UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of The Securities Exchange Act of 1934

Date of Report (Date of Earliest Event Reported): October 15, 2020

Sage Therapeutics, Inc.
(Exact name of registrant as specified in its charter)

DELAWARE	001-36544	27-4486580
(State or other jurisdiction of incorporation)	(Commission File Number)	(I.R.S. Employer Identification No.)

215 First Street Cambridge, MA	02142
(Address of principal executive offices)	(Zip Code)

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

Not Applicable
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

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

Title of each class	Trading symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.0001 per share	**SAGE**	**The Nasdaq Global Market**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☐

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

Item 8.01 Other Events.

On October 15, 2020, Sage Therapeutics, Inc. (the "Company") issued a press release announcing interim, topline data from the Company's ongoing Phase 3 open-label SHORELINE study evaluating zuranolone (SAGE-217) in the treatment of patients with major depressive disorder. A copy of the press release is filed as Exhibit 99.1 hereto and is incorporated by reference herein.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Press release issued by Sage Therapeutics, Inc. on October 15, 2020.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

SIGNATURES

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

Date: October 15, 2020

SAGE THERAPEUTICS, INC.

By: /s/ Jennifer Fitzpatrick
Jennifer Fitzpatrick
Vice President, Corporate Counsel

Sage Therapeutics Announces Positive Interim, Topline Zuranolone Safety and Tolerability Data from Open-Label SHORELINE Study in Patients with MDD

Zuranolone was generally well-tolerated at the 30 mg dose and by the initial patients treated with the 50 mg dose with an adverse event profile consistent with that seen in earlier trials

Nearly half of trial participants with positive response to initial 14-day course of zuranolone 30 mg did not need an additional zuranolone treatment course

For those who needed retreatment with the 30 mg dose, safety, tolerability and efficacy results were similar to those seen in the initial treatment course

CAMBRIDGE, Mass. – October 15, 2020 – Sage Therapeutics, Inc. (NASDAQ: SAGE), a biopharmaceutical company committed to developing novel therapies with the potential to transform the lives of people with debilitating brain disorders, today reported interim, topline results from a July data cut of the ongoing Phase 3 open-label SHORELINE Study. This clinical study was designed to naturalistically follow patients with major depressive disorder (MDD) and evaluate the safety and tolerability of zuranolone 30 mg in adults for up to one year. In May 2020, the protocol was amended to include a 50 mg dose of zuranolone. For the primary endpoint of safety and tolerability, the data analyzed to date show that zuranolone was generally well-tolerated in the 30 mg dose and among the initial patients treated with the 50 mg dose. Adverse events reported in the trial during the period analyzed were generally consistent with results seen in previous clinical trials.

Secondary endpoints included response and remission as evaluated by the 17-item Hamilton Rating Scale for Depression (HAMD-17) and the number of times a patient received retreatment. At the time of this analysis, patients with a clinical response (decrease in HAMD-17 baseline score of ³50%) to the initial 14-day course of zuranolone 30 mg used a mean number of 1.9 treatments per year. As the first naturalistic, longitudinal, clinical development trial conducted in MDD, the SHORELINE Study provides real world insight into the potential use of zuranolone, if successfully developed and approved as an as-needed treatment for MDD, and builds on the data assembled in the LANDSCAPE clinical program. The Company plans to report comprehensive data from the 30 mg dose in the first half of 2021 and will include additional subsets of data within the primary and secondary endpoints. Select data will be reserved for presentation at medical and scientific conferences and in peer-reviewed journal articles.

“This data from the SHORELINE Study show that medically-oriented, as needed treatment for depression has the potential to be a compelling option for many patients diagnosed with MDD,” said Jeff Jonas, M.D., chief executive officer at Sage Therapeutics. “Approximately 70% of patients who participated in the study only needed one or two treatment courses, a total of two to four weeks of treatment with zuranolone 30 mg, which we believe will be the minimally effective dose, if our development efforts are successful.”

Zuranolone 30 mg: Summary of July Results from SHORELINE Study

Sage’s Phase 3 SHORELINE Study is evaluating the safety and tolerability of zuranolone 30 mg and 50 mg in adults 18-75 who have MDD as defined by a baseline HAMD-17 total score ³20. The original study design included a zuranolone 30 mg dose administered once nightly for 14 days.

- 725 people with MDD (HAM-D ³ 20) were treated with a first dose of zuranolone 30 mg once daily for 14 days.
- The mean baseline HAM-D score (± SD) at entry into the study was 25.3 ± 4.1 (n=725).
- Of the 725 patients treated, 143 (19.7%) did not achieve response to the first course and exited the study. Subjects were required by protocol to achieve response to continue into the naturalistic follow-up period.

- At Day 15 of the initial course of patients who only received 30 mg in the study, the mean change from baseline was -14.9 ± 7.1 (n=640); 458 (71.6%) patients achieved response and 255 (39.8%) achieved remission (HAM-D £ 7).
- 304 (42%) patients were on pre-existing antidepressant therapy (ADT) which was continued, while 421 (58%) were on no ADT; there were no meaningful differences in efficacy outcomes between the two groups.

Safety and tolerability of initial treatment:

- In this first course of treatment with zuranolone 30 mg, the adverse events experienced by patients were similar in nature and frequency to those previously reported for completed zuranolone studies, with 447 (61.7%) patients reporting at least one adverse event.
- The most common adverse events (reported ³ 5%) were: somnolence (69; 9.5%), headache (63; 8.7%), and dizziness (39; 5.4%). Most adverse events were mild or moderate.
- Similar adverse events were reported regardless of the presence or absence of ADT.
- Causes of adverse event-related discontinuations during the 14-day course of treatment were varied, with the most common being dizziness, anxiety, or nausea (n=2 each). The overall rate of discontinuation due to treatment-emergent adverse events was 2.2%
- No events of loss of consciousness were reported at any time during the study.

Retreatment:

Among the 494 patient responders from the initial treatment cycle continuing in the study, 274 (55.5%) of patients used zuranolone in retreatment one or more times, while the remaining 220 (44.5%) were not retreated during their participation in the study.

- Of the 494 patients continuing in the study, 220 (44.5%) patients used only the single initial zuranolone course, while 132 (26.7%) used a total of 2 courses, 66 (13.4%) used a total of 3 courses, 51 (10.3%) used a total of 4 courses, and 27 (5.5%) used a total of 5 courses.
- The number of zuranolone retreatments used were similar regardless of the presence or absence of ADT.
- For patients using one or more retreatments with zuranolone, overall AE rates in treatment courses with greater than 50 patients were 151 (53.7%), 56 (38.1%), and 28 (35.9%) for the second, third, and fourth treatment courses, respectively.
- For those patients that used one or more retreatments, outcomes on efficacy measures and safety events were similar to those observed in the initial treatment course; and the presence or absence of ADTs did not change the results.

Initial Experience with Zuranolone 50 mg Dosing:

In May 2020, standard dosing with zuranolone in the SHORELINE Study was increased to 50 mg. Patients who started treatment at the 30 mg dose and were retreated after May 2020 started receiving zuranolone 50 mg rather than 30 mg. A new cohort of patients starting treatment at 50 mg was also initiated in May 2020.

- In this interim sample of patients who received zuranolone 50 mg after having received 30 mg previously (n=48), higher rates and levels of intensity with AEs of >5% (sedation, somnolence) were noted. Most adverse events were mild or moderate.
- In the 76 (38%) patients with safety data available from the 50 mg cohort, the adverse event profile was similar to that seen in patients who received 30 mg zuranolone. Events >5% of somnolence, dizziness, sedation, headache and tremor were observed to be more frequent in the 50 mg cohort, but were similar in severity to the events seen with 30 mg. Most adverse events were mild or moderate.
- For new 50 mg cohort (n=52) the mean HAM-D baseline score was 25.1 ± 3.1.
- At Day 15 of the initial course in this group, the mean HAM-D change from baseline was -15.9 ± 6.6; 39 (75.0%) achieved response and 25 (48.1%) achieved remission.

About the SHORELINE Study

The SHORELINE Study (217-MDD-303) is a Phase 3, open-label, 1-year longitudinal study evaluating the safety, tolerability, and need for repeat dosing with zuranolone in adults with MDD. The study comprises two cohorts, one with zuranolone 30 mg as a starting dose and one with zuranolone 50 mg as a starting dose both administered once nightly for 14 days. The need for repeated dosing is assessed every 14 days based on the results of a patient-reported PHQ-9 (³10) and HAMD-17 (³20) assessment. There was a minimum of 56 days between zuranolone 14-day courses, to allow for a maximum of five treatments for the follow-up period.

About Major Depressive Disorder

Major depressive disorder (MDD) is a common but serious mood disorder in which people experience depressive symptoms that impair their social, occupational, educational or other important functioning, such as a depressed mood or loss of interest or pleasure in daily activities, consistently for at least a two-week period. It is estimated that approximately 17 million people in the U.S. suffer from MDD each year. While antidepressants are widely used to treat MDD, large-scale studies have demonstrated the need for additional therapies.

About Zuranolone

Zuranolone (SAGE-217) is a once-daily, two-week therapy in development for the treatment of major depressive disorder (MDD) and postpartum depression (PPD). Zuranolone is an investigational oral neuroactive steroid (NAS) $GABA_A$ receptor positive allosteric modulator (PAM). The GABA system is the major inhibitory signaling pathway of the brain and central nervous system and contributes significantly to regulating brain function. Zuranolone has been granted Breakthrough Therapy Designation by the U.S. Food & Drug Administration.

About Sage Therapeutics

Sage Therapeutics is a biopharmaceutical company committed to developing novel therapies with the potential to transform the lives of people with debilitating disorders of the brain. We are pursuing new pathways with the goal of improving brain health, and our depression, neurology and neuropsychiatry franchise programs aim to change how brain disorders are thought about and treated. Our mission is to make medicines that matter so people can get better, sooner. For more information, please visit www.sagerx.com.

Forward-Looking Statements

Various statements in this release concern Sage's future expectations, plans and prospects, including without limitation: our views and expectations regarding: our plans and expected timelines; our belief in the potential profile and benefit of zuranolone, and the potential for successful development and approval;; our estimates as to the number of patients with MDD; the potential of our other product candidates, and the goals, opportunity and potential for our business. These statements constitute forward-looking statements as that term is defined in the Private Securities Litigation Reform Act of 1995. 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 contemplated in these forward-looking statements, including the risks that: results from interim data cuts from a clinical study may not be reflective of the results that will be achieved in the full study once completed; success in our non-clinical studies or in earlier clinical trials may not be repeated or observed in ongoing or future studies, and ongoing and future non-clinical and clinical results may not meet their primary or key secondary endpoints or be sufficient to file for or gain regulatory approval to market a product without further development work or may not support further development at all; we may encounter adverse results or adverse events at any stage of development that negatively impact further development or that require additional nonclinical and clinical work which may not yield positive results; we may encounter different or more severe adverse events at the higher doses we are studying in our new trials; we may encounter issues with the efficacy or durability of short-term treatment, or co-initiated treatment with zuranolone or safety and efficacy concerns with respect to retreatment that require additional studies be conducted; we may encounter delays in initiation or conduct of our ongoing and planned clinical trials, including slower than expected site initiation or enrollment, that

may impact our ability to meet our expected time-lines and increase our costs; we may not be able to mitigate the impact of COVID-19 on our clinical development timelines and the impact may be more significant than we expect and may negatively impact expected site initiation, enrollment or conduct in our clinical trials, or cause us to pause trials or not be able to use data, in each case which may significantly impact our ability to meet our expected time-lines or may significantly impact the integrity or sufficiency of the data from our trials or increase our costs or cause us to have to change our plans; the FDA may ultimately decide that the design or results of our completed and planned clinical trials for any of our product candidates, even if positive, are not sufficient for regulatory approval in the indications that are the focus of our development plan; other decisions or actions of the FDA or other regulatory agencies may affect the initiation, timing, design, size, progress and cost of clinical trials and our ability to proceed with further development; the actual size of the MDD patient population may be significantly lower than our estimates and, even if zuranolone is approved, it will only be approved or used to treat a subset of the relevant patient populations; we may encounter technical and other unexpected hurdles in the development and manufacture of our product candidates which may delay our timing or change our plans or increase our costs; as well as those risks more fully discussed in the section entitled "Risk Factors" in our most recent Quarterly Report on Form 10-Q, as well as discussions of potential risks, uncertainties, and other important factors in our subsequent filings with the Securities and Exchange Commission. In addition, any forward-looking statements represent our views only as of today, and should not be relied upon as representing our views as of any subsequent date. We explicitly disclaim any obligation to update any forward-looking statements.

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