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): May 3, 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 2.02 Results of Operations and Financial Condition

On May 3, 2022, Sage Therapeutics, Inc. announced its financial results for the quarter ended March 31, 2022. A copy of the press release is being furnished as Exhibit 99.1 to this Current Report on Form 8-K.

The information in this Current Report on Form 8-K and Exhibit 99.1 attached hereto is intended to be furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Press release issued by Sage Therapeutics, Inc. on May 3, 2022, furnished herewith.
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: May 3, 2022

SAGE THERAPEUTICS, INC.

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

Sage Therapeutics Announces First Quarter 2022 Financial Results and Highlights Pipeline and Business Progress

Rolling NDA submission for zuranolone in MDD underway, with full submission expected to be completed in the second half of 2022, associated NDA submission in PPD planned for early 2023

Topline data from Phase 3 SKYLARK Study evaluating 50 mg zuranolone for PPD on track for mid-2022

Six planned and ongoing Phase 2 studies across neuropsychiatry and neurology franchises, demonstrate focused execution across pipeline programs

Company leadership strengthened with appointment of Mark Pollack, M.D., as Senior Vice President, Medical Affairs

Conference call today at 8:00 a.m. ET

CAMBRIDGE, Mass. – May 3, 2022 – Sage Therapeutics, Inc. (Nasdaq: SAGE), a biopharmaceutical company leading the way to create a world with better brain health, today reported business highlights and financial results for the first quarter ended March 31, 2022.

"Current events have put a spotlight on the need for significant progress in brain health disorders, and at Sage, we've made a strong start to 2022 with the initiation of our rolling regulatory submission for zuranolone in major depressive disorder and meaningful progress across our entire pipeline," said Barry Greene, Chief Executive Officer at Sage Therapeutics. "We are currently executing four Phase 2 studies across our neuropsychiatry and neurology franchises, and we recently presented encouraging data from our SAGE-718 program in patients with mild cognitive impairment due to Parkinson's disease and mild cognitive impairment and mild dementia due to Alzheimer's disease at key scientific forums. Most importantly, across our programs we remain focused on innovation that emphasizes outcomes that are most important to patients, as we progress our mission to pioneer solutions to deliver life-changing brain health medicines, so every person can thrive."

First Quarter 2022 Portfolio Updates

Sage is advancing a portfolio of clinical programs featuring internally discovered novel chemical entities with the potential to become differentiated products intended to improve brain health by targeting the $GABA_A$ and NMDA receptor systems. Dysfunction in these systems is thought to be at the core of numerous neurological and neuropsychiatric disorders.

Depression Franchise

Sage's depression franchise features zuranolone, Sage's next-generation positive allosteric modulator (PAM) of $GABA_A$ receptors being evaluated in clinical development as a treatment for major depressive disorder (MDD) and postpartum depression (PPD), and ZULRESSO® (brexanolone) CIV injection, approved by the U.S. Food and Drug Association (FDA) as the first treatment specifically indicated for PPD. Zuranolone has received Breakthrough Therapy Designation for the treatment of MDD and Fast Track Designation for the treatment of PPD from the FDA.

Zuranolone is being evaluated, in collaboration with Biogen, as a potential rapid-acting, oral, once-daily, two-week treatment for MDD and PPD in the LANDSCAPE and NEST clinical development programs, respectively. The LANDSCAPE and NEST programs include five positive clinical trials in people with MDD and PPD, as well as the ongoing SKYLARK Study. Additionally, Shionogi completed a positive Phase 2 study with zuranolone in MDD. In the first quarter of this year, Sage and Biogen announced that the CORAL Study met the study objectives. 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 antidepressant treatments (ADTs) alone.

Yesterday, Sage and Biogen announced the initiation of a rolling New Drug Application (NDA) submission to the FDA for zuranolone in MDD with plans to complete the submission in the second half of 2022. An associated NDA filing for PPD is anticipated in early 2023 pending results from the SKYLARK Study.

The Company expects to achieve the following milestones across its depression franchise in 2022, with plans to share additional analyses from completed and ongoing studies at scientific forums throughout the year:

- Mid-2022:
  - SKYLARK (PPD-301) Study: Report topline data from the placebo-controlled Phase 3 study evaluating a two-week course of zuranolone 50 mg in women with PPD, with additional short-term follow-up.
- Late 2022:
  - Complete rolling NDA submission for zuranolone in MDD (2H 2022).
  - Announce topline data from the SUNBIRD Study, designed to evaluate the safe-use administration of ZULRESSO for the treatment of PPD in a patient's home (late 2022).
  - Present further zuranolone data, including analyses from the SHORELINE Study in MDD.

Neuropsychiatry Franchise

Sage's neuropsychiatry franchise features SAGE-718, the Company's first-in-class NMDA receptor PAM and lead neuropsychiatric drug candidate, in development as a potential oral therapy for cognitive disorders associated with NMDA receptor dysfunction, potentially including Huntington's disease (HD), Parkinson's disease (PD) and Alzheimer's disease (AD). SAGE-718 received Fast Track Designation from the FDA for development of SAGE-718 as a potential treatment for HD.

Sage is advancing a robust clinical program for SAGE-718 with multiple ongoing or planned Phase 2 studies, including the DIMENSION and SURVEYOR Studies in people with HD cognitive impairment, the lead indication for SAGE-718, the PRECEDENT Study in people with mild cognitive impairment (MCI) associated with PD and a Phase 2 study in people with MCI and mild dementia due to AD.

- DIMENSION (CIH-201) Study: Sage is currently enrolling the Phase 2 DIMENSION Study, a double-blind, placebo-controlled study in patients with HD cognitive impairment. The study is designed to evaluate the efficacy of once-daily dosed SAGE-718 over three months, with a target enrollment of approximately 178 patients. Sage expects the DIMENSION Study to include more than 40 clinical sites.
- SURVEYOR (CIH-202) Study: The SURVEYOR Study is a placebo-controlled Phase 2 study in people with HD cognitive impairment and healthy volunteers, with the goal of generating evidence linking efficacy signals on cognitive performance to domains of real-world functioning.
- PRECEDENT (CNP-202) Study: The Phase 2 PRECEDENT Study is a double-blind, placebo-controlled study in people with MCI due to PD. The study is designed to evaluate the safety and efficacy of SAGE-718 in patients with MCI due to PD over 42 days, followed by a controlled follow-up period.

Additionally, the Company recently presented data from completed SAGE-718 studies in PD and AD cognitive impairment at key scientific forums. Data from the Company's Phase 2 open label PARADIGM Study presented at the AD/PD 2022 Advances in Science & Therapy International Conference on Alzheimer's and Parkinson's Diseases and Related Neurological Disorders, showed that SAGE-718 given once daily for 14 days was associated with improvements in executive function and learning and memory at Day 14 in patients with MCI due to PD. Additionally, sustained effects and improving trends were seen out to Day 28. Data from the Phase 2 open-label LUMINARY Study in individuals with MCI and mild dementia due to AD presented at the American Academy of Neurology showed that SAGE-718 given once daily for 14 days was generally well-tolerated and associated with improved executive performance and learning and memory. At Day 14, improvements from baseline were observed in multiple tests of executive functioning and learning and memory. Statistically significant improvement was also observed in the Montreal Cognitive Assessment at Day 28.

The Company expects to achieve the following milestones across its neuropsychiatry franchise in 2022:

- Late 2022:
  - Phase 2/3 Study in HD (CIH-301): Initiate a Phase 2/3 open-label extension study of SAGE-718 in people with HD cognitive impairment.
  - Phase 2 Study in AD (CNA-202): Initiate a placebo-controlled Phase 2 study of SAGE-718 in people with MCI and mild dementia due to AD.

Sage also plans to share additional analyses from studies completed with SAGE-718 to date throughout 2022.

Neurology Franchise

Sage's neurology franchise features SAGE-324 and SAGE-689. SAGE-324, a next-generation PAM of $GABA_A$ receptors and Sage's lead neurology program, is in development as a potential oral therapy for neurological conditions, such as essential tremor (ET), epilepsy and PD. SAGE-689 is an intramuscular $GABA_A$ receptor PAM in development as a potential therapy for disorders associated with acute GABA hypofunction.

Sage and its collaborator, Biogen, are currently enrolling people in the Phase 2b KINETIC 2 placebo-controlled study of SAGE-324 in ET following positive results from the KINETIC Study. The KINETIC 2 Study is a Phase 2b dose-ranging study with the primary goal of defining the dose and frequency for SAGE-324 in ET with a good tolerability profile and a dosing schedule to maintain plasma concentrations needed for sustained tremor symptom control in treating ET.

Sage also plans to initiate a Phase 2 long-term open label safety study with SAGE-324. The study is designed to evaluate the long-term safety and tolerability of SAGE-324 in ET, with incidence of treatment-emergent adverse events as the primary endpoint.

SAGE-689 continues in Phase 1 development.

The Company expects to achieve the following milestones across its neurology franchise in 2022:

- Mid-2022:
  - Initiate a Phase 2 safety study with SAGE-324 in ET.
- Late 2022:
  - Complete enrollment in KINETIC 2 Study of SAGE-324 in ET.

Sage also plans to share additional analyses from studies completed with SAGE-324 to date throughout 2022.

Early Development

Sage is progressing its early development programs with IND-enabling studies underway for SAGE-319 and SAGE-421.

- **SAGE-319:** an oral, extrasynaptic $GABA_A$ receptor preferring PAM that Sage plans to study for potential use in disorders of social interaction.
- **SAGE-421:** an oral, NMDA receptor PAM that Sage plans to study for potential use in neurodevelopmental disorders and cognitive recovery and rehabilitation.

Business Updates

Sage announced today that Mark Pollack, M.D., joined the Company as Senior Vice President, Medical Affairs. Dr. Pollack will lead Sage's global medical affairs efforts across all Sage programs, with a focus on supporting the Company's external relationships with the scientific community. Dr. Pollack joins Sage from Myriad Genetics, where he served as Chief Medical Officer of the Neuroscience Business Unit. Additionally, Dr. Pollack brings 35 years of proven leadership in scientific research and medical practice, including positions as Chair of the Department of Psychiatry and Behavioral Sciences at Rush University Medical Center, Professor of Psychiatry at Massachusetts General Hospital and Harvard Medical School.

ANTICIPATED 2022 MILESTONES

- Zuranolone:
  - Report topline data from the SKYLARK Study in PPD (mid-2022).
  - Complete NDA submission in MDD (2H 2022).
  - Present further zuranolone data, including analyses from the SHORELINE Study in MDD.
- SAGE-718:
  - Initiate Phase 2/3 HD cognitive impairment open label extension study (late 2022).
  - Initiate placebo-controlled Phase 2 Study in people with mild cognitive impairment and mild dementia due to AD (late 2022).
- SAGE-324:
  - Initiate Phase 2 safety study in ET (mid-2022).
- ZULRESSO:
  - Announce topline data from the SUNBIRD Study, designed to evaluate the safe-use administration of ZULRESSO for the treatment of PPD in a patient's home (late 2022).

FINANCIAL RESULTS FOR THE FIRST QUARTER 2022

- **Cash Position:** Cash, cash equivalents and marketable securities as of March 31, 2022 were $1.6 billion compared to $1.7 billion at December 31, 2021.
- **Revenue:** Net revenue from sales of ZULRESSO was $1.6 million in the first quarter of 2022 and in the same period of 2021.
- **R&D Expenses:** Research and development expenses were $78.0 million, including $8.6 million of non-cash stock-based compensation expense, in the first quarter of 2022 compared to $58.1 million, including $9.3 million of non-cash stock-based compensation expense, in the same period of 2021, an increase of $19.9 million. The increase in spending was primarily due to increased spending on SAGE-324 and Sage's wholly owned pipeline including SAGE-718 and other programs, partially offset by decreased spending on zuranolone, primarily due to completion of the WATERFALL Study and the CORAL Study. The reimbursement from Biogen pursuant to the Sage/Biogen Collaboration and License Agreement was $18.5 million in the first quarter of 2022 compared to $22.1 million in the same period of 2021.
- **SG&A Expenses:** Selling, general and administrative expenses were $46.5 million, including $9.9 million of non-cash stock-based compensation expense, in the first quarter of 2022 compared to $39.8 million, including $12.7 million of non-cash stock-based compensation expense, in the same period of 2021, an increase of $6.7 million. The increase was primarily related to hiring employees to support ongoing activities in anticipation of potential future launches of our product candidates. The reimbursement from Biogen pursuant to the Sage/Biogen Collaboration and License Agreement was $1.5 million in the first quarter of 2022 compared to $2.7 million in the same period of 2021.
- **Net Loss:** Net loss was $122.1 million in the first quarter of 2022 compared to $95.8 million in the same period of 2021.

FINANCIAL GUIDANCE

- Sage anticipates cash, cash equivalents and marketable securities of approximately $1.3 billion at the end of 2022.
- The Company does not anticipate receipt of any milestone payments from collaborations in 2022.
- The Company believes its cash and cash equivalents, anticipated funding from our ongoing collaborations, and potential revenue, will support its operations into 2025.

Conference Call Information

Sage will host a conference call and webcast today, Tuesday, May 3, at 8:00 a.m. ET to discuss its first quarter 2022 financial results and recent corporate updates. 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 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.

Forward-Looking Statements

Various statements in this release concern Sage's future expectations, plans and prospects, including without limitation our statements regarding: plans for completion of our rolling NDA filing for zuranolone in MDD and associated submission for zuranolone in PPD, and the potential timing of such activities; our belief in the regulatory filing pathways for zuranolone; the potential profile and benefit of zuranolone in MDD and PPD; the potential for regulatory approval and commencement of commercialization of zuranolone; other planned next steps for the program; anticipated timelines for reporting clinical trial results, commencement of trials, and initiation of new activities; our plans for advancement of our pipeline; our belief in the potential profile and benefit of our product candidates; potential indications for our product candidates; the potential for success of our programs, and the opportunity to help patients in various indications; the mission and goals for our business; and our expectations with respect to 2022 year-end cash, no receipt of milestones from collaborations in 2022 and funding of future operations. 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 complete our rolling NDA submission for zuranolone in MDD and our planned submission in PPD and we may not be able to complete the submissions on the timelines we expect or at all; the FDA may find inadequacies and deficiencies in our NDA for zuranolone, including in the data we submit, despite prior discussions, and may decide not to accept the NDA for filing; even if the FDA accepts the NDA for filing, 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; even if our NDA is successfully filed and accepted, the FDA may not meet expected review timelines for our NDA; 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 the ongoing SKYLARK Study in PPD that negatively affect our ability to file an NDA for approval of zuranolone in PPD; results of ongoing or future studies may impact our ability to obtain approval of zuranolone or impair the potential profile of zuranolone; success in earlier clinical trials of any of our product candidates may not be repeated or observed in ongoing or future studies, and ongoing and future clinical trials may not meet their primary or key secondary endpoints which may substantially impair development; 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 ongoing and planned clinical trials, including as a result of slower than expected site initiation or enrollment, the need or decision to expand the trials or other changes, that may impact our ability to meet our expected timelines and increase our costs; 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 or may impair the potential for successful development; the anticipated benefits of our ongoing collaborations, including the achievement of events tied to milestone payments or the successful development or commercialization of products and generation of revenue, may never be

achieved; the need to align with our collaborators may hamper or delay our development and commercialization efforts or increase our costs; our business may be adversely affected and our costs may increase if any of our key collaborators fails to perform its obligations or terminates our collaboration; the internal and external costs required for our ongoing and planned activities, and the resulting impact on expense and use of cash, may be higher than expected which may cause us to use cash more quickly than we expect or change or curtail some of our plans or both; we may never be able to generate meaningful revenues from sales of ZULRESSO or to generate revenues at levels we expect or at levels necessary to justify our investment; we may not be successful in our efforts to gain regulatory approval of products beyond ZULRESSO and, even if successfully developed and approved, we may not achieve revenues from such products at the levels we expect; our expectations as to year-end cash and sufficiency of cash to fund future operations may prove not to be correct for these and other reasons such as changes in plans or actual events being different than our assumptions; we may be opportunistic in our future financing plans even if available cash is sufficient; additional funding may not be available on acceptable terms when we need it; the number of patients with the diseases or disorders for which our products are developed, the unmet need for additional treatment options and the potential market for our current or future products may be significantly smaller than we expect; any of our products that may be approved in the future may not achieve market acceptance or we may encounter reimbursement-related or other market-related issues that impact the success of our commercialization efforts; and we may encounter technical and other unexpected hurdles in the development and manufacture of our product candidates or the commercialization of our marketed product which may delay our timing or change our plans, increase our costs or otherwise negatively impact our business; as well as those risks more fully discussed in the section entitled "Risk Factors" in our most recent annual/quarterly report, 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.

Financial Tables

Sage Therapeutics, Inc. and Subsidiaries
Condensed Consolidated Statements of Operations
(in thousands, except share and per share data)
(unaudited)

	Three Months Ended March 31,	
	2022	2021
Product revenue, net	$ 1,582	$ 1,583
Operating costs and expenses:		
Cost of goods sold	286	187
Research and development	78,018	58,056
Selling, general and administrative	46,477	39,847
Total operating costs and expenses	124,781	98,090
Loss from operations	(123,199)	(96,507)
Interest income, net	1,168	708
Other income (expense), net	(24)	35
Net loss	$ (122,055)	$ (95,764)
Net loss per share - basic and diluted	$ (2.07)	$ (1.64)
Weighted average shares outstanding - basic and diluted	59,028,858	58,374,219

Sage Therapeutics, Inc. and Subsidiaries
Condensed Consolidated Balance Sheets
(in thousands)
(unaudited)

	March 31, 2022	December 31, 2021
Cash, cash equivalents and marketable securities	$1,625,241	$1,742,296
Total assets	$1,705,703	$1,825,288
Total liabilities	$ 87,201	$ 96,257
Total stockholders' equity	$1,618,502	$1,729,031

ZULRESSO (brexanolone) SELECT IMPORTANT SAFETY INFORMATION

This does not include all the information needed to use ZULRESSO safely and effectively. See full prescribing information for ZULRESSO.

WARNING: EXCESSIVE SEDATION AND SUDDEN LOSS OF CONSCIOUSNESS

See full prescribing information for complete boxed warning

Patients are at risk of excessive sedation or sudden loss of consciousness during administration of ZULRESSO.

Because of the risk of serious harm, patients must be monitored for excessive sedation and sudden loss of consciousness and have continuous pulse oximetry monitoring. Patients must be accompanied during interactions with their child(ren).

ZULRESSO is available only through a restricted program called the ZULRESSO REMS.

WARNINGS AND PRECAUTIONS

Suicidal Thoughts and Behaviors: Consider changing the therapeutic regimen, including discontinuing ZULRESSO, in patients whose PPD becomes worse or who experience emergent suicidal thoughts and behavior.

ADVERSE REACTIONS: Most common adverse reactions (incidence ≥5% and at least twice the rate of placebo) were sedation/somnolence, dry mouth, loss of consciousness, and flushing/hot flush.

USE IN SPECIFIC POPULATIONS

- **Pregnancy:** ZULRESSO may cause fetal harm. Healthcare providers are encouraged to register patients by calling the National Pregnancy Registry for Antidepressants at 1-844-405-6185 or visiting online at https://womensmentalhealth.org/clinical-and-researchprograms/pregnancyregistry/antidepressants/
- **Renal Impairment:** Avoid use of ZULRESSO in patients with end stage renal disease (ESRD)

Controlled Substance: ZULRESSO contains brexanolone, a Schedule IV controlled substance under the Controlled Substances Act.

To report SUSPECTED ADVERSE REACTIONS, contact Sage Therapeutics, Inc. at 1-844-4-SAGERX (1-844-472-4379) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see accompanying full Prescribing Information including Boxed Warning.

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