely affect the market price of our common stock by:

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

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 you 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.

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.

November 3, 2016 By: /s/ Jeffrey M. Jonas
Jeffrey M. Jonas, M.D.
Chief Executive Officer, President and Director

(Principal Executive Officer)

November 3, 2016 By: /s/ Kimi Iguchi
Kimi Iguchi
Chief Financial Officer

(Principal Financial and Accounting Officer)

EXHIBIT INDEX

| | | Incorporated by Reference to: | | | |
|---|---|---|---|---|---|
| | | | | Filing | |
| Exhibit | | Form or | Exhibit | Date with | SEC File |
| No. | Description | Schedule | No. | SEC | Number |
| 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 certification furnished in Exhibit 32.1 hereto is 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.