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): February 16, 2022

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 February 16, 2022, Sage Therapeutics, Inc. issued a press release announcing results from the CORAL Study, a Phase 3 trial comparing zuranolone 50 mg co-initiated with a standard of care antidepressant versus a standard of care antidepressant co-initiated with placebo in 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 February 16, 2022.
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: February 16, 2022

SAGE THERAPEUTICS, INC.

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

Sage Therapeutics and Biogen Announce the Phase 3 CORAL Study Met its Primary and Key Secondary Endpoints - Comparing Zuranolone 50 mg Co-initiated with Standard of Care Antidepressant vs. Standard of Care Co-initiated with Placebo in People with MDD

At the Day 3 primary endpoint, zuranolone 50 mg co-initiated with a standard of care antidepressant showed a statistically significant reduction in depressive symptoms

Key secondary endpoint demonstrates zuranolone co-initiated with an antidepressant was statistically significant in reducing depressive symptoms compared to an antidepressant co-initiated with placebo over the 2-week treatment period

Zuranolone 50 mg co-initiated with a standard of care antidepressant was generally well-tolerated with most TEAEs reported as mild or moderate and no new safety signals identified

Sage Therapeutics to host conference call today at 8:00 a.m. ET

CAMBRIDGE, Mass. – February 16, 2022 – Sage Therapeutics, Inc. (Nasdaq: SAGE), and Biogen Inc. (Nasdaq: BIIB) today announced the CORAL Study in people with major depressive disorder (MDD) met the trial objectives, demonstrating a rapid and statistically significant reduction in depressive symptoms at Day 3 and over the 2-week treatment period, achieving the primary and key secondary endpoints. This significance was demonstrated at the first measured time point, Day 3, with zuranolone 50 mg co-initiated with an open-label standard of care antidepressant (ADT) as assessed by change from baseline in the 17-item Hamilton Rating Scale for Depression (HAMD-17). The CORAL Study also met its key secondary endpoint, with zuranolone co-initiated with a standard of care ADT demonstrating a statistically significant improvement in depressive symptoms compared to ADT co-initiated with placebo, over the 2-week treatment period. Zuranolone was generally well-tolerated, and no new safety signals attributable to zuranolone were identified. In meeting its pre-defined objectives, the CORAL Study supports the potential of zuranolone, when co-initiated with standard of care, to accelerate the benefit of depression treatment compared to treatment with ADTs alone.

The CORAL Study was an active comparator trial comparing the combination of zuranolone 50 mg co-initiated with an active standard of care ADT to standard of care ADT co-initiated with placebo in people with MDD blinded to receipt of zuranolone or placebo. The trial demonstrated a mean change from baseline in HAMD-17 total score of -8.9 ± 0.39 (n=210) at Day 3 for people in the zuranolone co-initiated with ADT arm compared with -7.0 ± 0.38 (n=215) mean change from baseline for people in the ADT co-initiated with placebo arm. The key secondary endpoint measured the treatment effect over the 2-week treatment period at all scheduled visits (measured using equal weighted means for Days 3, 8, 12 and 15 of the study). The mean change over the treatment period for people who received zuranolone co-initiated with an ADT was -11.7 ±0.40 (n=210) compared with -10.1 ±0.39 (n=215) for people who received ADT co-initiated with placebo. Other secondary endpoints demonstrated a statistically significant reduction in HAMD-17 score in the zuranolone co-initiated with ADT arm compared to the ADT arm at Days 8 and 12, while Day 15 demonstrated numerical superiority and Day 42 showed equivalence.

Based on consistent findings suggesting a benefit of zuranolone in people with MDD with elevated anxiety across the LANDSCAPE program, the CORAL Study prospectively examined this population. In this CORAL Study subgroup (n=218 of 425 people (51.3%) with HAM-A total score ≥20 at baseline)

zuranolone co-initiated with an ADT was nominally statistically significant to ADT with placebo in reducing depressive symptoms as measured by the primary endpoint (-9.3 compared to -6.0; HAMD-17 total score change from baseline) and key secondary endpoint (-11.7 compared to -9.4; HAMD-17 total score change from baseline) demonstrating the potential to address the unmet need for this population, which has been historically less responsive to chronically administered ADTs.

“We believe the CORAL Study is clinically meaningful and with the addition of this data the LANDSCAPE program now demonstrates zuranolone has three potential real world uses for the treatment of MDD. The LANDSCAPE data support zuranolone as a monotherapy, and since many people in the previously completed studies were already on maintenance ADTs, we believe our data also support zuranolone as additive therapy. The CORAL Study further supports the use of zuranolone to accelerate the benefit of conventional ADTs in treating MDD with a well-tolerated safety profile,” said Barry Greene, Chief Executive Officer at Sage. “Including the CORAL Study, zuranolone now has six positive clinical studies, and we remain on track to start the rolling submission for a New Drug Application in MDD early this year with completion targeted for the second half of 2022.”

“These positive results from the CORAL Study indicate that zuranolone co-initiated with standard of care may offer more rapid relief from depressive symptoms than current standard of care taken alone,” said Priya Singhal, M.D., M.P.H., Head of Global Safety and Regulatory Sciences and Interim Head of R&D at Biogen. “Based on the collective results observed across the LANDSCAPE clinical development program, we believe that zuranolone has the potential to offer a new clinically meaningful treatment option for people with major depressive disorder.”

In the CORAL Study, zuranolone 50 mg co-initiated with a standard of care ADT was generally well-tolerated with no new safety signals identified. The majority of people in the study experienced treatment emergent adverse events (TEAEs) that were mild or moderate in severity, consistent with previous data in the LANDSCAPE program. The adverse events occurring 10% or higher in the zuranolone plus ADT arm were somnolence (18.4%), dizziness (13.2%) and headache (11.8%). In the ADT plus placebo arm the AEs occurring 10% or greater were headache (14.7%) and nausea (23.4%). The CORAL Study safety data support the known safety profile of zuranolone based on clinical trials to date.

“The CORAL Study results were particularly interesting because the data demonstrated that zuranolone worked within days to provide rapid reduction in depressive symptoms as compared to current ADTs, which in clinical practice can take weeks or months to work,” said Sagar Parikh, MD, Professor of Depression and Clinical Neuroscience, and Psychiatry Sciences, University of Michigan. “In my experience, people with MDD deserve to feel better as soon as possible with a treatment with tolerable side effects. These data suggest that zuranolone has the potential to offer this option and to provide physicians the opportunity to think differently about treating MDD.”

The Phase 3 CORAL Study builds on the foundational data assembled within the LANDSCAPE clinical program to date. Data from this program has been presented at numerous medical and scientific conferences, and the companies plan to present additional data from the CORAL Study in future scientific forums.

CORAL Study Summary Results

The CORAL Study was a Phase 3, randomized, double-blind, placebo-controlled trial, which enrolled 440 people with MDD (n=220 per treatment arm). People in the study received zuranolone 50 mg co-initiated with an open-label standard of care ADT or open-label standard of care ADT co-initiated with placebo once nightly for 14 days. Results for the primary and key secondary efficacy endpoints during the treatment period are outlined in the following table and all favor zuranolone.

- The mean (SD) baseline HAMD-17 score at entry into the study was 26.8 (2.5) in the zuranolone co-initiated with ADT arm and 26.6 (2.6) in the ADT co-initiated with placebo arm.
- 180 (84.9%) people in the study who received zuranolone co-initiated with ADT, and 177 (81.2%) people who received ADT co-initiated with placebo, completed the study.

	Zuranolone 50 mg co-initiated with an ADT LS Mean HAMD-17 Total Score CFB (n= 210)	ADT co-initiated with placebo LS Mean HAMD-17 Total Score CFB (n=215)	p value
Day 3 Primary Endpoint	-8.9	-7.0	0.0004
Key Secondary Endpoint *LS Mean Change in HAMD-17 total score using equal weights for Days 3, 8, 12, and 15 (over the blinded treatment period)*	-11.7	-10.1	0.0054

ADT = antidepressant; CFB = change from baseline; HAMD-17 = 17-item Hamilton Depression Rating Scale; LS Mean = Least Squares Mean

Mean CFB in HAMD-17 Total Score at Each Time Point in the Blinded Treatment Period (Applied to Calculate the Key Secondary Endpoint)

	Zuranolone 50 mg co-initiated with an ADT LS Mean HAMD-17 Total Score CFB	ADT co-initiated with placebo LS Mean HAMD-17 Total Score CFB	p value
Day 3 Primary Endpoint	-8.9	-7.0	0.0004
Day 8	-11.3	-9.2	0.0012
Day 12	-12.8	-11.4	0.0381
Day 15	-13.7	-12.9	0.2477

ADT = antidepressant; CFB = change from baseline; HAMD-17 = 17-item Hamilton Depression Rating Scale; LS Mean = Least Squares Mean

Safety and tolerability of zuranolone 50 mg co-initiated with an ADT:

- Over the study period, the AEs 10% or higher in either treatment arm (zuranolone with an ADT vs. ADT with placebo) were: somnolence (18.4% vs 8.3%), dizziness (13.2% vs 7.3%), headache (11.8% vs 14.7%), and nausea (9.0% vs 23.4%).
- The percentage of people reporting TEAEs leading to discontinuation of study drug were 6.6% in the zuranolone co-initiated with an ADT arm, and 3.7% in the ADT co-initiated placebo arm, respectively. Similarly, the percentage of people reporting TEAEs leading to discontinuation of ADT were 7.5% in the zuranolone co-initiated with an ADT arm, and 5.5% in the ADT co-initiated placebo arm, respectively.
- No evidence of increased suicidal ideation/behavior was identified with zuranolone when co-initiated with an ADT compared with ADT co-initiated with placebo as measured by the Columbia-Suicide Severity Rating Scale (C-SSRS), and systematic evaluations revealed no evidence of withdrawal symptoms in either study arm.

Conference Call Information

Sage will host a conference call and webcast on February 16 at 8:00 a.m. ET to review the totality of the CORAL Study. The live webcast can be accessed on the investor page of Sage's website at investor.sagerx.com. A replay of the webcast will be available on Sage's website approximately two hours after the completion of the event and will be archived for up to 30 days.

About the CORAL Study

The CORAL Study (217-MDD-305) was a Phase 3, randomized, double-blind, placebo-controlled trial assessing the efficacy and safety of zuranolone 50 mg co-initiated with an open-label standard of care antidepressant (ADT) compared to a standard of care ADT co-initiated with placebo in adults with MDD. In the study, 440 people were enrolled. People in the study were randomized to receive zuranolone 50 mg with a standard of care ADT or a standard of care ADT co-initiated with placebo once nightly for two weeks. People in the study were then followed for four weeks during which they continued their ADT. The study included five ADTs across different SSRI and SNRIs (sertraline, escitalopram, citalopram, duloxetine, desvenlafaxine) that represent the most commonly used ADTs. The choice of ADT was made by the clinician. The primary endpoint was the change in baseline 17-item Hamilton Rating Scale for Depression (HAMD-17) total score at Day 3.

About Major Depressive Disorder (MDD)

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 more than 19 million adults in the U.S. and more than 260 million people worldwide suffer from depression. While antidepressants are widely used to treat MDD, large-scale studies have demonstrated the need for additional therapies with a differentiated profile.

About Zuranolone

Zuranolone (SAGE-217/BIIB125) is a once-daily, two-week, investigational drug 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 to regulating brain function.

Zuranolone is being evaluated in the LANDSCAPE and NEST clinical trial programs. The two development programs include multiple studies examining use of zuranolone in several thousand people with a variety of dosing, clinical endpoints, and treatment paradigms. The LANDSCAPE program includes five studies of zuranolone in people with MDD (MDD-201B, MOUNTAIN, SHORELINE, WATERFALL, and CORAL Studies). The NEST program includes two placebo-controlled studies of zuranolone in people with PPD (ROBIN and SKYLARK Studies). Additionally, Shionogi recently completed a Phase 2 study of zuranolone in Japan in people with MDD.

About Sage Therapeutics

Sage Therapeutics is a biopharmaceutical company fearlessly leading the way to create a world with better brain health. Our mission is to pioneer solutions to deliver life-changing brain health medicines, so every person can thrive. For more information, please visit. www.sagerx.com.

About Biogen

As pioneers in neuroscience, Biogen discovers, develops, and delivers worldwide innovative therapies for people living with serious neurological diseases as well as related therapeutic adjacencies. One of the world's first global biotechnology companies, Biogen was founded in 1978 by Charles Weissmann, Heinz Schaller, Sir Kenneth Murray, and Nobel Prize winners Walter Gilbert and Phillip

Sharp. Today, Biogen has a leading portfolio of medicines to treat multiple sclerosis, has introduced the first approved treatment for spinal muscular atrophy, and is providing the first and only approved treatment to address a defining pathology of Alzheimer's disease. Biogen is also commercializing biosimilars and focusing on advancing the industry's most diversified pipeline in neuroscience that will transform the standard of care for patients in several areas of high unmet need.

In 2020, Biogen launched a bold 20-year, $250 million initiative to address the deeply interrelated issues of climate, health, and equity. Healthy Climate, Healthy Lives™ aims to eliminate fossil fuels across the company's operations, build collaborations with renowned institutions to advance the science to improve human health outcomes, and support underserved communities.

We routinely post information that may be important to investors on our website at www.biogen.com. Follow us on social media - Twitter, LinkedIn, Facebook, YouTube.

Forward-Looking Statements

Sage Therapeutics Safe Harbor

Various statements in this release concern Sage's future expectations, plans and prospects, including without limitation our statements regarding: the potential for zuranolone, if approved; our belief in the potential profile, benefit and impact of zuranolone in the treatment of MDD, if approved, and the unmet need for new treatment options; our estimates as to the number of people with MDD; our future plans and expected activities; and the mission and goals 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: we may experience delays or unexpected hurdles in our efforts to file a new drug application ("NDA") and seek approval of zuranolone in the treatment of MDD or PPD; even if we are successful in our efforts to file an NDA for zuranolone, the FDA may find that the data included in the NDA are not sufficient for approval and may not approve the NDA; the FDA may decide that the design, conduct or results of our completed and ongoing clinical trials for zuranolone, even if positive, are not sufficient for approval in MDD or PPD and may require additional trials or data which may significantly delay and put at risk our efforts to obtain approval and may not be successful; other decisions or actions of the FDA or other regulatory agencies may affect our efforts with respect to zuranolone and our plans, progress or results; we may experience negative results in ongoing or future studies of zuranolone that negatively affect our ability to obtain approval of zuranolone or that impair the potential profile of zuranolone; unexpected concerns may arise from additional data, analysis or results from any of our completed studies; we may encounter 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 delays in initiation, conduct or completion of our planned activities that may impact our ability to meet our expected timelines; the number of people with MDD and potential market for zuranolone as a treatment for MDD, if approved, may be substantially smaller than our estimates; the unmet need for additional treatment options in MDD, the potential benefit for zuranolone and market acceptance of zuranolone, if approved, may not be as significant as we expect; and we may encounter technical and other unexpected hurdles in the development and manufacture of zuranolone or any of our other product candidates which may delay our timing or change our plans or prospects, or otherwise negatively impact our business; 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.

Biogen Safe Harbor

This news release contains forward-looking statements, including statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995, relating to the potential, benefits, safety and efficacy of zuranolone; the potential clinical effects of zuranolone; the clinical development program for zuranolone; clinical development programs, clinical trials and data readouts and presentations for zuranolone; the potential treatment of MDD; the potential of Biogen's commercial business and pipeline programs, including zuranolone; the anticipated benefits and potential of Biogen's collaboration arrangement with Sage; and risks and uncertainties associated with drug development and commercialization. These forward-looking statements may be accompanied by words such as "aim," "anticipate," "believe," "could," "estimate," "expect," "forecast," "intend," "may," "plan," "potential," "possible," "will," "would" and other words and terms of similar meaning. Drug development and commercialization involve a high degree of risk and only a small number of research and development programs result in commercialization of a product. Results in early-stage clinical trials may not be indicative of full results or results from later stage or larger scale clinical trials and do not ensure regulatory approval. You should not place undue reliance on these statements, or the scientific data presented.

These statements involve risks and uncertainties that could cause actual results to differ materially from those reflected in such statements, including without limitation, uncertainty of success in the development and potential commercialization of zuranolone; unexpected concerns may arise from additional data, analysis or results of clinical studies of zuranolone; regulatory authorities may require additional information or further studies, or may fail or refuse to approve or may delay approval of Biogen's drug candidates, including zuranolone; the occurrence of adverse safety events; the risks of other unexpected hurdles, costs or delays; failure to protect and enforce data, intellectual property and other proprietary rights and uncertainties relating to intellectual property claims and challenges; product liability claims; third party collaboration risks; and the direct and indirect impacts of the ongoing COVID-19 pandemic on our business, results of operations and financial condition. The foregoing sets forth many, but not all, of the factors that could cause actual results to differ from Biogen's expectations in any forward-looking statement. Investors should consider this cautionary statement as well as the risk factors identified in Biogen's most recent annual or quarterly report and in other reports Biogen has filed with the U.S. Securities and Exchange Commission. These statements are based on Biogen's current beliefs and expectations and speak only as of the date of this news release. Biogen does not undertake any obligation to publicly update any forward-looking statements, whether as a result of new information, future developments or otherwise.

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