

Sage Therapeutics, Inc.
Form 424B5
February 25, 2019
Table of Contents

Filed Pursuant to Rule 424(b)(5)
Registration No. 333-228879

The information in this preliminary prospectus supplement is not complete and may be changed. A registration statement relating to these securities has been filed with the Securities and Exchange Commission and is effective. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities and they are not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to completion

Preliminary prospectus supplement dated February 25, 2019

Prospectus supplement

(To prospectus dated December 18, 2018)

\$500,000,000

Common stock

We are selling up to \$500,000,000 of our common stock in this offering.

Our common stock is traded on The Nasdaq Global Market under the symbol SAGE. On February 22, 2019, the last reported sale price on The Nasdaq Global Market of our common stock was \$153.97 per share.

Investing in our common stock involves risks. See Prospectus Supplement Summary Risks Related to Our Business beginning on page S-14 of this prospectus supplement and Risk Factors beginning on page S-19 of this prospectus supplement and in our Annual Report on Form 10-K for the year ended December 31, 2018, which is incorporated herein by reference.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus supplement or the accompanying prospectus. Any representation to the contrary is a criminal offense.

| | Per share | Total |
|---|-----------|-------|
| Public offering price | \$ | \$ |
| Underwriting discounts and commissions(1) | \$ | \$ |
| Proceeds, before expenses, to Sage Therapeutics, Inc. | \$ | \$ |

(1) We have agreed to reimburse the underwriters for certain FINRA-related expenses. See Underwriting. We have granted the underwriters an option for a period of 30 days from the date of this prospectus supplement to purchase up to approximately \$75,000,000 of additional shares of our common stock at the public offering price, less the underwriting discount.

The underwriters expect to deliver the shares of common stock against payment to the investors on or about _____, 2019.

Goldman Sachs & Co. LLC

J.P. Morgan

The date of this prospectus supplement is _____, 2019.

Table of Contents

Table of contents

Prospectus supplement

| | Page |
|--|-------------|
| <u>About this prospectus supplement</u> | S-1 |
| <u>Where you can find additional information; incorporation by reference</u> | S-3 |
| <u>Special note regarding forward-looking statements</u> | S-4 |
| <u>Prospectus supplement summary</u> | S-7 |
| <u>The offering</u> | S-17 |
| <u>Risk factors</u> | S-19 |
| <u>Use of proceeds</u> | S-21 |
| <u>Dilution</u> | S-22 |
| <u>Description of capital stock</u> | S-24 |
| <u>Dividend policy</u> | S-29 |
| <u>Underwriting</u> | S-30 |
| <u>Material U.S. federal income tax considerations for non-U.S. holders</u> | S-38 |
| <u>Legal matters</u> | S-42 |
| <u>Experts</u> | S-42 |

Prospectus

| | Page |
|--|-------------|
| <u>About this prospectus</u> | 1 |
| <u>Where you can find additional information</u> | 3 |
| <u>Incorporation of certain information by reference</u> | 4 |
| <u>Cautionary statement regarding forward-looking statements</u> | 5 |
| <u>Risk factors</u> | 7 |
| <u>About the company</u> | 8 |
| <u>Description of securities</u> | 9 |
| <u>Use of proceeds</u> | 11 |
| <u>Selling stockholders</u> | 12 |
| <u>Plan of distribution</u> | 13 |
| <u>Legal matters</u> | 15 |
| <u>Experts</u> | 15 |

Table of Contents

About this prospectus supplement

This document is part of the registration statement that we filed with the Securities and Exchange Commission, or the SEC, using a shelf registration process and consists of two parts. The first part is this prospectus supplement, including the documents incorporated by reference, which describes the specific terms of this offering. The second part, the accompanying prospectus, including the documents incorporated by reference, gives more general information, some of which may not apply to this offering. Generally, when we refer to the prospectus, we are referring to both parts combined. This prospectus supplement may add to, update or change information in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement or the accompanying prospectus.

If information in this prospectus supplement is inconsistent with the accompanying prospectus or with any document incorporated by reference that was filed with the SEC before the date of this prospectus supplement, you should rely on this prospectus supplement. This prospectus supplement, the accompanying prospectus and the documents incorporated by reference into each include important information about us, the securities being offered and other information you should know before investing in our securities. You should also read and consider information in the documents we have referred you to in the sections of this prospectus supplement entitled *Where You Can Find Additional Information* and *Incorporation of Certain Information by Reference* and in the sections of the accompanying prospectus entitled *Where You Can Find Additional Information* and *Incorporation of Certain Information by Reference*.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference herein were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

We take no responsibility for, and can provide no assurances as to the reliability of, any information that is in addition to or different from that contained or incorporated by reference in this prospectus supplement and the accompanying prospectus. We are not offering to sell these securities in any jurisdiction where the offer or sale is not permitted. You should not assume that the information contained or incorporated by reference in this prospectus supplement or the accompanying prospectus is accurate as of any date other than as of the date of this prospectus supplement or the accompanying prospectus, as the case may be, or in the case of the documents incorporated by reference, the date of such documents, regardless of the time of delivery of this prospectus supplement and the accompanying prospectus or any sale of our securities. Our business, financial condition, liquidity, results of operations and prospects may have changed since those dates.

All references in this prospectus supplement or the accompanying prospectus to the Company, we, us, or our mean Sage Therapeutics, Inc. and our subsidiaries, unless we state otherwise or the context otherwise requires. We own various U.S. federal trademark applications and unregistered trademarks, including our corporate logo. This prospectus supplement and the information incorporated herein by reference contain references to trademarks, service marks and trade names owned by us or other companies. Solely for convenience, trademarks, service marks and trade names referred to in this prospectus supplement and the information incorporated herein, including logos, artwork, and other visual displays, may appear without the ® or ™ symbols, but such references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensor to these trademarks, service marks and trade names.

Edgar Filing: Sage Therapeutics, Inc. - Form 424B5

We do not intend our use or display of other companies' trade names, service marks or trademarks to imply a relationship with, or endorsement or sponsorship of us by, any other companies. All trademarks, service marks

S-1

Table of Contents

and trade names included or incorporated by reference into this prospectus supplement or any related free writing prospectus are the property of their respective owners.

No action is being taken in any jurisdiction outside the United States, or the U.S., to permit a public offering of the securities or possession or distribution of this prospectus supplement or the accompanying prospectus in that jurisdiction. Persons who come into possession of this prospectus supplement or the accompanying prospectus in jurisdictions outside the U.S. are required to inform themselves about and to observe any restrictions as to this offering and the distribution of this prospectus supplement or the accompanying prospectus applicable to that jurisdiction.

S-2

Table of Contents

Where you can find additional information; incorporation by reference

We have filed with the SEC a registration statement on Form S-3 under the Securities Act of 1933, as amended, or the Securities Act, with respect to the common stock offered by this prospectus supplement. This prospectus supplement, filed as part of the registration statement, does not contain all the information set forth in the registration statement and its exhibits and schedules, portions of which have been omitted as permitted by the rules and regulations of the SEC. For further information about us, we refer you to the registration statement and to its exhibits and schedules.

We file annual, quarterly and current reports, proxy statements and other information with the SEC. The SEC maintains a website at www.sec.gov that contains periodic and current reports, proxy and information statements, and other information regarding registrants that are filed electronically with the SEC.

These documents are also available, free of charge, through the Investors & Media section of our website, which is located at www.sagerx.com. Information contained on our website is not incorporated by reference into this prospectus supplement or the accompanying prospectus and you should not consider information on our website to be part of this prospectus supplement or the accompanying prospectus.

The SEC allows us to incorporate by reference the information and reports we file with it, which means that we can disclose important information to you by referring you to these documents. The information incorporated by reference is an important part of this prospectus supplement and accompanying prospectus, and information that we file after the date hereof with the SEC will automatically update and supersede the information already incorporated by reference. We are incorporating by reference the documents listed below, which we have already filed with the SEC, and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities and Exchange Act of 1934, as amended, or the Exchange Act, except as to any portion of any future report or document that is not deemed filed under such provisions, after the date of this prospectus supplement and prior to the termination of this offering:

Annual Report on Form 10-K for the year ended December 31, 2018, as filed with the SEC on February 19, 2019;

The information specifically incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2017 from our definitive proxy statement on Schedule 14A (other than information furnished rather than filed), which was filed with the SEC on April 30, 2018;

Current Reports on Form 8-K filed with the SEC on January 7, 2019 and January 23, 2019 (in each case, except for information contained therein which is furnished rather than filed); and

The description of our common stock contained in our registration statement on Form 8-A, which was filed with the SEC on July 15, 2014, including any amendment or report filed for the purpose of updating such description.

Upon request, we will provide, without charge, to each person, including any beneficial owner, to whom a copy of this prospectus is delivered a copy of the documents incorporated by reference into this prospectus. You may request a copy of these filings, and any exhibits we have specifically incorporated by reference as an exhibit in this prospectus, at no cost by writing or telephoning us at the following:

Edgar Filing: Sage Therapeutics, Inc. - Form 424B5

Sage Therapeutics, Inc., 215 First Street, Cambridge, Massachusetts, 02142, Attention: Secretary, (617) 299-8380.

You may also access these documents, free of charge, on the SEC's website at www.sec.gov or on our website at www.sagerx.com. Information contained on our website is not incorporated by reference into this prospectus, and you should not consider any information on, or that can be accessed from, our website as part of this prospectus supplement or the accompanying prospectus.

S-3

Table of Contents

Special note regarding forward-looking statements

This prospectus supplement, the accompanying prospectus and the information incorporated by reference herein and therein contain statements that are not historical facts and are considered forward-looking within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act. These forward-looking statements contain projections about the advancement and potential of our product candidates, our future results of operations or our financial position and other plans and expectations with respect to our activities. In some cases you can identify these statements by forward-looking words such as anticipate, believe, could, continue, estimate, expect, intend, should, will, would, plan, projected or the negative of such words or other similar words or phrases. We believe it is important to communicate our future expectations to our investors. However, there may be events in the future that we are not able to accurately predict or control, and that may cause our actual results to differ materially from the expectations we describe in our forward-looking statements.

Investors are cautioned not to unduly rely on forward-looking statements because these statements are based on the beliefs and assumptions of our management based on information currently available to management and they relate to future events or our future financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements. 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 prospectus supplement, and potentially in other indications, and the goals and vision for our business;

our expectations as to the sufficiency of the data generated from the clinical trials and non-clinical studies of our proprietary intravenous, or IV, formulation of brexanolone, known as ZULRESSO (brexanolone) injection, to support approval by the U.S. Food and Drug Administration, or FDA, of our new drug application, or NDA, for ZULRESSO in the treatment of postpartum depression, or PPD, and the potential timing of such a decision;

our expectations as to the FDA following the joint recommendation of the Psychopharmacologic Drugs Advisory Committee, or PDAC, and Drug Safety and Risk Management, or DSaRM, Advisory Committee supporting the benefit/risk profile of ZULRESSO in the treatment of PPD when administered in healthcare settings certified under a Risk Evaluation and Mitigation Strategies, or REMS, program;

our expectations as to the timing of a potential launch of ZULRESSO in the U.S. as a treatment for PPD, if our NDA is approved by the FDA; our views as to our readiness for such a launch; our plans with respect to the size, readiness and focus of our field force; our plans with respect to possible pricing of ZULRESSO; and our expectations with respect to the availability of healthcare facilities qualified and willing to be certified under the REMS as sites of care for administration of ZULRESSO, and the potential for expanding sites of care in the future;

our views as to the anticipated rate and degree of market acceptance, prescription and use of ZULRESSO, if approved, including the impact of: limitations on sites of care for administration of ZULRESSO to REMS certified healthcare facilities; the risk/benefit profile of ZULRESSO; implementation of the REMS program; pricing; and the potential scope, level and availability of reimbursement;

our plans to further clarify and evaluate the potential development and regulatory pathway for our proprietary formulation of brexanolone in the European Union, or EU, including our planned activities, and our plans and expectations with respect to the potential development of our other product candidates for markets outside the United States;

S-4

Table of Contents

our expectations as to the sufficiency of our planned development program for SAGE-217 in major depressive disorder and PPD, if successful, to support filing of an NDA with the FDA; our statements regarding the potential for approval in such indications in the U.S.; and our view of the potential product profile and market for SAGE-217 and our other product candidates, if successfully developed and approved;

our estimates regarding the timing of commencement or completion of clinical trials for our product candidates;

our ability, within the expected time-frames, to initiate clinical trials and non-clinical studies of existing or future product candidates, including pivotal clinical trials, and to successfully complete and announce the results of ongoing and future clinical trials;

our estimates regarding expenses, use of cash, potential future revenues, timing of future cash needs, and capital requirements;

our expectations as to the potential to achieve future revenues and the potential timing of such revenues;

our use of proceeds from this offering;

our expectations with respect to the availability of supplies of ZULRESSO, SAGE-217 and our other product candidates, and the expected performance of our third-party manufacturers;

our ability to obtain and maintain intellectual property protection for our proprietary assets and other forms of exclusivity relevant to our business;

the estimated number of patients with diseases or disorders of interest to us; the size of the potential markets for our product candidates; the potential for our product candidates in those markets, if approved; and our ability to serve those markets;

the level of costs we may incur in connection with our activities, the possible timing and sources of future financings, and our ability to obtain additional financing when needed to fund future operations;

the potential for success of competing products that are or become available for the indications that we are pursuing or may pursue in the future;

the potential risk of loss of key scientific or management personnel; and

other risks and uncertainties, including those listed under the Risk Factors section and under Prospectus Supplement Summary Risks Related to Our Business.

These forward-looking statements are neither promises nor guarantees of future performance, and are subject to a variety of risks and uncertainties, many of which are beyond our control, which could cause actual results to differ materially from those indicated by these forward-looking statements, including, without limitation: the risk the FDA may, despite the recommendation of the Advisory Committee, decide that the clinical and nonclinical data from our ZULRESSO development program in PPD are not sufficient to support the grant of regulatory approval in the U.S., and may require additional trials, analyses or data; the risk that we may not be able, or willing, to meet requirements for submission of a marketing authorization application, or MAA, to the European Medicines Agency, or EMA, for ZULRESSO, or if an MAA is filed, the risk that the MAA will not be approved; the risk that we may not be successful in our development of SAGE-217 or of any of our other product candidates in any indication we are currently pursuing or may in the future pursue; the risk that regulatory authorities may require additional trials or nonclinical studies or additional analyses or data with respect to SAGE-217 prior to filing or approval of an NDA; the possibility that we may experience slower than expected clinical site initiation or slower than expected identification and enrollment of evaluable patients in our ongoing or future clinical trials; the potential for delays or problems in gaining approval to conduct a clinical trial or in analyzing data or the need for additional analysis, data or patients; the potential that future nonclinical and clinical results may not be positive and may not support further development of our product candidates or be sufficient to gain regulatory approval to market the relevant product; the potential for unexpected adverse events or other safety or tolerability issues arising in the conduct of our clinical trials or nonclinical studies to impact our ability to continue clinical trials or further development of the applicable product candidate or to gain

Table of Contents

regulatory approval; the risk that our estimates of the prevalence of the diseases for which we are developing our product candidates may be significantly lower than we expect; the risk that internal and external costs required for our activities, and to build our organization, and the resulting use of cash, may be higher than we expect, or we may conduct additional clinical trials or pre-clinical studies, or engage in new activities, requiring additional expenditures and using cash more quickly than anticipated; the risk that even if ZULRESSO or any of our other product candidates is approved, we may not be able to obtain pricing, reimbursement, availability of sites of care, or market acceptance at the levels we expect, and we may not meet our expectations with respect to revenues; and the risk that we may encounter other unexpected hurdles or issues in the development, manufacture and potential future commercialization of our product candidates that may impact our timing, progress or results, as well as those risks more fully discussed in the Risk Factors section and under Risks Related to Our Business in this prospectus supplement, the section of the accompanying prospectus entitled Risk Factors and the risk factors and cautionary statements described in other documents that we file from time to time with the SEC, specifically under Item 1A: Risk Factors in our Annual Report on Form 10-K for the year ended December 31, 2018 and our Current Reports on Form 8-K.

Given these uncertainties, readers should not place undue reliance on our forward-looking statements. These forward-looking statements speak only as of the date on which the statements were made and are not guarantees of future performance. Except as may be required by applicable law, we do not undertake or intend to update any forward-looking statements after the date of this prospectus supplement or the respective dates of documents incorporated by reference herein or therein that include forward-looking statements.

Table of Contents

Prospectus supplement summary

This summary highlights selected information contained elsewhere or incorporated by reference in this prospectus supplement and the accompanying prospectus. This summary may not contain all the information that you should consider before investing in our securities. You should read this entire prospectus supplement and the accompanying prospectus carefully, especially the risks of investing in our common stock discussed under Risk Factors beginning on page S-19 of this prospectus supplement, along with our consolidated financial statements and notes to those consolidated financial statements and the other information incorporated by reference in this prospectus supplement and the accompanying prospectus, before making an investment decision. This prospectus supplement may add to, update or change information in the accompanying prospectus.

Overview

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

The following table summarizes the status of our development programs as of the date of this prospectus supplement.

Our lead product candidate is ZULRESSO (brexanolone) injection, a proprietary intravenous, or IV, formulation of brexanolone for which we have filed a new drug application, or NDA, with the United States Food and Drug Administration, or the FDA, seeking approval to market and sell the product in the treatment of postpartum depression, or PPD. Brexanolone is chemically identical to allopregnanolone, a naturally occurring neuroactive steroid that acts as a positive allosteric modulator of GABA_A receptors. PPD is a common biological complication of childbirth, and is characterized by significant depressive symptoms that typically commence

Table of Contents

during the third trimester of pregnancy or in the months following childbirth. Our NDA for ZULRESSO is currently under FDA review. On November 2, 2018, the Psychopharmacologic Drugs Advisory Committee, or PDAC, and Drug Safety and Risk Management, or DSaRM, Advisory Committee of the FDA jointly voted, by a vote of 17 to 1, that our data support a positive benefit/risk profile for ZULRESSO in the treatment of PPD when administered by qualified staff in a healthcare facility certified under a Risk Evaluation and Mitigation Strategies, or REMS, program. In November 2018, the FDA extended the previously disclosed December 19, 2018 Prescription Drug User Fee Act, or PDUFA, target date for a decision on the NDA for ZULRESSO by a period of three months to March 19, 2019. The launch of ZULRESSO in the U.S., if approved, will follow anticipated scheduling of brexanolone as a controlled substance by the Drug Enforcement Administration, or DEA, which we expect to be completed 90 days after FDA approval. We anticipate that ZULRESSO, if approved, will launch in the U.S. in June 2019.

PPD is a common biological complication of childbirth, and is characterized by significant depressive symptoms that typically commence during the third trimester of pregnancy or within the months following childbirth. PPD symptoms may include sadness and depressed mood; anxiety or agitation; loss of interest in daily activities; changes in eating and sleeping habits; feeling overwhelmed; fatigue and decreased energy; inability to concentrate; hypervigilance about the baby or lack of interest in the baby; and feelings of worthlessness, shame or guilt. In the U.S., estimates of new mothers identified with PPD each year vary state-to-state from 8 to 20 percent, with an overall average of 11.5 percent. Based on these data, we estimate that 400,000 or more women in the U.S. each year may experience PPD, and that approximately 50% are formally diagnosed. We estimate that 20 to 30% of women diagnosed with PPD will experience severe symptoms. PPD can lead to devastating consequences for a woman and for her family. Suicide is the leading cause of maternal death following childbirth. There are no pharmacological therapies specifically approved for PPD. Current standard of care for PPD is comprised of psychotherapy and, in women with moderate or severe PPD, the cautious use of pharmacological therapies such as selective serotonin reuptake inhibitors, or SSRIs, and serotonin and norepinephrine reuptake inhibitors, or SNRIs.

In November 2017, we announced positive top-line results from our Hummingbird Phase 3 clinical program studying our proprietary IV formulation of brexanolone in PPD. The Hummingbird Phase 3 program was comprised of two multicenter, randomized, double-blind, parallel-group, placebo-controlled Phase 3 trials designed to evaluate the safety and effectiveness of brexanolone in women with PPD. One study (202B) evaluated women with severe PPD and the other study (202C) evaluated women with moderate PPD, in each case as defined by the study criteria. Entry criteria for participants included symptoms of PPD that began no earlier than the third trimester and no later than the first four weeks following delivery in women who were no more than six months post-partum at the time of screening. In November 2017, we announced that both trials, at all doses, achieved the primary endpoint, a statistically significant mean reduction from baseline in the 17-item Hamilton Rating Scale for Depression, or HAMD-17, total score at 60 hours in the brexanolone group compared to the placebo group (Study 202B: $p=0.0252$ for 90 $\mu\text{g}/\text{kg}/\text{h}$ dose and $p=0.0013$ for 60 $\mu\text{g}/\text{kg}/\text{h}$ dose; Study 202C: $p=0.0160$ for 90 $\mu\text{g}/\text{kg}/\text{h}$ dose).

In Study 202B, 122 women with severe PPD, as measured by a HAMD-17 total score of 26 or above, prior to randomization were dosed in one of three treatment groups: brexanolone 90 $\mu\text{g}/\text{kg}/\text{hour}$, brexanolone 60 $\mu\text{g}/\text{kg}/\text{hour}$, or placebo, on a 1:1:1 basis. Brexanolone 90 $\mu\text{g}/\text{kg}/\text{hour}$ treatment was associated with a statistically significant mean reduction in HAMD-17 total score of 17.7 points from baseline at 60 hours compared with a 14.0 point mean reduction in HAMD-17 total score associated with placebo ($p=0.0252$). Brexanolone 60 $\mu\text{g}/\text{kg}/\text{hour}$ treatment was associated with a statistically significant mean reduction in HAMD-17 total score of 19.9 points from baseline at 60 hours compared with a 14.0 point mean reduction in HAMD-17 total score associated with placebo ($p=0.0013$). Reduction in HAMD-17 total score in the brexanolone group versus placebo were first observed at 48 hours, with statistical significance only in the 60 μg group, and the effect at 60 hours was maintained at the 30-day follow-up period with statistical significance for both brexanolone dose groups. Improvement in the Clinical Global Impression Improvement,

S-8

Table of Contents

or CGI-I, scale at 60 hours was consistent with the primary endpoint ($p=0.0095$ for 90 $\mu\text{g}/\text{kg}/\text{h}$ dose and $p=0.0131$ for 60 $\mu\text{g}/\text{kg}/\text{h}$ dose).

In Study 202C, 104 patients with moderate PPD, as measured by a HAMD-17 total score of 20 to 25, were dosed in one of two treatment groups (brexanolone 90 $\mu\text{g}/\text{kg}/\text{hour}$ or placebo) on a 1:1 basis. Brexanolone treatment was associated with a statistically significant mean reduction in HAMD-17 total score of 14.2 points from baseline at 60 hours ($p=0.016$) compared with a 12.0 point mean reduction in HAMD-17 total score associated with placebo. Statistical significance was first observed at 48 hours and remained through Day 7, but was not observed at Day 30. However, the effect observed at 60 hours was maintained through the 30-day follow-up period. Improvement in the CGI-I scale at 60 hours was consistent with the primary endpoint ($p=0.0005$).

Brexanolone IV was generally well tolerated in both trials with similar rates of adverse events across all treatment groups. The most common adverse reactions in the trials were sedation/somnolence, dizziness, dry mouth, flushing and loss of consciousness. Adverse events leading to discontinuation occurred in 2% of patients and were sedation-related or related to infusion site pain. In the Hummingbird program, in patients treated with brexanolone, approximately 4% of patients experienced loss of consciousness and less than 1% experienced an altered state of consciousness during the infusion. All of these patients recovered with dose interruption, and no further intervention was necessary.

We currently have a sales, marketing, and market access teams in place in anticipation of a potential launch as well as a patient support team located in Raleigh, North Carolina. If approved, administration of ZULRESSO will be limited to healthcare facilities that have been certified under a REMS program under the supervision of qualified staff to mitigate the potential for harm associated with the risk of excessive sedation and loss of consciousness during administration of ZULRESSO. As part of the proposed REMS, patients who are prescribed ZULRESSO will be required to enroll in a patient registry to allow us to compile additional information to further our understanding of the risk of a loss of consciousness during administration and management of the risk. Given the mode of administration, the nature of the REMS and the limitation on the administration of ZULRESSO to a healthcare facility setting certified under the REMS, we expect that use of ZULRESSO, if approved for marketing and sale in the U.S., will, at least initially, be focused primarily on women with more severe symptoms of PPD, which we estimate is about 20 to 30% of women diagnosed with PPD.

We have received PRIority MEDicines, or PRIME, designation from the European Medicines Agency, or EMA, in the European Union, or EU, for our proprietary formulation of brexanolone as a potential treatment for PPD. In October 2018, we received scientific advice from the EMA regarding the potential regulatory pathway for a marketing authorization application, or MAA, filing in the EU. We anticipate having additional discussions with the EMA to help further clarify and evaluate what data and information would be needed, and what other requirements would need to be met, for a potential MAA filing.

Our next most advanced product candidate is SAGE-217, an oral compound, that is currently in Phase 3 clinical development in PPD and major depressive disorder, or MDD. SAGE-217 is a novel neuroactive steroid that, like brexanolone, is a positive allosteric modulator of GABA_A receptors, targeting both synaptic and extrasynaptic GABA_A receptors. The FDA has granted Breakthrough Therapy designation and Fast Track designation to SAGE-217 in the treatment of MDD.

We have completed two positive placebo-controlled pivotal clinical trials with SAGE-217, one in MDD completed in 2017 and one in PPD for which top-line results were announced in January 2019. The PPD study evaluated the effect of SAGE-217 30 mg on depressive symptoms in 151 women with severe PPD. After two weeks of outpatient treatment, patients treated with SAGE-217 had a statistically significant improvement of 17.8 points in the Hamilton

Rating Scale for Depression (HAMD-17) score, compared to 13.6 for placebo (primary endpoint, $p=0.0028$), with statistically significant reductions in HAMD-17 compared to placebo maintained through the end of the four-week follow-up. Remission was achieved in 45% of patients treated with SAGE-217 for two weeks as measured by the

S-9

Table of Contents

HAMD-17 compared with 23% of patients receiving placebo ($p=0.0110$). Results from secondary endpoints were statistically significant and consistent with the primary endpoint. SAGE-217 was generally well-tolerated with a safety profile consistent with that seen in earlier SAGE-217 trials. Overall reports of AEs were similar between SAGE-217 (58%) and placebo (51%). Two subjects experienced serious adverse events (SAEs), one subject in each group. The most common adverse events in the SAGE-217 treatment group were: somnolence, headache, dizziness, upper respiratory tract infection, diarrhea, and sedation.

Our development plan for SAGE-217 is subject to ongoing discussions with the FDA. The ongoing Phase 3 clinical trials for SAGE-217 in MDD are: a placebo-controlled Phase 3 clinical trial in patients with MDD, known as the Mountain Study, in which we are studying two weeks of treatment with SAGE-217 followed by four weeks of follow-up and an ongoing open-label retreatment study, known as the Shoreline Study, evaluating initial treatment with SAGE-217, treatment-free intervals, and as needed retreatment, in patients with MDD in which patients will be followed for up to a year after treatment. Dosing in the Mountain Study commenced in December 2018, and we expect to report top-line results from this study in the fourth quarter of 2019 or the first quarter of 2020. We plan to add an open-label extension trial to the Mountain Study under a separate protocol to continue to follow patients from the Mountain Study after completion for up to six months. As part of our Phase 3 clinical development program for SAGE-217 in depression, we also plan to initiate a placebo-controlled trial to evaluate fixed interval SAGE-217 monotherapy (treatment without traditional antidepressants) for up to a year, which we believe will help us meet the expected requirements for a potential NDA filing, and inclusion of maintenance dosing as part of the label, if our development efforts are successful. In addition, we are conducting a placebo-controlled polysomnography Phase 3 clinical trial of SAGE-217 in patients with MDD who have co-morbid insomnia, known as the Rainforest Study. We expect to report top-line results from the Rainforest Study and the Shoreline Study in 2020.

We are also exploring SAGE-217 in other indications, including bipolar depression and sleep disorders. We expect to report topline results from a small open-label Phase 2 clinical trial of SAGE-217 in bipolar depression in the first half of 2019.

The FDA's breakthrough therapy designation for SAGE-217 in MDD is based on the positive results of a double-blind, placebo-controlled Phase 2 clinical trial of SAGE-217 in patients with moderate to severe MDD. In the trial, treatment for 14 days with SAGE-217 was associated with a statistically significant mean reduction from baseline in the HAMD-17 total score at Day 15 (the time of the primary endpoint) of 17.6 points for the SAGE-217 group, compared to 10.7 for the placebo group ($p<0.0001$). Statistically significant mean improvements in the HAMD-17 score compared to placebo were observed by the morning following the first dose through Week 4, and the effects of SAGE-217 remained numerically greater than placebo through the end of follow-up at Week 6, but the results at week 6 were not statistically significant. At Day 15, 64 percent of patients who received SAGE-217 achieved remission, defined as a score of 7 or less on the HAM-D score, compared with 23 percent of patients who received placebo ($p=0.0005$). SAGE-217 was generally well-tolerated in the trial with no serious or severe adverse events. The overall number of reports of adverse events was similar between drug (53%) and placebo (46%). A low rate of discontinuations due to adverse events was reported.

In 2018, we entered into a collaboration with Shionogi & Co., Ltd., or Shionogi, under which we granted rights to Shionogi for the development and commercialization of SAGE-217 in Japan, Taiwan and South Korea. Shionogi has commenced Phase 1 clinical studies in Japan to evaluate the safety and tolerability of SAGE-217 in Japanese and Caucasian subjects.

In addition to SAGE-217, we have a portfolio of other novel compounds that target GABA_A receptors. SAGE-324 is a novel neuroactive steroid that, like brexanolone and SAGE-217, targets synaptic and extrasynaptic GABA_A receptors. We are considering developing SAGE-324 for a number of neurological conditions, including essential tremor and

certain epileptiform disorders. Results from a recently completed Phase 1 single ascending dose clinical trial of SAGE-324 demonstrated that the profile of SAGE-324 includes

S-10

Table of Contents

good oral bioavailability and a pharmacokinetic profile consistent with once-daily dosing. SAGE-324 demonstrated clear target engagement in the brain using pharmaco-EEG (β -band power) as a functional biomarker. SAGE-324 was generally well-tolerated with no serious adverse events and with a safety profile consistent with GABA_A positive allosteric modulation. A Phase 1 multiple ascending dose clinical trial of SAGE-324 is ongoing. We also recently initiated a Phase 1 clinical trial to determine the safety, tolerability and pharmacokinetics of SAGE-324 in a small number of patients with essential tremor. We expect to report top-line results from the Phase 1 multiple ascending dose clinical trial and the Phase 1 essential tremor clinical trial of SAGE-324 in the second half of 2019. Our portfolio also includes SAGE-689, a novel GABA_A receptor positive allosteric modulator, with which we have conducted non-clinical studies to date, and other compounds at earlier stages of development with a focus on both acute and chronic CNS disorders.

Our second area of focus is the development of novel compounds that target the NMDA receptor. The first product candidate selected for development from this program is SAGE-718, an oxysterol-based positive allosteric modulator of the NMDA receptor, which we are exploring in certain cognition-related disorders impacted by NMDA receptor dysfunction, currently in Phase 1 development. Indications involving NMDA receptor hypofunction include certain types, aspects or subpopulations of a number of diseases such as depression, Huntington's disease, Alzheimer's disease, attention deficit hyperactivity disorder, schizophrenia, and neuropathic pain. We completed a Phase 1 single ascending dose trial of SAGE-718 in 2017 and a Phase 1 multiple ascending dose trial in 2018. The primary objective of these trials was to assess the safety, tolerability, and pharmacokinetics of SAGE-718 in healthy volunteers. Results from these Phase 1 clinical trials of SAGE-718 demonstrated that the profile of SAGE-718 includes good oral bioavailability and a pharmacokinetic profile consistent with once-daily dosing. SAGE-718 was generally well-tolerated with no serious adverse events reported. We are continuing our SAGE-718 Phase 1 clinical program with target engagement biomarker studies in healthy volunteers, focused on electrophysiology and imaging, which are ongoing and for which we expect to report results in the first half of 2019. We also recently initiated a Phase 1 clinical trial to determine the safety, tolerability and pharmacokinetics of SAGE-718 in a small number of patients with early manifest Huntington's disease. We expect to report top-line results from this trial in the second half of 2019.

We expect to continue to focus our research and development efforts on allosteric modulation of the GABA_A and NMDA receptor systems in the brain. Our earlier stage efforts include the GABA_A receptor modulator compounds and programs such as SAGE-105 and our ST-320 and ST-210 programs, and additional compounds targeting the NMDA receptor such as SAGE-904, another positive allosteric modulator of the NMDA receptor. IND-enabling studies of SAGE-904 are ongoing. The GABA_A and NMDA receptor systems are broadly accepted as impacting many psychiatric and neurological disorders, spanning disorders of mood, seizure, cognition, anxiety, sleep, pain, and movement, among others. We believe that we may have the opportunity to develop molecules from our internal portfolio to address a number of these disorders in the future. Our ability to identify and develop such novel CNS therapies is enabled by our proprietary chemistry platform that is centered, as a starting point, on knowledge of the chemical scaffolds of certain endogenous neuroactive steroid compounds. We believe our knowledge of the chemistry and activity of allosteric modulators allows us to efficiently design molecules with different characteristics. This diversity enables us to regulate important properties such as half-life, brain penetration and receptor pharmacology to develop product candidates that have the potential for better selectivity, increased tolerability, and fewer off-target side effects than either current CNS therapies or previous therapies which have failed in development.

We have not generated any revenue from product sales to date. We have incurred net losses in each year since our inception, and we have an accumulated deficit of \$963.3 million as of December 31, 2018. Our net losses were \$372.9 million for the year ended December 31, 2018 and \$270.1 million for the year ended December 31, 2017. These losses have resulted principally from costs incurred in connection with research and development activities and general and administrative costs associated with our operations. We expect to incur significant expenses and increasing operating losses for the foreseeable future.

S-11

Table of Contents

Our strategy

Our goal is to be the leading biopharmaceutical company focused on development and commercialization of novel proprietary therapies for the treatment of life-altering CNS disorders. Our current focus is on building on our multi-franchise opportunities in depression, neuropsychiatry, and neurology. Key elements of our strategy are to:

Obtain regulatory approval of ZULRESSO (brexanolone) injection, our proprietary IV formulation of brexanolone in the treatment of PPD in the U.S.;

Commercialize ZULRESSO in the U.S., if and when approved;

Advance Phase 3 clinical development of SAGE-217 in MDD; continue to explore SAGE-217 at earlier stages in other indications; and file for regulatory approval of SAGE-217 in the U.S., if our development efforts are successful;

Support our collaboration with Shionogi for SAGE-217 in Japan, Taiwan and South Korea, and continue to evaluate opportunities for our product candidates in other global markets;

Advance SAGE-324 through completion of ongoing Phase 1 clinical trials, with potential future development in essential tremor, certain epileptiform disorders and other neurological conditions;

Advance SAGE-718 through completion of ongoing Phase 1 clinical trials, with potential future development in indications involving NMDA receptor hypofunction;

Evaluate the market potential and regulatory pathways for our product candidates in the European Union, or EU, and other countries outside the U.S., and move forward where and when it may make business and strategic sense for us to proceed;

Advance one or more of our early clinical-stage product candidates into Phase 2 clinical development; and advance one or more of our non-clinical stage compounds into Phase 1 clinical development;

Bring to market any of our other CNS product candidates that are successfully developed and approved;

Continue our research and development efforts to evaluate the potential for our existing product candidates in the treatment of additional CNS indications, and the identification of new drug candidates and new areas of interest;

Enhance the probability of our success by developing unique assets with differentiated features, and focus our internal development activities on indications where we can make well-informed, rapid go/no-go decisions; and

Utilize the strengths of our proprietary chemistry platform and scientific know-how to expand our portfolio of new chemical entities to lessen our long-term reliance on the success of any one program and to facilitate long-term growth.

S-12

Table of Contents

Company information

We were incorporated in Delaware in April 2010. Our mailing address and executive offices are located at 215 First Street, Cambridge, Massachusetts, 02142, and our telephone number is (617) 299-8380. We maintain an Internet website at the following address: www.sagerx.com. The information on, or that can be accessed through, our website does not constitute part of this prospectus supplement or the accompanying prospectus, and you should not rely on any such information in making the decision whether to purchase our common stock. Our common stock trades on The Nasdaq Global Market under the symbol SAGE .

S-13

Table of Contents

Risks related to our business

We are a clinical-stage biopharmaceutical company, and our business and ability to execute our business strategy are subject to a number of risks of which you should be aware before you decide to buy our common stock. In particular, you should consider the following risks, which are discussed more fully in the section entitled "Risk Factors" in our Annual Report on Form 10-K for the fiscal year ended December 31, 2018, which is incorporated herein by reference:

We currently do not have any products approved for marketing and sale, and may never be able to successfully gain approval to market and sell any drug product. We depend heavily on the success of ZULRESSO (brexanolone) injection, our proprietary IV formulation of brexanolone, which is the subject of an NDA currently under review by the FDA. We cannot be certain that the FDA will approve our NDA for ZULRESSO on the timelines we expect or at all. The FDA may, despite prior advice, decide that the clinical and nonclinical data from our brexanolone development program in PPD are not sufficient to support the grant of regulatory approval. We cannot be certain that we will file an MAA with the EMA seeking approval of brexanolone in the EU, or that the EMA will approve the MAA, if filed.

Even if ZULRESSO is approved for marketing and sale in the U.S., there is no assurance that our launch or commercialization efforts will be successful or that we will be able to generate revenues or profits at the levels or on the timing we expect or at levels necessary to support our goals. We have never marketed, sold or distributed for commercial use any pharmaceutical product. If ZULRESSO is approved, administration of ZULRESSO will be limited to healthcare facilities that are trained and certified under a REMS, program under the supervision of qualified staff. We do not yet have agreement with the FDA on the details of the REMS program. As part of the proposed REMS program, patients receiving ZULRESSO will be required to enroll in a registry to gather information to help further characterize the risk of loss of consciousness during administration and management of the risk. Implementing these requirements and finding and certifying sites of care for administration of ZULRESSO will be challenging and complex and may take time depending on the type of facility. Certain healthcare facilities may not have the infrastructure to support administration of ZULRESSO or to implement the REMS program or the registry, or may not be willing to do so as a result of the limitations, restrictions and other requirements related to administration of ZULRESSO or the REMS or for other reasons. Similarly, women with PPD who need treatment may find it too onerous to undergo an infusion or to be treated at a healthcare facility or to be enrolled in the registry or may be concerned about the risk/benefit profile. Given the mode of administration, the nature of the REMS and the limitation on the administration of ZULRESSO to a healthcare facility setting certified under the REMS, we expect that use of ZULRESSO, if approved for marketing and sale in the U.S., will, at least initially, and potentially beyond the initial launch period, be focused primarily on women with more severe symptoms of PPD.

If we receive regulatory approval to market or sell ZULRESSO, if approved, but are unable to establish adequate sales, marketing and distribution capabilities, whether independently or with third parties, or sufficient, accessible and acceptable REMS certified healthcare facilities for administration of ZULRESSO, or if we do not achieve a sufficient level of market acceptance, or if we are unable to do any of the foregoing in a timely manner and on commercially reasonable terms, our business, results of operations, financial condition and prospects will be materially adversely affected.

We may face issues related to market acceptance and use of any of our products, if approved, including: challenges related to the IV mode of administration of ZULRESSO; limitations in the number, accessibility and acceptability of settings for administration due to the requirement for a REMS certified healthcare facility or the other requirements of the REMS program; financial burdens of treatment for the patient or site of care; or competition from lower cost anti-depressants. Any of these issues could impair our ability to successfully commercialize the product or to generate substantial revenues or profits or to meet our expectations with respect to the amount or timing of revenues or profits.

S-14

Table of Contents

Our future business prospects also depend heavily on our ability to successfully develop and gain regulatory approval of our other product candidates beyond brexanolone. SAGE-217, our lead next generation compound, is in clinical development for MDD, PPD, bipolar depression and sleep disorders, and other product candidates, including SAGE-324 and SAGE-718, are at earlier stages. We cannot be certain we will be able to initiate or complete ongoing and planned clinical trials and nonclinical studies of our product candidates, or announce results, on the time-lines we expect. We cannot be certain that the results of clinical trials or nonclinical studies of any of our product candidates will be positive or support further development. Positive results from earlier nonclinical studies and clinical trials of our product candidates are not necessarily predictive of the results of later nonclinical studies and clinical trials with the same or different compounds. Even if trials of our product candidates are positive the FDA may, despite prior advice, require additional trials or nonclinical studies or additional analyses or data prior to filing or approval of an NDA. If we cannot replicate the positive results from our earlier nonclinical studies and clinical trials of our product candidates in our later nonclinical studies and clinical trials or if other negative data is generated, we may be unable to successfully develop, obtain regulatory approval for and commercialize our product candidates.

A Fast Track designation or Breakthrough Therapy designation by the FDA and PRIME designation by the EMA may not actually lead to a faster development or regulatory review or approval process. Changes in regulatory requirements, regulatory authority guidance or unanticipated events during our nonclinical studies and clinical trials of our product candidates may occur, which may result in changes in requirements with respect to nonclinical studies and clinical trial protocols or result in the need for additional nonclinical studies and clinical trial requirements, which could result in increased costs to us and could delay our development timeline.

The number of patients with PPD, MDD, and the other diseases and disorders for which we are developing product candidates has not been established with precision. In estimating the potential prevalence of indications we are pursuing, or may in the future pursue, including our estimates as to the prevalence of PPD, we have applied assumptions and assessments with respect to available information that may not prove to be correct. 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, our estimates of the prevalence of PPD are higher than estimates reported in some of the published literature or results obtained from certain studies analyzing limited claims databases. We believe this difference is due to variations in methodologies and a possible under-diagnosis of PPD as a result of lack of screening and under-reporting, and patients being reluctant to seek treatment in clinical practice. The actual number of patients with PPD, MDD, or any other indication in which we elect to pursue development of our product candidates may, however, be significantly lower than our estimates. In addition, our products, if approved, may be approved for use or used in only a subset of the patients with these diseases or disorders. If the actual number of patients with these diseases or disorders or any other diseases or disorders we elect to pursue with our product candidates, or the subset that is appropriate for use of our product candidates or who actually use our products, if approved, is smaller than we anticipate, we may encounter difficulties in enrolling patients in our clinical trials, thereby delaying completion of our clinical trials or 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.

The identification of serious adverse events or other undesirable side effects during the use of brexanolone, SAGE-217, SAGE-324, SAGE-718 or any of our other product candidates in ongoing or planned clinical

trials, emergency-use cases, investigator sponsored trials, expanded access programs, or nonclinical studies may adversely affect our development of such product candidates or our ability to obtain regulatory approval, or may affect market acceptance, if the product is approved.

S-15

Table of Contents

Even if we receive marketing approval for ZULRESSO or our other 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 the FDA will recommend controlled substances scheduling of brexanolone and may recommend scheduling with respect to any of our other product candidates. In such event, prior to a product launch, the U.S. Drug Enforcement Agency, or DEA, will need to determine the controlled substance schedule of such product, taking into account the recommendation of the FDA. The DEA review period is typically completed 90 days after FDA approval. The process may delay our ability to market any such product if it is approved. Even if we receive marketing approval in the U.S., we may never seek or receive regulatory approval outside the U.S.

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 private and governmental healthcare payors, and we may not be able to achieve such acceptance at satisfactory levels. 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 at acceptable levels or at all, and any pricing and reimbursement approval we may obtain may be subject to significant hurdles or restrictions on reimbursement.

With respect to some of our product candidates, we are dependent on licensed intellectual property. If we were to lose our rights to licensed intellectual property, we may not be able to continue developing or commercializing those product candidates, if approved.

If we are unable to adequately protect our proprietary technology, or obtain and maintain issued patents or other forms of data and market exclusivity 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 rely completely on third party suppliers to manufacture our product candidates for nonclinical studies and clinical trials, and we intend to continue to rely on third parties to produce nonclinical, clinical and commercial supplies of our product candidates in the future. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the requirements of the FDA and other applicable regulatory authorities, or if we are unable to secure supply, we would need to find alternative manufacturing facilities which may adversely impact our ability to develop, obtain regulatory approval of and commercialize our product candidates or the timing of such events.

As of December 31, 2018, our cash, cash equivalents and marketable securities were \$922.8 million. Under Accounting Standards Update, or ASU, 2014-15, *Presentation of Financial Statements Going Concern* (Subtopic 205-40), or, ASC 205-40, we have the responsibility to evaluate whether conditions or events raise substantial doubt about our ability to meet our future financial obligations as they become due within one year after the date the financial statements are issued. Under ASC 205-40, this evaluation initially cannot take into consideration the potential mitigating effects of plans that have not been fully implemented as of the date the financial statements are issued. We expect that, based on our current operating plans, our

existing cash, cash equivalents and marketable securities will be sufficient to fund our current planned operations for at least the next twelve months. However, until such time, if ever, as we can generate substantial product revenue and achieve profitability, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements and other sources of funding. 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 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 itself.

S-16

Table of Contents

The offering

| | |
|--|---|
| Common stock offered by us | \$500,000,000 of shares of common stock |
| Common stock outstanding following the offering | shares of common stock. |
| Underwriters' option to purchase additional shares | We have granted the underwriters an option to purchase up to an additional \$75.0 million of shares of common stock. The underwriters can exercise this option at any time within 30 days from the date of this prospectus supplement. |
| Use of proceeds | <p>We expect to receive from this offering approximately \$500.0 million (or approximately \$575.0 million if the underwriters exercise their option to purchase additional shares in full), before deducting estimated underwriting discounts and commissions and estimated offering expenses. We intend to use the net proceeds from this offering to fund our:</p> <ul style="list-style-type: none">Advancing of our development and commercial capabilities with the goal of building the leading CNS biotech company, including building on our multi-franchise opportunities in depression, neurology and neuropsychiatry;Planned U.S. commercial launch of ZULRESSO for the treatment of PPD, if approved;Continued investment in SAGE-217 development, including ongoing or planned clinical trials in MDD, bipolar depression, insomnia, and initial pre-commercial planning activities;Continued advancement of our neurology franchise, led by SAGE-324 in development for essential tremor and epileptiform disorders;Continued advancement of our neuropsychiatry franchise, led by SAGE-718 in development for certain cognition-related disorders such as Huntington's disease; |

Working capital, capital expenditures and general corporate purposes.

See [Use of Proceeds](#) for additional information.

The Nasdaq Global Market symbol [SAGE](#)

Risk factors [Investing in our securities involves risks. See \[Risk Factors\]\(#\) beginning on page S-19 of this prospectus supplement and other information included or incorporated by reference into this prospectus supplement and the accompanying prospectus for a discussion of the factors you should carefully consider before deciding to invest in our securities.](#)

Table of Contents

The number of shares of our common stock to be outstanding after the offering is based on 46,888,263 shares of common stock outstanding as of December 31, 2018, and excludes:

7,530,767 shares of common stock issuable upon the exercise of stock options outstanding as of December 31, 2018, at a weighted average exercise price of \$93.22 per share;

82,700 shares of common stock issuable upon the vesting of restricted stock units outstanding as of December 31, 2018;

2,099,811 shares of common stock reserved for future issuance under our 2014 Stock Option and Incentive Plan, or the 2014 Plan, and Amended and Restated 2016 Inducement Equity Plan, or 2016 Plan, as of December 31, 2018, plus any future increases in the number of shares of common stock reserved for issuance under the 2014 Plan pursuant to the evergreen provision of the 2014 Plan; and

232,244 shares of common stock reserved for future issuance under our 2014 Employee Stock Purchase Plan as of December 31, 2018.

Except as otherwise indicated, all information in this prospectus supplement assumes:

no exercise by the underwriters of their option to purchase up to an additional \$75,000,000 of shares of common stock in this offering; and

no exercise of stock options after December 31, 2018.

Table of Contents

Risk factors

*Investing in our securities involves a high degree of risk. In addition to the other information contained in this prospectus supplement, the accompanying prospectus and in the documents we incorporate by reference, you should carefully consider the risks discussed below and under the heading **Risk Factors** in our Annual Report on Form 10-K for the fiscal year ended December 31, 2018, filed with the SEC on February 19, 2019, as updated by our subsequent filings under the Exchange Act, before making a decision about investing in our securities. Such risks and uncertainties and those discussed below are not the only ones facing us. Additional risks and uncertainties not presently known to us, or that we currently see as immaterial, may also harm our business. If any of these risks occur, our business, financial condition and operating results could be harmed, the trading price of our common stock could decline and you could lose part or all of your investment.*

Risks related to this offering and our common stock

The price of our common stock historically has been volatile, which may affect the price at which you could sell the common stock.

For the year to date, the market price for our common stock has varied between a high closing price of \$160.93 on February 15, 2019 and a low closing price of \$89.33 on January 3, 2019. This volatility may affect the price at which you could sell the common stock. Our stock price is likely to continue to be volatile and subject to significant price and volume fluctuations in response to market and other factors, including the other factors discussed in our Annual Report on Form 10-K for the year ended December 31, 2018 or in future periodic reports; variations in our quarterly operating results from our expectations or those of securities analysts or investors; downward revisions in securities analysts' estimates; and announcement by us or our competitors of significant acquisitions, strategic partnerships, joint ventures or capital commitments.

We have broad discretion in the use of the net proceeds from this offering and our existing cash and may not use them effectively.

Our management will have broad discretion in the application of the net proceeds from this offering, including for any of the purposes described in the section entitled **Use of Proceeds**, as well as our existing cash, and you will be relying on the judgment of our management regarding such application. You will not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used appropriately. Our management might not apply the net proceeds or our existing cash in ways that ultimately increase the value of your investment. If we do not invest or apply the net proceeds from this offering or our existing cash in ways that enhance stockholder value, we may fail to achieve expected results, which could cause our stock price to decline. Pending their use, we may invest the net proceeds from this offering in short-term, investment-grade, interest-bearing securities. These investments may not yield a favorable return to our stockholders.

If you purchase our common stock in this offering, you will incur immediate and substantial dilution in the book value of your shares.

Investors purchasing shares of common stock in this offering will pay a price per share that substantially exceeds the as adjusted book value per share of our tangible assets as of December 31, 2018 after subtracting our liabilities. As a result, investors purchasing shares of common stock in this offering will incur immediate dilution of \$ per share, based on the difference between the public offering price of \$ per share, and the as adjusted net tangible book value per share of our outstanding common stock based on 46,888,263 shares of common stock outstanding as of December 31, 2018.

This dilution is due to the substantially lower price paid by some of our investors who purchased shares prior to this offering as compared to the price offered to the public in this offering, and the exercise of stock options

S-19

Table of Contents

granted to our employees. In addition, as of December 31, 2018, options to purchase 7,530,767 shares of our common stock at a weighted average exercise price of \$93.22 per share and 82,700 shares of common stock issuable upon the vesting of restricted stock units were outstanding. The exercise of any of these options or the vesting of our restricted stock units would result in additional dilution. As a result of the dilution to investors purchasing shares in this offering, investors may receive significantly less than the purchase price paid in this offering, if anything, in the event of our liquidation. Further, because we will need to raise additional capital to fund our future activities, we may in the future sell substantial amounts of common stock or securities convertible into or exchangeable for common stock.

These future issuances of common stock or common stock-related securities, together with the exercise of outstanding options and any additional shares issued in connection with acquisitions, if any, may result in further dilution. For a further description of the dilution that you will experience immediately after this offering, see Dilution.

Sales of a substantial number of shares of our common stock in the public market or sales under existing 10b5-1 plans by our Section 16 officers could cause our stock price to fall.

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

In addition, the sale of substantial amounts of our common stock could adversely impact its price. As of December 31, 2018, 46,888,263 shares of our common stock and options to purchase 7,530,767 shares of our common stock (of which 2,846,158 were exercisable as of that date) were outstanding. The sale or the availability for sale of a large number of shares of our common stock in the public market could cause the price of our common stock to decline.

We along with our directors and executive officers have agreed that for a period of 90 days (with respect to us and our executive officers), and 30 days (with respect to our directors) after the date of this prospectus supplement, subject to specified exceptions, including trades under existing 10b5-1 plans, we or they will not offer, sell, contract to sell, pledge or otherwise dispose of, directly or indirectly, any shares of our common stock or securities convertible into or exchangeable or exercisable for any shares of our common stock. These lock-up periods affect approximately 1,138,106 shares of our common stock as of December 31, 2018. Certain of our representatives may, in their sole discretion, release all or some portion of the shares subject to lock-up agreements at any time and for any reason. Sales of a substantial number of such shares upon expiration of the lock-up and market stand-off agreements, the perception that such sales may occur, or early release of these agreements, could cause our market price to fall or make it more difficult for you to sell your common stock at a time and price that you deem appropriate.

A number of our Section 16 officers and directors have established 10b5-1 plans under which their shares of our stock will be sold at prices and in amounts established in the plans. These sales may occur during or after the lock-up period. Sales of stock by any of our directors, executive officers or principal stockholders, including under 10b5-1 plans, could have a material adverse effect on the trading price of our common stock.

The market price of our common stock may be adversely affected by market conditions affecting the stock markets in general, including price and trading fluctuations on The Nasdaq Global Market.

Market conditions may result in volatility in the level of, and fluctuations in, market prices of stocks generally and, in turn, our common stock and sales of substantial amounts of our common stock in the market, in each case being unrelated or disproportionate to changes in our operating performance. The overall weakness in the economy has recently contributed to the extreme volatility of the markets which may have an effect on the market price of our

common stock.

S-20

Table of Contents

Use of proceeds

We expect to receive approximately \$500.0 million from the sale of shares of common stock offered hereby before deducting underwriting discounts and commissions and estimated offering expenses payable by us, or approximately \$575.0 million if the underwriters exercise their option in full to purchase \$75.0 million of additional shares of common stock.

We intend to use the net proceeds from this offering to fund our:

Advancing of our development and commercial capabilities with the goal of building the leading CNS biotech company, including building on our multi-franchise opportunities in depression, neurology and neuropsychiatry;

Planned U.S. commercial launch of ZULRESSO for the treatment of PPD, if approved;

Continued investment in SAGE-217 development, including ongoing or planned clinical trials in MDD, bipolar depression, insomnia, and initial pre-commercial planning activities;

Continued advancement of our neurology franchise, led by SAGE-324 in development for essential tremor and epileptiform disorders;

Continued advancement of our neuropsychiatry franchise, led by SAGE-718 in development for certain cognition-related disorders such as Huntington's disease; and

Working capital, capital expenditures and general corporate purposes.

The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the scope and results of our regulatory activities, the progress of our development efforts, the status of and results from nonclinical studies and ongoing clinical trials or any clinical trials we may commence in the future, the scope, timing and results of our commercial activities, if ZULRESSO is approved, the nature and scope of our initial pre-commercial planning activities for our other product candidates, and the nature and scope of our ex-U.S. operations, as well as any collaborations that we may enter into with third parties for our product candidates and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering.

Pending our use of the net proceeds from this offering, we intend to invest the net proceeds in a variety of capital preservation investments, including short-term, investment-grade, interest-bearing instruments and U.S. government securities.

Table of Contents**Dilution**

If you invest in our common stock in this offering, your ownership interest will be diluted to the extent of the difference between the price per share of our common stock in this offering and the as adjusted net tangible book value per share of our common stock immediately after this offering.

As of December 31, 2018, we had net tangible book value of approximately \$863.0 million, or \$18.40 per share of our common stock, based upon 46,888,263 shares of our common stock outstanding as of that date. Historical net tangible book value per share is equal to our total tangible assets, less total liabilities, divided by the number of outstanding shares of our common stock. Dilution in net tangible book value per share represents the difference between the amount per share paid by purchasers of shares of common stock in this offering and the net tangible book value per share of our common stock immediately after this offering.

After giving effect to the sale of _____ shares of common stock in this offering at a price of \$ _____ per share and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of December 31, 2018 would have been approximately \$ _____ billion, or approximately \$ _____ per share of common stock. This represents an immediate increase in as adjusted net tangible book value of \$ _____ per share to our existing stockholders and an immediate dilution of \$ _____ per share to investors participating in this offering at an assumed public offering price.

Dilution per share to new investors is determined by subtracting net tangible book value per share after this offering from the public offering price per share paid by new investors. The following table illustrates this per share dilution (assuming the underwriters do not exercise in full their option to purchase additional shares):

| | |
|---|----------|
| Public offering price per share | \$ |
| Historical net tangible book value per share as of December 31, 2018 | \$ 18.40 |
| Increase in net tangible book value per share attributable to new investors | |

As adjusted net tangible book value per share after this offering

| | |
|-------------------------------------|----|
| Dilution per share to new investors | \$ |
|-------------------------------------|----|

The foregoing table and discussion is based on 46,888,263 shares of common stock outstanding as of December 31, 2018, and excludes:

7,530,767 shares of common stock issuable upon the exercise of stock options outstanding as of December 31, 2018, at a weighted average exercise price of \$93.22 per share;

82,700 shares of common stock issuable upon the vesting of restricted stock units outstanding as of December 31, 2018;

Edgar Filing: Sage Therapeutics, Inc. - Form 424B5

2,099,811 shares of common stock reserved for future issuance under the 2014 Plan and 2016 Plan, as of December 31, 2018, plus any future increases in the number of shares of common stock reserved for issuance under the 2014 Plan pursuant to the evergreen provision of the 2014 Plan; and

232,244 shares of common stock reserved for future issuance under our 2014 Employee Stock Purchase Plan as of December 31, 2018.

If the underwriters exercise in full their option to purchase an assumed additional shares of common stock at a price of \$ per share, the as adjusted net tangible book value after this offering would be \$ per share, representing an increase in net tangible book value of \$ per share to existing stockholders and immediate dilution in net tangible book value of \$ per share to investors purchasing our common stock in this offering.

S-22

Table of Contents

To the extent that any options are exercised, new options are issued under our equity incentive plans, our outstanding restricted stock units vest or we otherwise issue additional shares of common stock in the future (including shares issued in connection with acquisitions), there will be further dilution to new investors.

In addition, we may choose to raise additional capital due to market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

S-23

Table of Contents

Description of capital stock

This section describes the general terms of our common stock. For more detailed information, a holder of our common stock should refer to our certificate of incorporation and our by-laws, copies of which are filed with the SEC as exhibits to the registration statement of which this prospectus supplement and the accompanying prospectus are a part.

General

Our authorized capital stock consists of 120,000,000 shares of common stock, \$0.0001 par value per share, and 5,000,000 shares of preferred stock, \$0.0001 par value per share. As of December 31, 2018, there were 46,888,263 shares of our common stock outstanding and no shares of preferred stock were outstanding.

The following summary description of our capital stock is based on the provisions of our amended and restated certificate of incorporation and amended and restated bylaws and the applicable provisions of the Delaware General Corporation Law. This information is qualified entirely by reference to the applicable provisions of our amended and restated certificate of incorporation, amended and restated bylaws and the Delaware General Corporation Law.

Common stock

We are authorized to issue one class of common stock. Holders of our common stock are entitled to one vote for each share of common stock held of record for the election of directors and on all matters submitted to a vote of stockholders. Holders of our common stock are entitled to receive dividends ratably, if any, as may be declared by our board of directors out of legally available funds, subject to any preferential dividend rights of any preferred stock then outstanding. Upon our dissolution, liquidation or winding up, holders of our common stock are entitled to share ratably in our net assets legally available after the payment of all our debts and other liabilities, subject to the preferential rights of any preferred stock then outstanding. Holders of our common stock have no preemptive, subscription, redemption or conversion rights. The rights, preferences and privileges of holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future. Except as described under *Anti-takeover effects of Delaware law and provisions of our certificate of incorporation and by-laws* below, a majority vote of the holders of common stock is generally required to take action under our amended and restated certificate of incorporation and amended and restated by-laws.

Preferred stock

Our board of directors is authorized, without action by the stockholders, to designate and issue up to an aggregate of 5,000,000 shares of preferred stock in one or more series. Our board of directors can designate the rights, preferences and privileges of the shares of each series and any of its qualifications, limitations or restrictions. Our board of directors may authorize the issuance of preferred stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of common stock. The issuance of preferred stock, while providing flexibility in connection with possible future financings and acquisitions and other corporate purposes could, under certain circumstances, have the effect of restricting dividends on our common stock, diluting the voting power of our common stock, impairing the liquidation rights of our common stock, or delaying, deferring or preventing a change in control of our company, which might harm the market price of our common stock. See also *Anti-takeover effects of Delaware law and provisions of our certificate of incorporation and by-laws* *Provisions of our amended and restated certificate of incorporation and amended and restated by-laws* *Undesignated Preferred Stock* below.

Table of Contents

Our board of directors will make any determination to issue such shares based on its judgment as to our Company's best interests and the best interests of our stockholders. We have no shares of preferred stock outstanding and we have no current plans to issue any shares of preferred stock following completion of this offering.

Anti-takeover effects of Delaware Law, our certificate of incorporation and our by-laws

Certain provisions of the Delaware General Corporation Law and of our amended and restated certificate of incorporation and amended and restated by-laws could have the effect of delaying, deferring or discouraging another party from acquiring control of us. These provisions, which are summarized below, are expected to discourage certain types of coercive takeover practices and inadequate takeover bids and, as a consequence, they might also inhibit temporary fluctuations in the market price of our common stock that often result from actual or rumored hostile takeover attempts. These provisions are also designed in part to encourage anyone seeking to acquire control of us to first negotiate with our board of directors. These provisions might also have the effect of preventing changes in our management. It is possible that these provisions could make it more difficult to accomplish transactions that stockholders might otherwise deem to be in their best interests. However, we believe that the advantages gained by protecting our ability to negotiate with any unsolicited and potentially unfriendly acquirer outweigh the disadvantages of discouraging such proposals, including those priced above the then-current market value of our common stock, because, among other reasons, the negotiation of such proposals could improve their terms.

Delaware takeover statute

We are subject to the provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly held Delaware corporation from engaging in a business combination with an interested stockholder for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions:

before the stockholder became interested, our board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;

upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances, but not the outstanding voting stock owned by the interested stockholder; or

at or after the time the stockholder became interested, the business combination was approved by our board of directors and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

Section 203 defines a business combination to include:

Edgar Filing: Sage Therapeutics, Inc. - Form 424B5

any merger or consolidation involving the corporation and the interested stockholder;

any sale, transfer, lease, pledge, exchange, mortgage or other disposition involving the interested stockholder of 10% or more of the assets of the corporation;

subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;

S-25

Table of Contents

subject to exceptions, any transaction involving the corporation that has the effect of increasing the proportionate share of the stock of any class or series of the corporation beneficially owned by the interested stockholder; or

the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

In general, Section 203 defines an interested stockholder as any entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by the entity or person.

Provisions of our amended and restated certificate of incorporation and amended and restated by-laws

Our amended and restated certificate of incorporation and amended and restated by-laws include a number of provisions that may have the effect of delaying, deferring or discouraging another party from acquiring control of us and encouraging persons considering unsolicited tender offers or other unilateral takeover proposals to negotiate with our board of directors rather than pursue non-negotiated takeover attempts. These provisions include the items described below.

Board composition and filling vacancies

In accordance with our amended and restated certificate of incorporation, our board is divided into three classes serving staggered three-year terms, with one class being elected each year. Our amended and restated certificate of incorporation also provides that directors may be removed only for cause and then only by the affirmative vote of the holders of 75% or more of the shares then entitled to vote at an election of directors. Furthermore, any vacancy on our board of directors, however occurring, including a vacancy resulting from an increase in the size of our board, may only be filled by the affirmative vote of a majority of our directors then in office even if less than a quorum.

No written consent of stockholders

Our amended and restated certificate of incorporation provides that all stockholder actions are required to be taken by a vote of the stockholders at an annual or special meeting, and that stockholders may not take any action by written consent in lieu of a meeting. This limit may lengthen the amount of time required to take stockholder actions and would prevent the amendment of our by-laws or removal of directors by our stockholder without holding a meeting of stockholders.

Meetings of stockholders

Our amended and restated by-laws provide that only a majority of the members of our board of directors then in office may call special meetings of stockholders and only those matters set forth in the notice of the special meeting may be considered or acted upon at a special meeting of stockholders. Our amended and restated by-laws limit the business that may be conducted at an annual meeting of stockholders to those matters properly brought before the meeting.

Advance notice requirements

Our amended and restated by-laws establish advance notice procedures with regard to stockholder proposals relating to the nomination of candidates for election as directors or new business to be brought before meetings of our stockholders. These procedures provide that notice of stockholder proposals must be timely given in writing to our

corporate secretary prior to the meeting at which the action is to be taken. Generally, to be timely, notice must be received at our principal executive offices not less than 90 days or more than 120 days prior to the first anniversary date of the annual meeting for the preceding year. The notice must contain certain information specified in our amended and restated by-laws.

S-26

Table of Contents

Amendment to by-laws and certificate of incorporation

As required by the Delaware General Corporation Law, any amendment of our amended and restated certificate of incorporation must first be approved by a majority of our board of directors, and if required by law or our amended and restated certificate of incorporation, must thereafter be approved by a majority of the outstanding shares entitled to vote on the amendment, and a majority of the outstanding shares of each class entitled to vote thereon as a class, except that the amendment of the provisions relating to stockholder action, directors, limitation of liability and the amendment of our amended and restated by-laws and amended and restated certificate of incorporation must be approved by not less than 75% of the outstanding shares entitled to vote on the amendment, and not less than 75% of the outstanding shares of each class entitled to vote thereon as a class. Our amended and restated by-laws may be amended by the affirmative vote of a majority of the directors then in office, subject to any limitations set forth in the amended and restated by-laws; and may also be amended by the affirmative vote of at least 75% of the outstanding shares entitled to vote on the amendment, or, if the board of directors recommends that the stockholders approve the amendment, by the affirmative vote of the majority of the outstanding shares entitled to vote on the amendment, in each case voting together as a single class.

Undesignated preferred stock

Our amended and restated certificate of incorporation provides for 5,000,000 authorized shares of preferred stock. The existence of authorized but unissued shares of preferred stock may enable our board of directors to render more difficult or to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise. For example, if in the due exercise of its fiduciary obligations, our board of directors were to determine that a takeover proposal is not in the best interests of us or our stockholders, our board of directors could cause shares of preferred stock to be issued without stockholder approval in one or more private offerings or other transactions that might dilute the voting or other rights of the proposed acquirer or insurgent stockholder or stockholder group. In this regard, our amended and restated certificate of incorporation grants our board of directors broad power to establish the rights and preferences of authorized and unissued shares of preferred stock. The issuance of shares of preferred stock could decrease the amount of earnings and assets available for distribution to holders of shares of common stock. The issuance may also adversely affect the rights and powers, including voting rights, of these holders and may have the effect of delaying, deterring or preventing a change in control of us.

Exclusive jurisdiction of certain actions

Our amended and restated certificate of incorporation requires, to the fullest extent permitted by law, that derivative actions brought in our name, actions against our directors, officers and employees for breach of fiduciary duty and other similar actions may be brought only in the Court of Chancery in the State of Delaware, unless we otherwise consent. Although we believe this provision benefits us by providing increased consistency in the application of Delaware law in the types of lawsuits to which it applies, the provision may have the effect of discouraging lawsuits against our directors and officers.

Table of Contents

Transfer agent and registrar

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A.

S-28

Table of Contents

Dividend policy

We have never declared or paid dividends on our capital stock. We do not anticipate paying any dividends on our capital stock in the foreseeable future. We currently intend to retain all available funds and any future earnings to fund the development and growth of our business. Any future determination to declare dividends will be subject to the discretion of our board of directors and will depend on various factors, including applicable laws, our results of operations, financial condition, future prospects and any other factors deemed relevant by our board of directors. Investors should not purchase our common stock with the expectation of receiving cash dividends.

S-29

Table of Contents**Underwriting**

We are offering the shares of common stock described in this prospectus supplement through Goldman Sachs & Co. LLC and J.P. Morgan Securities LLC, which are acting as the joint book-running managers of the offering and underwriters. We have entered into an underwriting agreement with the underwriters. Subject to the terms and conditions of the underwriting agreement, we have agreed to sell to the underwriters, and each underwriter has severally agreed to purchase, at the public offering price less the underwriting discounts and commissions set forth on the cover page of this prospectus supplement, the number of shares of common stock listed next to its name in the following table:

| Underwriter | Number of shares |
|----------------------------|-----------------------------|
| Goldman Sachs & Co. LLC | |
| J.P. Morgan Securities LLC | |
| Total | |

The underwriters are committed to purchase all the shares offered by us if they purchase any shares. The underwriting agreement also provides that if an underwriter defaults, the purchase commitments of non-defaulting underwriters may also be increased or the offering may be terminated.

We have agreed to indemnify the underwriter against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the underwriter may be required to make in respect of those liabilities.

The underwriters propose to offer the shares of common stock directly to the public at the initial public offering price set forth on the cover page of this prospectus supplement and to certain dealers at that price less a concession not in excess of \$ per share. Any such dealers may resell shares to certain other brokers or dealers at a discount of up to \$ per share from the initial public offering price. After the initial offering of the shares to the public, the offering price and other selling terms may be changed by the underwriters. Sales of shares made outside of the United States may be made by affiliates of the underwriters. The offering of the shares by the underwriters is subject to receipt and acceptance and subject to the underwriters' right to reject any order in whole or in part.

The underwriters have an option to buy up to \$75.0 million of additional shares of common stock from us at the public offering price, less the underwriting discount, to cover sales of shares by the underwriters which exceed the number of shares specified in the table above. The underwriters have 30 days from the date of this prospectus supplement to exercise this option to purchase additional shares. If any shares are purchased with this option to purchase additional shares, the underwriters will purchase shares in approximately the same proportion as shown in the table above. If any additional shares of common stock are purchased, the underwriters will offer the additional shares on the same terms as those on which the shares are being offered.

The underwriting fee is equal to the public offering price per share of common stock less the amount paid by the underwriters to us per share of common stock. The underwriting fee is \$ per share. The following table shows the per share and total underwriting discounts and commissions to be paid to the underwriters and proceeds before expenses to us, assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

| | Without option | With option |
|--|-----------------------|--------------------|
| Per share underwriting discounts and commissions | \$ | \$ |
| Total underwriting discounts and commissions | \$ | \$ |
| Proceeds, before expenses, to us | \$ | \$ |

S-30

Table of Contents

We estimate that the total expenses of this offering, including registration, filing and listing fees, printing fees and legal and accounting expenses, but excluding the underwriting discounts and commissions, will be approximately \$350,000. We have agreed to reimburse the underwriters for all expenses related to the clearance of the offering with the Financial Industry Regulatory Authority (in an amount not to exceed \$20,000).

A prospectus supplement in electronic format may be made available on the web sites maintained by one or more underwriters, or selling group members, if any, participating in the offering. The underwriters may agree to allocate a number of shares to underwriters and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the representatives to underwriters and selling group members that may make Internet distributions on the same basis as other allocations.

In connection with this offering, we and each of our directors and executive officers have agreed that, for a period of 90 days, with respect to us and our executive officers and 30 days with respect to our directors, after the date of this prospectus supplement, subject to specified exceptions, not to sell or transfer any common stock or securities convertible into, exchangeable for, exercisable for, or repayable with common stock without first obtaining the written consent of Goldman Sachs & Co. LLC and J.P. Morgan Securities LLC. Specifically, we and these other persons have agreed, with certain limited exceptions, not to directly or indirectly:

offer, pledge, sell or contract to sell any common stock,

sell any option or contract to purchase any common stock,

purchase any option or contract to sell any common stock,

grant any option, right or warrant for the sale of any common stock,

lend or otherwise dispose of or transfer any common stock,

publicly disclose the intention to make any such offer, sale, pledge or disposition of any common stock,

request or demand that we file a registration statement related to the common stock, or

enter into any swap or other agreement that transfers, in whole or in part, the economic consequence of ownership of any common stock whether any such swap or transaction is to be settled by delivery of shares or other securities, in cash or otherwise.

The restrictions described in the immediately preceding paragraph do not apply to:

the sale of shares of our common stock to the underwriters pursuant to the terms of the underwriting agreement,

the issuance by us of shares of our common stock upon the exercise or conversion of a security outstanding on the date of this prospectus supplement,

the issuance by us of shares of our common stock or other securities convertible into or exercisable for shares of common stock issued in connection with a joint venture, marketing or distribution arrangement, collaboration agreement, intellectual property license agreement, or any acquisition of assets or not less than a majority or controlling portion of the equity of another entity, provided that (x) the aggregate number of shares of common stock or securities convertible into or exercisable for common stock that we may issue shall not exceed 5.0% of the total number of shares of common stock issued and outstanding immediately following the completion of this offering, and (y) all recipients of any such securities shall enter into lock-up agreements,

sales of securities acquired in open market transactions after the date of the this offering,

transfers of shares of our common stock or other securities as bona fide gifts or by will or intestacy to the legal representative, heir, beneficiary or a member of the immediate family of the person or entity in a transaction not involving a disposition for value,

Table of Contents

in the case of lock-up agreements signed by directors and officers, transfers or dispositions of shares of our common stock or other securities to any trust for the direct or indirect benefit of the director or officer signing the lock-up agreement or the immediate family of such person, in each case for estate planning purposes,

in the case of a lock-up agreement signed by a trust, distributions of shares of our common stock or any security directly or indirectly convertible into our common stock to its beneficiaries in a transaction not involving a disposition for value,

in the case of lock-up agreements signed by a corporation, limited liability company, partnership or other entity, distribution of shares of our common stock or any security directly or indirectly convertible into shares of our common stock to members, stockholders, limited partners, subsidiaries or affiliates of such entity or to any investment fund or other entity that controls or manages such entity in a transaction not involving a disposition for value,

transfers to us pursuant to agreements under which we have the option to repurchase shares or securities upon termination of service of the person or entity, provided that the repurchase price for any such shares or securities shall not exceed the original purchase price paid to the Company for such shares or securities,

the receipt by the person or entity from us of shares of our common stock upon the exercise of options, provided that any such shares of common stock received upon such exercise shall be subject to the same restrictions,

the establishment of a trading plan pursuant to Rule 10b5-1 under the Exchange Act for the transfer of common stock, provided that such plan does not provide for any transfers of common stock, and no filing with the SEC or other public announcement shall be required or voluntarily made by the director or officer or any other person in connection therewith, in each case during the applicable 90-day or 30-day restricted period, or any extension thereof pursuant to the lock-up agreement, or

sales or transfers of common stock made pursuant to a trading plan that satisfies the requirements of Rule 10b5-1 under the Exchange Act that has been entered into prior to the date of the lock-up agreement, provided that no amendments or other modifications are made to such plans and that, to the extent a public announcement or filing under the Exchange Act, if any, is required or voluntarily made by or on behalf of the director, officer or the Company regarding any such sales or transfers, such announcement or filing shall include a statement to the effect that the sale or transfer was made pursuant to a trading plan pursuant to Rule 10b5-1.

This lock-up provision applies to common stock and to securities convertible into or exchangeable or exercisable for or repayable with common stock. It also applies to common stock owned now or acquired later by the person executing the agreement or for which the person executing the agreement later acquires the power of disposition.

In connection with this offering, the underwriters may engage in stabilizing transactions, which involves making bids for, purchasing and selling shares of common stock in the open market for the purpose of preventing or retarding a

decline in the market price of the common stock while this offering is in progress. These stabilizing transactions may include making short sales of the common stock, which involves the sale by the underwriters of a greater number of shares of common stock than they are required to purchase in this offering, and purchasing shares of common stock on the open market to cover positions created by short sales. Short sales may be covered shorts, which are short positions in an amount not greater than the underwriters' option to purchase additional shares referred to above, or may be naked shorts, which are short positions in excess of that amount. The underwriters may close out any covered short position either by exercising their option to purchase additional shares, in whole or in part, or by purchasing shares in the open market. In making this determination, the underwriters will consider, among other things, the price of shares available for purchase in the open market compared to the price at which the underwriters may purchase shares through the option to purchase additional shares. A naked short position is more likely to be created if the underwriters are concerned that there may be

S-32

Table of Contents

downward pressure on the price of the common stock in the open market that could adversely affect investors who purchase in this offering. To the extent that the underwriters create a naked short position, they will purchase shares in the open market to cover the position.

The underwriters have advised us that, pursuant to Regulation M of the Securities Act of 1933, they may also engage in other activities that stabilize, maintain or otherwise affect the price of the common stock, including the imposition of penalty bids. This means that if the representatives of the underwriters purchase common stock in the open market in stabilizing transactions or to cover short sales, the representatives can require the underwriters that sold those shares as part of this offering to repay the underwriting discount received by them.

These activities may have the effect of raising or maintaining the market price of the common stock or preventing or retarding a decline in the market price of the common stock, and, as a result, the price of the common stock may be higher than the price that otherwise might exist in the open market. If the underwriters commence these activities, they may discontinue them at any time. The underwriters may carry out these transactions on the Nasdaq Global Market, in the over-the-counter market or otherwise.

In addition, in connection with this offering certain of the underwriters (and selling group members) may engage in passive market making transactions in our common stock on The Nasdaq Global Market prior to the pricing and completion of this offering. Passive market making consists of displaying bids on The Nasdaq Global Market no higher than the bid prices of independent market makers and making purchases at prices no higher than these independent bids and effected in response to order flow. Net purchases by a passive market maker on each day are generally limited to a specified percentage of the passive market maker's average daily trading volume in the common stock during a specified period and must be discontinued when such limit is reached. Passive market making may cause the price of our common stock to be higher than the price that otherwise would exist in the open market in the absence of these transactions. If passive market making is commenced, it may be discontinued at any time.

The underwriters and their respective affiliates are full service financial institutions engaged in various activities, which may include sales and trading, commercial and investment banking, advisory, investment management, investment research, principal investment, hedging, market making, brokerage and other financial and non-financial activities and services. Certain of the underwriters and their respective affiliates have provided, and may in the future provide, a variety of these services to the issuer and to persons and entities with relationships with the issuer, for which they received or will receive customary fees and expenses.

In addition, in the ordinary course of their business activities, the underwriters and their affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers. Such investments and securities activities may involve securities and/or instruments of ours or our affiliates. The underwriters and their affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Other than in the U.S., no action has been taken by us or the underwriters that would permit a public offering of the securities offered by this prospectus supplement in any jurisdiction where action for that purpose is required. The securities offered by this prospectus supplement may not be offered or sold, directly or indirectly, nor may this prospectus supplement or any other offering material or advertisements in connection with the offer and sale of any such securities be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus supplement comes are advised to inform themselves about and to observe any restrictions relating to the

offering and the distribution of this prospectus supplement. This prospectus supplement does not constitute an offer to sell or a solicitation of an offer to buy any securities offered by this prospectus supplement in any jurisdiction in which such an offer or a solicitation is unlawful.

S-33

Table of Contents

Notice to prospective investors in Canada

The shares of common stock may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus Exemptions or subsection 73.3(1) of the Securities Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions and Ongoing Registrant Obligations. Any resale of the common stock must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus supplement (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 (or, in the case of securities issued or guaranteed by the government of a non-Canadian jurisdiction, section 3A.4) of National Instrument 33-105 Underwriting Conflicts (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

Notice to prospective investors in the European Economic Area

In relation to each Member State of the European Economic Area, each, a Relevant Member State, no offer of shares may be made to the public in that Relevant Member State other than:

- A. to any legal entity which is a qualified investor as defined in the Prospectus Directive;
- B. to fewer than 150 natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the representatives; or
- C. in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of shares shall require the Company or the representatives to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

Each person in a Relevant Member State who initially acquires any shares or to whom any offer is made will be deemed to have represented, acknowledged and agreed that it is a qualified investor within the meaning of the law in that Relevant Member State implementing Article 2(1)(e) of the Prospectus Directive. In the case of any shares being offered to a financial intermediary as that term is used in Article 3(2) of the Prospectus Directive, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the shares acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer of any shares to the public other than their offer or resale in a Relevant Member State to qualified investors as so defined or in circumstances in which the prior

consent of the representatives has been obtained to each such proposed offer or resale.

The Company, the representatives and their affiliates will rely upon the truth and accuracy of the foregoing representations, acknowledgements and agreements.

For the purpose of the above provisions, the expression an offer to the public in relation to any shares in any Relevant Member State means the communication in any form and by any means of sufficient information on the

Table of Contents

terms of the offer and the shares to be offered so as to enable an investor to decide to purchase or subscribe the shares, as the same may be varied in the Relevant Member State by any measure implementing the Prospectus Directive in the Relevant Member State and the expression "Prospectus Directive" means Directive 2003/71/EC, as amended, including by Directive 2010/73/EU.

Notice to prospective investors in the United Kingdom

In addition, in the United Kingdom, this document is being distributed only to, and is directed only at, and any offer subsequently made may only be directed at persons who are "qualified investors" (as defined in the Prospectus Directive) (i) who have professional experience in matters relating to investments falling within Article 19 (5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended, or the Order, and/or (ii) who are high net worth companies (or persons to whom it may otherwise be lawfully communicated) falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as "relevant persons"). This document must not be acted on or relied on in the United Kingdom by persons who are not relevant persons. In the United Kingdom, any investment or investment activity to which this document relates is only available to, and will be engaged in with, relevant persons.

Notice to prospective investors in Switzerland

The shares may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange, or SIX, or on any other stock exchange or regulated trading facility in Switzerland. This document has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this document nor any other offering or marketing material relating to the shares or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this document nor any other offering or marketing material relating to the offering, the Company, the shares have been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of shares will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA (FINMA), and the offer of shares has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes (CISA). The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of shares.

Notice to prospective investors in the Dubai International Financial Centre

This prospectus supplement relates to an Exempt Offer in accordance with the Offered Securities Rules of the Dubai Financial Services Authority, or the DFSA. This prospectus supplement is intended for distribution only to persons of a type specified in the Offered Securities Rules of the DFSA. It must not be delivered to, or relied on by, any other person. The DFSA has no responsibility for reviewing or verifying any documents in connection with Exempt Offers. The DFSA has not approved this prospectus supplement nor taken steps to verify the information set forth herein and has no responsibility for the prospectus supplement. The shares to which this prospectus supplement relates may be illiquid and/or subject to restrictions on their resale. Prospective purchasers of the shares offered should conduct their own due diligence on the shares. If you do not understand the contents of this prospectus supplement you should consult an authorized financial advisor.

Notice to prospective investors in Australia

Edgar Filing: Sage Therapeutics, Inc. - Form 424B5

No placement document, prospectus, product disclosure statement or other disclosure document has been lodged with the Australian Securities and Investments Commission in relation to the offering. This prospectus does not

S-35

Table of Contents

constitute a prospectus, product disclosure statement or other disclosure document under the Corporations Act 2001 (the Corporations Act), and does not purport to include the information required for a prospectus, product disclosure statement or other disclosure document under the Corporations Act.

Any offer in Australia of the shares may only be made to persons, or the Exempt Investors, who are sophisticated investors (within the meaning of section 708(8) of the Corporations Act), professional investors (within the meaning of section 708(11) of the Corporations Act) or otherwise pursuant to one or more exemptions contained in section 708 of the Corporations Act so that it is lawful to offer the shares without disclosure to investors under Chapter 6D of the Corporations Act.

The shares applied for by Exempt Investors in Australia must not be offered for sale in Australia in the period of 12 months after the date of allotment under the offering, except in circumstances where disclosure to investors under Chapter 6D of the Corporations Act would not be required pursuant to an exemption under section 708 of the Corporations Act or otherwise or where the offer is pursuant to a disclosure document which complies with Chapter 6D of the Corporations Act. Any person acquiring shares must observe such Australian on-sale restrictions.

This prospectus contains general information only and does not take account of the investment objectives, financial situation or particular needs of any particular person. It does not contain any securities recommendations or financial product advice. Before making an investment decision, investors need to consider whether the information in this prospectus is appropriate to their needs, objectives and circumstances, and, if necessary, seek expert advice on those matters.

Notice to prospective investors in Hong Kong

The shares have not been offered or sold and will not be offered or sold in Hong Kong, by means of any document, other than (a) to professional investors as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance; or (b) in other circumstances which do not result in the document being a prospectus as defined in the Companies Ordinance (Cap. 32) of Hong Kong or which do not constitute an offer to the public within the meaning of that Ordinance. No advertisement, invitation or document relating to the shares has been or may be issued or has been or may be in the possession of any person for the purposes of issue, whether in Hong Kong or elsewhere, which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to professional investors as defined in the Securities and Futures Ordinance and any rules made under that Ordinance.

Notice to prospective investors in Japan

The shares have not been and will not be registered under the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948, as amended) and, accordingly, will not be offered or sold, directly or indirectly, in Japan, or for the benefit of any Japanese Person or to others for re-offering or resale, directly or indirectly, in Japan or to any Japanese Person, except in compliance with all applicable laws, regulations and ministerial guidelines promulgated by relevant Japanese governmental or regulatory authorities in effect at the relevant time. For the purposes of this paragraph, Japanese Person shall mean any person resident in Japan, including any corporation or other entity organized under the laws of Japan.

Notice to prospective investors in Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for

S-36

Table of Contents

subscription or purchase, of Non-CIS Securities may not be circulated or distributed, nor may the Non-CIS Securities be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore, or the SFA, (ii) to a relevant person pursuant to Section 275(1), or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275, of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the Non-CIS Securities are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

- (a) a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or
- (b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor, securities (as defined in Section 239(1) of the SFA) of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the Non-CIS Securities pursuant to an offer made under Section 275 of the SFA except:
 - (a) to an institutional investor or to a relevant person defined in Section 275(2) of the SFA, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;
 - (b) where no consideration is or will be given for the transfer;
 - (c) where the transfer is by operation of law;
 - (d) as specified in Section 276(7) of the SFA; or
 - (e) as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore.

Table of Contents

**Material U.S. federal income tax considerations for
non-U.S. holders of common stock**

The following discussion is a summary of the material U.S. federal income tax considerations applicable to non-U.S. holders (as defined below) with respect to their ownership and disposition of shares of our common stock issued pursuant to this offering. For purposes of this discussion, a non-U.S. holder means a beneficial owner of our common stock that is for U.S. federal income tax purposes:

a non-resident alien individual;

a foreign corporation or any other foreign organization taxable as a corporation for U.S. federal income tax purposes; or

a foreign estate or trust, the income of which is not subject to U.S. federal income tax on a net income basis. This discussion does not address the tax treatment of partnerships or other entities that are pass-through entities for U.S. federal income tax purposes or persons that hold their common stock through partnerships or other pass-through entities. A partner in a partnership or other pass-through entity that will hold our common stock should consult his, her or its tax advisor regarding the tax consequences of acquiring, holding and disposing of our common stock through a partnership or other pass-through entity, as applicable.

This discussion is based on current provisions of the U.S. Internal Revenue Code of 1986, as amended, which we refer to as the Code, existing and proposed U.S. Treasury Regulations promulgated thereunder, current administrative rulings and judicial decisions, all as in effect as of the date of this prospectus and, all of which are subject to change or to differing interpretation, possibly with retroactive effect. Any such change or differing interpretation could alter the tax consequences to non-U.S. holders described in this prospectus. There can be no assurance that the Internal Revenue Service, which we refer to as the IRS, will not challenge one or more of the tax consequences described herein. We assume in this discussion that a non-U.S. holder holds shares of our common stock as a capital asset within the meaning of Section 1221 of the Code, generally property held for investment.

This discussion does not address all aspects of U.S. federal income taxation that may be relevant to a particular non-U.S. holder in light of that non-U.S. holder's individual circumstances nor does it address any U.S. state, local or non-U.S. taxes, the alternative minimum tax, the Medicare tax on net investment income, the rules regarding qualified small business stock within the meaning of Section 1202 of the Code, or any other aspect of any U.S. federal tax other than the income tax. This discussion also does not consider any specific facts or circumstances that may apply to a non-U.S. holder and does not address the special tax rules applicable to particular non-U.S. holders, such as:

insurance companies;

tax-exempt or governmental organizations;

financial institutions;

brokers or dealers in securities;

regulated investment companies;

pension plans;

controlled foreign corporations, passive foreign investment companies, and corporations that accumulate earnings to avoid U.S. federal income tax;

qualified foreign pension funds, or entities wholly owned by a qualified foreign pension fund ;

persons deemed to sell our common stock under the constructive sale provisions of the Code;

S-38

Table of Contents

persons that hold our common stock as part of a straddle, hedge, conversion transaction, synthetic security or other integrated investment; and

certain U.S. expatriates.

This discussion is for general information only and is not tax advice. Accordingly, all prospective non-U.S. holders of our common stock should consult their tax advisors with respect to the U.S. federal, state, local and non-U.S. tax consequences of the purchase, ownership and disposition of our common stock.

Distributions on our common stock

Distributions, if any, on our common stock will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. If a distribution exceeds our current and accumulated earnings and profits, the excess will be treated as a tax-free return of the non-U.S. holder's investment, up to such holder's tax basis in the common stock. Any remaining excess will be treated as capital gain, subject to the tax treatment described below in **Gain on sale or other taxable disposition of our common stock**. Any such distributions will also be subject to the discussions below under the sections titled **Backup withholding and information reporting** and **Withholding and information reporting requirements FATCA**.

Subject to the discussion in the following two paragraphs in this section, dividends paid to a non-U.S. holder generally will be subject to withholding of U.S. federal income tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the U.S. and such holder's country of residence.

Dividends that are treated as effectively connected with a trade or business conducted by a non-U.S. holder within the U.S. and, if an applicable income tax treaty so provides, that are attributable to a permanent establishment or a fixed base maintained by the non-U.S. holder within the U.S., are generally exempt from the 30% withholding tax if the non-U.S. holder satisfies applicable certification and disclosure requirements. However, such U.S. effectively connected income, net of specified deductions and credits, is taxed at the same graduated U.S. federal income tax rates applicable to U.S. persons (as defined in the Code). Any U.S. effectively connected income received by a non-U.S. holder that is a corporation may also, under certain circumstances, be subject to an additional branch profits tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the U.S. and such holder's country of residence.

A non-U.S. holder of our common stock who claims the benefit of an applicable income tax treaty between the U.S. and such holder's country of residence generally will be required to provide a properly executed IRS Form W-8BEN or W-8BEN-E (or successor form) to the applicable withholding agent and satisfy applicable certification and other requirements. Non-U.S. holders are urged to consult their tax advisors regarding their entitlement to benefits under a relevant income tax treaty. A non-U.S. holder that is eligible for a reduced rate of U.S. withholding tax under an income tax treaty may obtain a refund or credit of any excess amounts withheld by timely filing a U.S. tax return with the IRS.

Gain on sale or other taxable disposition of our common stock

Subject to the discussions below under **Backup withholding and information reporting** and **Withholding and information reporting requirements FATCA**, a non-U.S. holder generally will not be subject to any U.S. federal income tax on any gain realized upon such holder's sale or other taxable disposition of shares of our common stock unless:

the gain is effectively connected with the non-U.S. holder's conduct of a U.S. trade or business and, if an applicable income tax treaty so provides, is attributable to a permanent establishment or a fixed-base maintained by such non-U.S. holder in the U.S., in which case the non-U.S. holder generally will be taxed on a net income basis at the graduated U.S. federal income tax rates applicable to U.S. persons (as defined in the Code) and, if the non-U.S. holder is a foreign corporation, the branch profits tax described above in Distributions on our common stock also may apply;

S-39

Table of Contents

the non-U.S. holder is a nonresident alien individual who is present in the U.S. for 183 days or more in the taxable year of the disposition and certain other conditions are met, in which case the non-U.S. holder will be subject to a 30% tax (or such lower rate as may be specified by an applicable income tax treaty between the U.S. and such holder's country of residence) on the net gain derived from the disposition, which may be offset by certain U.S. source capital losses of the non-U.S. holder, if any (even though the individual is not considered a resident of the U.S.), provided that the non-U.S. holder has timely filed U.S. federal income tax returns with respect to such losses; or

we are, or have been, at any time during the five-year period preceding such sale of other taxable disposition (or the non-U.S. holder's holding period, if shorter) a U.S. real property holding corporation, unless our common stock is regularly traded on an established securities market and the non-U.S. holder holds no more than 5% of our outstanding common stock, directly or indirectly, actually or constructively, during the shorter of the 5-year period ending on the date of the disposition or the period that the non-U.S. holder held our common stock. Generally, a corporation is a U.S. real property holding corporation only if the fair market value of its U.S. real property interests equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. Although there can be no assurance, we do not believe that we are, or have been, a U.S. real property holding corporation, or that we are likely to become one in the future. No assurance can be provided that our common stock will be regularly traded on an established securities market for purposes of the rules described above.

Backup withholding and information reporting

We must report annually to the IRS and to each non-U.S. holder the gross amount of the distributions on our common stock paid to such holder and the tax withheld, if any, with respect to such distributions. Non-U.S. holders may have to comply with specific certification procedures to establish that the holder is not a U.S. person (as defined in the Code) in order to avoid backup withholding at the applicable rate with respect to dividends on our common stock. Dividends paid to non-U.S. holders subject to withholding of U.S. federal income tax, as described above in

Distributions on our common stock, generally will be exempt from U.S. backup withholding.

Information reporting and backup withholding will generally apply to the proceeds of a disposition of our common stock by a non-U.S. holder effected by or through the U.S. office of any broker, U.S. or foreign, unless the holder certifies its status as a non-U.S. holder and satisfies certain other requirements, or otherwise establishes an exemption. Generally, information reporting and backup withholding will not apply to a payment of disposition proceeds to a non-U.S. holder where the transaction is effected outside the U.S. through a non-U.S. office of a broker. However, for information reporting purposes, dispositions effected through a non-U.S. office of a broker with substantial U.S. ownership or operations generally will be treated in a manner similar to dispositions effected through a U.S. office of a broker.

Non-U.S. holders should consult their tax advisors regarding the application of the information reporting and backup withholding rules to them. Copies of information returns may be made available to the tax authorities of the country in which the non-U.S. holder resides or is incorporated under the provisions of a specific treaty or agreement. Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules from a payment to a non-U.S. holder can be refunded or credited against the non-U.S. holder's U.S. federal income tax liability, if any, provided that an appropriate claim is filed with the IRS in a timely manner.

Withholding and information reporting requirements FATCA

Edgar Filing: Sage Therapeutics, Inc. - Form 424B5

Provisions of the Code commonly referred to as the Foreign Account Tax Compliance Act, or FATCA, generally impose a U.S. federal withholding tax at a rate of 30% on payments of dividends on our common stock paid to a foreign entity unless (i) if the foreign entity is a foreign financial institution, such foreign entity undertakes

S-40

Table of Contents

certain due diligence, reporting, withholding, and certification obligations, (ii) if the foreign entity is not a foreign financial institution, such foreign entity identifies certain of its U.S. investors, if any, or (iii) the foreign entity is otherwise exempt under FATCA. Such withholding may also apply to payments of proceeds of sales or other dispositions of our common stock, although under recently proposed U.S. Treasury Regulations no withholding would apply to payments of gross proceeds. The preamble to the proposed regulations specifies that taxpayers (including withholding agents) are permitted to rely on the proposed regulations pending finalization. Under certain circumstances, a non-U.S. holder may be eligible for refunds or credits of this withholding tax. An intergovernmental agreement between the U.S. and an applicable foreign country may modify the requirements described in this paragraph. Non-U.S. holders should consult their tax advisors regarding the possible implications of this legislation on their investment in our common stock and the entities through which they hold our common stock, including, without limitation, the process and deadlines for meeting the applicable requirements to prevent the imposition of the 30% withholding tax under FATCA.

The preceding discussion of U.S. federal income tax considerations is for general information only. It is not tax advice. Each prospective investor should consult its own tax advisor regarding the particular U.S. federal, state and local and non-U.S. tax consequences of purchasing, holding and disposing of our common stock, including the consequences of any proposed change in applicable laws.

Table of Contents

Legal matters

Certain legal matters with respect to the securities offered by this prospectus supplement will be passed upon for us by Goodwin Procter LLP, Boston, Massachusetts. Certain legal matters will be passed upon for the underwriters by Ropes & Gray LLP, Boston, Massachusetts.

Experts

The financial statements and management's assessment of the effectiveness of internal control over financial reporting (which is included in Management's Report on Internal Control over Financial Reporting) incorporated in this prospectus supplement by reference to the Annual Report on Form 10-K for the year ended December 31, 2018 have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

S-42

Table of Contents

PROSPECTUS

Sage Therapeutics, Inc.

Common Stock

Preferred Stock

Warrants

Units

Debt Securities

By this prospectus, we or any selling stockholder may offer and sell from time to time, in one or more offerings, common stock, preferred stock, warrants, debt securities or any combination thereof as described in this prospectus. The warrants may be convertible into or exercisable or exchangeable for common stock or preferred stock, the preferred stock may be convertible into or exchangeable for common stock and the debt securities may be convertible into or exchangeable for common stock or preferred stock. You should carefully read this prospectus, any prospectus supplement and any free writing prospectus, as well as any documents incorporated in any of the foregoing by reference, before you invest in our securities. This prospectus may not be used to sell our securities unless accompanied by a prospectus supplement. The prospectus supplement or any related free writing prospectus may also add to, update, supplement or clarify information contained in this prospectus.

Our common stock is traded on The NASDAQ Global Market under the symbol **SAGE**.

We or any selling stockholder may offer and sell our securities to or through one or more agents, underwriters, dealers or other third parties or directly to one or more purchasers on a continuous or delayed basis. If agents, underwriters or dealers are used to sell our securities, we or any selling stockholder will name them and describe their compensation in a prospectus supplement. The price to the public of our securities and the net proceeds we expect to receive from the sale of such securities will also be set forth in a prospectus supplement. We will not receive any proceeds from the sale of securities by selling stockholders.

INVESTING IN OUR SECURITIES INVOLVES A HIGH DEGREE OF RISK. YOU SHOULD REVIEW CAREFULLY THE RISKS AND UNCERTAINTIES REFERENCED UNDER THE HEADING RISK FACTORS ON PAGE 7 OF THIS PROSPECTUS AS WELL AS THOSE CONTAINED IN THE APPLICABLE PROSPECTUS SUPPLEMENT AND ANY RELATED FREE WRITING PROSPECTUS, AND IN THE OTHER DOCUMENTS THAT ARE INCORPORATED BY REFERENCE INTO THIS PROSPECTUS OR THE APPLICABLE PROSPECTUS SUPPLEMENT.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is December 18, 2018.

Table of Contents**TABLE OF CONTENTS**

| | Page |
|--|-------------|
| <u>ABOUT THIS PROSPECTUS</u> | 1 |
| <u>WHERE YOU CAN FIND ADDITIONAL INFORMATION</u> | 3 |
| <u>INCORPORATION OF CERTAIN INFORMATION BY REFERENCE</u> | 4 |
| <u>CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS</u> | 5 |
| <u>RISK FACTORS</u> | 7 |
| <u>ABOUT THE COMPANY</u> | 8 |
| <u>DESCRIPTION OF SECURITIES</u> | 9 |
| <u>USE OF PROCEEDS</u> | 11 |
| <u>SELLING STOCKHOLDERS</u> | 12 |
| <u>PLAN OF DISTRIBUTION</u> | 13 |
| <u>LEGAL MATTERS</u> | 15 |
| <u>EXPERTS</u> | 15 |

We are responsible for the information contained and incorporated by reference in this prospectus, in any accompanying prospectus supplement, and in any related free writing prospectus we prepare or authorize. We have not authorized anyone to give you any other information, and we take no responsibility for any other information that others may give you. If you are in a jurisdiction where offers to sell, or solicitations of offers to purchase, the securities offered by this documentation are unlawful, or if you are a person to whom it is unlawful to direct these types of activities, then the offer presented in this document does not extend to you. The information contained in this document speaks only as of the date of this document, unless the information specifically indicates that another date applies. Our business, financial condition, results of operations and prospectus may have changed since those dates.

Table of Contents

ABOUT THIS PROSPECTUS

This prospectus is part of an automatic shelf registration statement that we filed with the Securities and Exchange Commission, or the SEC, as a well-known seasoned issuer as defined in Rule 405 under the Securities Act of 1933, as amended, or the Securities Act. Under this shelf registration, we and/or selling stockholders may offer shares of our common stock and preferred stock, various series of warrants to purchase common stock or preferred stock, debt securities or any combination thereof, from time to time in one or more offerings. This prospectus only provides you with a general description of the securities we and/or selling stockholders may offer. Each time we and/or selling stockholders offer a type or series of securities under this prospectus, we will provide a prospectus supplement that will contain more specific information about the specific terms of the offering. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to these offerings. This prospectus may not be used to sell our securities unless accompanied by a prospectus supplement. Each such prospectus supplement and any free writing prospectus that we may authorize to be provided to you may also add, update or change information contained in this prospectus or in documents incorporated by reference into this prospectus. We urge you to carefully read this prospectus, any applicable prospectus supplement and any related free writing prospectus, together with the information incorporated herein by reference as described under the headings **Where You Can Find Additional Information** and **Incorporation of Certain Information by Reference** before you invest in our securities.

Neither we nor any selling stockholder have authorized anyone to provide you with information in addition to or different from that contained in this prospectus, any applicable prospectus supplement and any related free writing prospectus. We take no responsibility for, and can provide no assurances as to the reliability of, any information not contained in this prospectus, any applicable prospectus supplement or any related free writing prospectus that we or a selling stockholder may authorize to be provided to you. This prospectus is an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. You should assume that the information in this prospectus, any applicable prospectus supplement or any related free writing prospectus is accurate only as of the date on the front of the document and that any information incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus, any applicable prospectus supplement or any related free writing prospectus, or any sale of a security.

This prospectus contains summaries of certain provisions contained in some of the documents described herein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been filed, will be filed or will be incorporated by reference as exhibits to the registration statement of which this prospectus is a part, and you may obtain copies of those documents as described below under the heading **Where You Can Find Additional Information**.

Unless otherwise mentioned or unless the context requires otherwise, throughout this prospectus, any applicable prospectus supplement and any related free writing prospectus, the words **SAGE**, **Sage**, **we**, **us**, **our**, the **company** or similar references refer to Sage Therapeutics, Inc. and its subsidiaries; and the term **securities** refers collectively to our common stock, preferred stock, warrants to purchase common stock or preferred stock, debt securities, or any combination of the foregoing securities.

We own various U.S. federal trademark registrations and applications and unregistered trademarks, including our corporate logo. This prospectus and the information incorporated herein by reference contains references to trademarks, service marks and trade names owned by us or other companies. Solely for convenience, trademarks, service marks and trade names referred to in this prospectus and the information incorporated herein, including logos, artwork, and other visual displays, may appear without the ® or ™ symbols, but such references are not intended to

indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensor to these trademarks, service marks and trade names. We do not intend our use or display of other companies' trade names, service marks or trademarks to imply a relationship with, or

Table of Contents

endorsement or sponsorship of us by, any other companies. All trademarks, service marks and trade names included or incorporated by reference into this prospectus, any applicable prospectus supplement or any related free writing prospectus are the property of their respective owners.

Table of Contents

WHERE YOU CAN FIND ADDITIONAL INFORMATION

This prospectus is part of a registration statement that we have filed with the SEC. Certain information in the registration statement has been omitted from this prospectus in accordance with the rules of the SEC. We are subject to the information requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act, and, in accordance therewith, file annual, quarterly and special reports, proxy statements and other information with the SEC. You may read and copy any document we file at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C., 20549. You may call the SEC at 1-800-SEC-0330 for further information on the operation of the Public Reference Room. These documents also may be accessed through the SEC's Electronic Data Gathering, Analysis and Retrieval system, or EDGAR, via electronic means, including the SEC's home page on the Internet (*www.sec.gov*).

We have the authority to designate and issue more than one class or series of stock having various preferences, conversion and other rights, voting powers, restrictions, limitations as to dividends, qualifications and terms and conditions of redemption. See Description of Securities. We will furnish a full statement of the relative rights and preferences of each class or series of our stock which has been so designated and any restrictions on the ownership or transfer of our stock to any stockholder upon request and without charge. Written requests for such copies should be directed to Sage Therapeutics, Inc., 215 First Street, Cambridge, Massachusetts, 02142, Attention: Secretary, or by telephone request to (617) 299-8380. Our website is located at *http://www.sagerx.com*. Information contained on our website is not incorporated by reference into this prospectus, and you should not consider any information on, or that can be accessed from, our website as part of this prospectus or any accompanying prospectus supplement.

Table of Contents

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference the information and reports we file with it, which means that we can disclose important information to you by referring you to these documents. The information incorporated by reference is an important part of this prospectus, and information that we file after the date hereof with the SEC will automatically update and supersede the information already incorporated by reference. We are incorporating by reference the documents listed below, which we have already filed with the SEC, and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, except as to any portion of any future report or document that is not deemed filed under such provisions, after the date of this prospectus and prior to the termination of this offering:

Annual Report on Form 10-K for the year ended December 31, 2017, as filed with the SEC on February 22, 2018;

The information specifically incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2017, from our definitive proxy statement on Schedule 14A (other than information furnished rather than filed), which was filed with the SEC on April 30, 2018;

Quarterly Report on Form 10-Q filed with the SEC for the quarters ended March 31, 2018, June 30, 2018, and September 30, 2018, as filed with the SEC on May 3, 2018, August 7, 2018 and November 6, 2018, respectively;

Current Reports on Form 8-K filed with the SEC on January 8, 2018, January 31, 2018, February 7, 2018, February 9, 2018, February 13, 2018, February 22, 2018, May 3, 2018, May 30, 2018, June 8, 2018, June 12, 2018, June 14, 2018, August 7, 2018, November 2, 2018, November 6, 2018, and November 20, 2018 (in each case, except for information contained therein which is furnished rather than filed); and

The description of our common stock contained in our registration statement on Form 8-A, which was filed with the SEC on July 15, 2014, including any amendment or report filed for the purpose of updating such description.

Upon request, we will provide, without charge, to each person, including any beneficial owner, to whom a copy of this prospectus is delivered a copy of the documents incorporated by reference into this prospectus. You may request a copy of these filings, and any exhibits we have specifically incorporated by reference as an exhibit in this prospectus, at no cost by writing or telephoning us at the following:

Sage Therapeutics, Inc., 215 First Street, Cambridge, Massachusetts, 02142, Attention: Secretary, (617) 299-8380.

You may also access these documents, free of charge on the SEC's website at www.sec.gov or on our website at www.sagerx.com. Information contained on our website is not incorporated by reference into this prospectus, and you should not consider any information on, or that can be accessed from, our website as part of this prospectus or any accompanying prospectus supplement.

Edgar Filing: Sage Therapeutics, Inc. - Form 424B5

This prospectus is part of a registration statement we filed with the SEC. We have incorporated exhibits into this registration statement. You should read the exhibits carefully for provisions that may be important to you.

Neither we nor any selling stockholder have authorized anyone to provide you with information other than what is incorporated by reference or provided in this prospectus or any prospectus supplement. Neither we nor any selling stockholder are making an offer of these securities in any state where such offer is not permitted. You should not assume that the information in this prospectus or in the documents incorporated by reference is accurate as of any date other than the date on the front of this prospectus or those documents.

Table of Contents

CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, including the documents that we incorporate by reference, contains forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act. Any statements about our expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and may be forward-looking. These statements are often, but are not always, made through the use of words or phrases such as may, will, could, should, expects, intends, plans, anticipates, believes, estimates, predicts, continue, and similar expressions, or the negative of these terms, or similar expressions. Accordingly, these statements involve estimates, assumptions and uncertainties which could cause actual results to differ materially from those expressed in them. Any forward-looking statements are qualified in their entirety by reference to the factors discussed throughout this prospectus, and in particular those factors referenced in the section Risk Factors.

This prospectus, including the sections entitled About this Prospectus and Risk Factors, contains forward-looking statements that are based on our management's belief and assumptions and on information currently available to our management. These statements relate to future events or our future financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements. Forward-looking statements include, but are not limited to, statements about:

the accuracy of our estimates regarding expenses, use of cash, the potential for future revenues, timing of future cash needs, and our ability to obtain additional financing when needed;

the initiation, timing, progress and results of our clinical trials, nonclinical studies, and research and development programs, including our ability to complete successfully, within expected time frames, our ongoing and future clinical trials and nonclinical studies and to advance our product candidates to the next stages of development;

our plans with respect to filing for regulatory approval for our product candidates if development is successful, and the potential to obtain regulatory approval of our product candidates and to commercialize our products, if approval is obtained;

our plans and expectations with respect to potential future commercial activities, if regulatory approval for our product candidates is obtained;

the implementation of our business model, strategic plans for our business, product candidates and technology; and

the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates and technology.

These forward-looking statements are neither promises nor guarantees of future performance, and are subject to a variety of risks and uncertainties, many of which are beyond our control, which could cause actual results to differ materially from those indicated by these forward-looking statements, including, without limitation: the potential that future clinical and non-clinical results may not support further development of our product candidates; the potential for unexpected adverse events to impact our ability to continue clinical trials or further development of a product candidate or to impact commercialization of any marketed product; the risk that we may not be successful in our efforts to obtain regulatory approval of any product candidate; the risk that we may not be successful in our commercialization efforts with respect to products, if any, that receive regulatory approval; the risk that we may encounter delays or other unexpected hurdles or issues in the development or manufacture of our product candidates or in connection with the commercialization of approved products, if any, that may impact our timing, progress, results or financial expectations, as well as those risks more fully discussed in the Risk Factors section and under the sections of any accompanying prospectus supplement entitled Risk Factors and the risk factors and cautionary statements described in other documents that we file from time to

Table of Contents

time with the SEC, specifically under Item 1A: Risk Factors and elsewhere in our most recent Annual Report on Form 10-K for the period ending December 31, 2017, our Quarterly Reports on Form 10-Q and our Current Reports on Form 8-K.

Given these uncertainties, readers should not place undue reliance on our forward-looking statements. These forward-looking statements speak only as of the date on which the statements were made and are not guarantees of future performance. Except as may be required by applicable law, we do not undertake to update any forward-looking statements after the date of this prospectus supplement or the respective dates of documents incorporated by reference herein or therein that include forward-looking statements.

Table of Contents

RISK FACTORS

Investing in our securities involves a high degree of risk. You should carefully consider the risks described in the documents incorporated by reference in this prospectus and any prospectus supplement, as well as other information we include or incorporate by reference into this prospectus and any applicable prospectus supplement, before making an investment decision. Our business, financial condition or results of operations could be materially adversely affected by the materialization of any of these risks. The trading price of our securities could decline due to the materialization of any of these risks, and you may lose all or part of your investment. This prospectus and the documents incorporated herein by reference also contain forward-looking statements that involve risks and uncertainties. Actual results could differ materially from those anticipated in these forward-looking statements as a result of certain factors, including the risks described in the documents incorporated herein by reference, including (i) our most recent Annual Report on Form 10-K for the year ended December 31, 2017, which is on file with the SEC and is incorporated by reference into this prospectus, (ii) our most recent quarterly report on Form 10-Q for the quarterly period ended September 30, 2018, which is on file with the SEC and is incorporated by reference into this prospectus, and (iii) other documents we file with the SEC that are deemed incorporated by reference into this prospectus.

Table of Contents

ABOUT THE COMPANY

We are a clinical-stage biopharmaceutical company committed to developing novel medicines to transform the lives of patients with life-altering central nervous system disorders. We have a portfolio of novel product candidates targeting critical CNS receptor systems, GABA_A and NMDA. Our lead program, ZULRESSO (brexanolone) injection, a proprietary IV formulation of brexanolone, has completed Phase 3 clinical development for postpartum depression and a new drug application is currently under review with the U.S. Food and Drug Administration. We are developing next generation modulators, including SAGE-217, SAGE-324 and SAGE-718, in various CNS disorders.

We were incorporated under the laws of the state of Delaware in April 2010. Our principal executive office is located at 215 First Street, Cambridge, Massachusetts, 02142, and our telephone number is (617) 299-8380. Our website address is www.sagerx.com. The information on, or that can be accessed through, our website does not constitute part of this prospectus, and you should not rely on any such information in making the decision whether to purchase our common stock. Our common stock trades on The NASDAQ Global Market under the symbol SAGE .

Table of Contents

DESCRIPTION OF SECURITIES

We and/or any selling stockholder may offer shares of our common stock and preferred stock, various series of warrants to purchase common stock or preferred stock, debt securities, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt, or any combination thereof from time to time in one or more offerings under this prospectus at prices and on terms to be determined at the time of any offering. This prospectus provides you with a general description of the securities we and/or any selling stockholder may offer. Each time we and/or any selling stockholder offer a type or series of securities under this prospectus, we will provide a prospectus supplement and/or free writing prospectus that will describe the specific amounts, prices and other important terms of the securities.

Common Stock. We and/or any selling stockholder may issue and/or sell, as applicable, shares of our common stock from time to time. Holders of shares of our common stock are entitled to one vote for each share held of record on all matters to be voted on by stockholders and do not have cumulative voting rights. Subject to the preferences that may be applicable to any then outstanding preferred stock, the holders of our outstanding shares of common stock are entitled to receive dividends, if any, as may be declared from time to time by our board of directors out of legally available funds. In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities, subject to the satisfaction of any liquidation preference granted to the holders of any outstanding shares of preferred stock.

Preferred Stock. We may issue shares of our preferred stock from time to time, in one or more series. Our board of directors will determine the rights, preferences and privileges of the shares of each wholly unissued series, and any qualifications, limitations or restrictions thereon, including dividend rights, conversion rights, preemptive rights, terms of redemption or repurchase, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of any series. Convertible preferred stock will be convertible into our common stock or exchangeable for other securities. Conversion may be mandatory or at the holder's option and would be at prescribed conversion rates.

If we sell any series of preferred stock under this prospectus, we will fix the rights, preferences and privileges of the preferred stock of such series, as well as any qualifications, limitations or restrictions thereon, in the certificate of designation relating to that series. We will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of any certificate of designation that describes the terms of the series of preferred stock we are offering before the issuance of that series of preferred stock. We urge you to read the applicable prospectus supplement and any free writing prospectus that we may authorize to be provided to you related to the series of preferred stock being offered, as well as the complete certificate of designation that contains the terms of the applicable series of preferred stock.

Warrants. We may issue warrants for the purchase of common stock and/or preferred stock in one or more series. We may issue warrants independently or together with common stock and/or preferred stock, and the warrants may be attached to or separate from these securities. We urge you to read the applicable prospectus supplement and any free writing prospectus that we may authorize to be provided to you related to the particular series of warrants being offered, as well as the complete warrant agreements and warrant certificates that contain the terms of the warrants. Forms of the warrant agreements and forms of warrant certificates containing the terms of the warrants being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

We will evidence each series of warrants by warrant certificates that we will issue. Warrants may be issued under an applicable warrant agreement that we enter into with a warrant agent. We will indicate the name and address of the warrant agent, if applicable, in the prospectus supplement relating to the particular series of warrants being offered.

Table of Contents

Units. We may issue, in one or more series, units consisting of common stock, preferred stock, and/or warrants for the purchase of common stock and/or preferred stock in any combination. We urge you to read the applicable prospectus supplement and any free writing prospectus that we may authorize to be provided to you related to the series of units being offered, as well as the complete unit agreement that contains the terms of the units. We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of unit agreement and any supplemental agreements that describe the terms of the series of units we are offering before the issuance of the related series of units.

We will evidence each series of units by unit certificates that we will issue. Units may be issued under a unit agreement that we enter into with a unit agent. We will indicate the name and address of the unit agent, if applicable, in the prospectus supplement relating to the particular series of units being offered.

Debt Securities. We may issue debt securities, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. The features of any debt securities we issue will be described in a prospectus supplement. We urge you, however, to read the applicable prospectus supplement and any free writing prospectus that we may authorize to be provided to you related to the particular series of debt securities being offered, as well as the complete indenture that contains the terms of the debt securities. We will file as exhibits to the registration statement of which this prospectus is a part, any supplemental agreements that describe the terms of the series of debt securities we are offering before the issuance of the related series of debt securities.

We may evidence each series of debt securities we will issue by an indenture that we enter into with a trustee. We will indicate the name and address of the trustee, if applicable, in the prospectus supplement relating to the particular series of debt securities being offered.

Table of Contents

USE OF PROCEEDS

Except as described in any prospectus supplement or in any related free writing prospectus that we may authorize to be provided to you, the net proceeds received by us from our sale of the securities described in this prospectus will be added to our general funds and will be used for our general corporate purposes. From time to time, we may engage in additional public or private financings of a character and amount which we may deem appropriate. Unless otherwise set forth in a prospectus supplement, we will not receive any proceeds from the sale of securities by any selling stockholder.

Table of Contents

SELLING STOCKHOLDERS

Selling stockholders are persons or entities that, directly or indirectly, have acquired or will from time to time acquire from us, our securities. Such selling stockholders may be parties to registration rights agreements with us, or we otherwise may have agreed or will agree to register their securities for resale. The initial purchasers of our securities, as well as their transferees, pledges, donees or successors, all of whom we refer to as selling stockholders, may from time to time offer and sell our securities pursuant to this prospectus and any applicable prospectus supplement.

The applicable prospectus supplement will set forth the name of each of the selling stockholders and the number of securities beneficially owned by such selling stockholder that are covered by such prospectus supplement. The applicable prospectus supplement will also disclose whether any of the selling stockholders has held any position or office with, has been employed by or otherwise has had a material relationship with us during the three years prior to the date of the applicable prospectus supplement.

Table of Contents

PLAN OF DISTRIBUTION

We and/or any selling stockholder may sell our securities from time to time in one or more transactions. We and/or any selling stockholder may sell our securities to or through agents, underwriters, dealers, remarketing firms or other third parties or directly to one or more purchasers or through a combination of any of these methods. In some cases, we and/or any selling stockholder or dealers acting with us and/or any selling stockholder or on behalf of us and/or any selling stockholder may also purchase our securities and reoffer them to the public. We and/or any selling stockholder may also offer and sell, or agree to deliver, our securities pursuant to, or in connection with, any option agreement or other contractual arrangement.

Agents whom we designate may solicit offers to purchase our securities.

We and/or any selling stockholder will name any agent involved in offering or selling our securities, and disclose any commissions that we will pay to the agent, in the applicable prospectus supplement.

Unless we and/or any selling stockholder indicate otherwise in the applicable prospectus supplement, agents will act on a best efforts basis for the period of their appointment.

Agents may be deemed to be underwriters under the Securities Act, of any of our securities that they offer or sell.

We and/or any selling stockholder may use an underwriter or underwriters in the offer or sale of our securities.

If we and/or any selling stockholder use an underwriter or underwriters, we will execute an underwriting agreement with the underwriter or underwriters at the time that we reach an agreement for the sale of our securities.

We and/or any selling stockholder will include the names of the specific managing underwriter or underwriters, as well as the names of any other underwriters, and the terms of the transactions, including the compensation the underwriters and dealers will receive, in the applicable prospectus supplement.

The underwriters will use the applicable prospectus supplement, together with the prospectus, to sell our securities.

We may use a dealer to sell our securities.

If we and/or any selling stockholder use a dealer, we will sell our securities to the dealer, as principal.

The dealer will then sell our securities to the public at varying prices that the dealer will determine at the time it sells our securities.

We and/or any selling stockholder will include the name of the dealer and the terms of the transactions with the dealer in the applicable prospectus supplement.

We and/or any selling stockholder may solicit directly offers to purchase our securities, and we may directly sell our securities to institutional or other investors. We and/or any selling stockholder will describe the terms of direct sales in the applicable prospectus supplement.

We and/or any selling stockholder may engage in at-the-market offerings into an existing trading market in accordance with Rule 415(a)(4) of the Securities Act.

We and/or any selling stockholder will indemnify agents, underwriters and dealers against certain liabilities, including liabilities under the Securities Act. Agents, underwriters and dealers, or their affiliates, may be customers of, engage in transactions with or perform services for us or our respective affiliates, in the ordinary course of business.

Table of Contents

We and/or any selling stockholder may authorize agents and underwriters to solicit offers by certain institutions to purchase our securities at the public offering price under delayed delivery contracts.

If we and/or any selling stockholder use delayed delivery contracts, we will disclose that we are using them in the prospectus supplement and will tell you when we will demand payment and when delivery of our securities will be made under the delayed delivery contracts.

These delayed delivery contracts will be subject only to the conditions that we describe in the prospectus supplement.

We and/or any selling stockholder will describe in the applicable prospectus supplement the commission that underwriters and agents soliciting purchases of our securities under delayed delivery contracts will be entitled to receive.

Unless otherwise specified in connection with a particular underwritten offering of our securities, the underwriters will not be obligated to purchase offered securities unless specified conditions are satisfied, and if the underwriters do purchase any offered securities, they will purchase all offered securities.

In connection with underwritten offerings of the offered securities and in accordance with applicable law and industry practice, the underwriters in certain circumstances are permitted to engage in certain transactions that stabilize the price of our securities. Such transactions consist of bids or purchases for the purpose of pegging, fixing or maintaining the price of our securities. If the underwriters create a short position in our securities in connection with the offering (i.e., if they sell more securities than are set forth on the cover page of the applicable prospectus supplement), the underwriters may reduce that short position by purchasing our securities in the open market or as otherwise provided in the applicable prospectus supplement. The underwriters may also impose a penalty bid, whereby selling concessions allowed to dealers participating in the offering may be reclaimed if the securities sold by them are repurchased in connection with stabilization transactions. In general, purchases of a security for the purpose of stabilization or to reduce a short position could cause the price of the security to be higher than it might be in the absence of such purchases. The imposition of a penalty bid might also have an effect on the price of our securities to the extent that it were to discourage resales of our securities. The underwriters are not required to engage in these activities and may end any of these activities at any time.

We and/or any selling stockholder may effect sales of securities in connection with forward sale, option or other types of agreements with third parties. Any distribution of securities pursuant to any forward sale agreement may be effected from time to time in one or more transactions that may take place through a stock exchange, including block trades or ordinary broker's transactions, or through broker-dealers acting either as principal or agent, or through privately-negotiated transactions, or through an underwritten public offering, or through a combination of any such methods of sale, at market prices prevailing at the time of sale, prices relating to such prevailing market prices or at negotiated or fixed prices.

The specific terms of the lock-up provisions, if any, in respect of any given offering will be described in the applicable prospectus supplement.

In compliance with the guidelines of the Financial Industry Regulatory Authority, or FINRA, the maximum consideration or discount to be received by any FINRA member or independent broker dealer may not exceed 8.0% of

the aggregate amount of the securities offered by this prospectus.

Table of Contents

LEGAL MATTERS

The validity of the securities being offered by this prospectus will be passed upon by Goodwin Procter LLP, Boston, Massachusetts.

EXPERTS

The financial statements and management's assessment of the effectiveness of internal control over financial reporting (which is included in Management's Report on Internal Control over Financial Reporting) incorporated in this Prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2017 have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

Table of Contents

\$500,000,000

Sage Therapeutics, Inc.

Common stock

Prospectus supplement

Goldman Sachs & Co. LLC

J.P. Morgan

, 2019