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): August 2, 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 August 2, 2022, Sage Therapeutics, Inc. announced its financial results for the quarter ended June 30, 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 August 2, 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: August 2, 2022

SAGE THERAPEUTICS, INC.

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

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

Rolling NDA submission for zuranolone in MDD and PPD remains on track, with completion expected in the second half of 2022

Announced positive topline data from the Phase 3 SKYLARK Study evaluating 50 mg zuranolone for PPD

Enrolling multiple Phase 2 studies across neuropsychiatry and neurology franchises, additional trials expected to initiate throughout 2022

Cash and cash equivalents, anticipated funding from ongoing collaborations, and potential revenue, expected to support operations into 2025

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

CAMBRIDGE, Mass. – August 2, 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 second quarter ended June 30, 2022.

"The first half of 2022 has been marked by important clinical and regulatory achievements across our entire pipeline, paving the way for continued focused execution throughout the remainder of the year," said Barry Greene, Chief Executive Officer at Sage Therapeutics. "We are making progress on the NDA submission for zuranolone and building our organization to support a potential launch. Based on the consistent clinical profile of zuranolone, we believe it has the potential, if approved, to address the significant unmet need for people suffering from MDD and PPD and we are working with a sense of urgency toward our goal of bringing zuranolone to them. Beyond zuranolone, we are continuing to advance our pipeline, with the presentation of multiple data sets at key upcoming scientific congresses. I believe our progress this year, combined with the strong foundation we've built, supports our growth as a leader in brain health and a top-tier biopharmaceutical company."

Second 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 designed to improve brain health by targeting the GABAA 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 various affective disorders, and ZULRESSO® (brexanolone) CIV injection, approved by the U.S. Food and Drug Association (FDA) as the first treatment specifically indicated for postpartum depression (PPD). Zuranolone has received Breakthrough Therapy and Fast Track Designation for the treatment of major depressive disorder (MDD) and Fast Track Designation for the treatment of PPD from the FDA.

Zuranolone is being evaluated as a potential rapid-acting, once-daily, oral two-week treatment for MDD and PPD in the LANDSCAPE and NEST clinical development programs, respectively. Across seven positive clinical trials, zuranolone has demonstrated rapid and sustained relief of depressive symptoms in people with MDD and PPD. In the second quarter of this year, Sage and its collaborator, Biogen, announced that the SKYLARK Study of zuranolone in PPD met its primary and all key secondary endpoints.

In June 2022, Sage and Biogen announced that the rolling NDA submission that was previously initiated will seek approval for both MDD and PPD in one filing. The Companies plan to complete submission of the single NDA for zuranolone for the treatment of both MDD and PPD to the FDA in the second half of this year, accelerating previously planned timelines for PPD.

The Company also shared insights from the terminated RAINFOREST and REDWOOD Studies today. The RAINFOREST Study was designed to investigate the efficacy and safety of 30 mg zuranolone in comorbid MDD and insomnia. The REDWOOD Study was designed to study fixed schedule intermittent dosing of 30 mg zuranolone throughout the course of a year. Both studies were terminated in 2020 based on the Company's plans to advance the program with the 50 mg dose of zuranolone.

The RAINFOREST Study, which enrolled 87 patients, was terminated prior to achieving the planned sample size. As the study was not fully enrolled, the statistical analysis plan was invalid. The study directionality showed that zuranolone may benefit sleep efficiency, with numerical improvement in objective measures of quality of sleep, including wake after sleep onset, total sleep time, latency to persistent sleep, median number of awakenings, and mean duration of awakenings, and differences on endpoints involving REM sleep. The REDWOOD Study did not enroll enough patients for efficacy analyses to be performed. There were no new safety findings from the study. In the open-label SHORELINE Study, a large naturalistic study in the zuranolone development program, 80% of patients who responded to initial treatment with zuranolone 50 mg received only 1 or 2 treatment courses during their time in the year-long study, with a median time to the second treatment course of 249 days also with no new safety findings.

Additionally, Sage today announced that the SUNBIRD Study evaluating the safe-use administration of ZULRESSO as a treatment for PPD in a woman's home has completed enrollment. Sage does not plan any label changes from this study.

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

- Late 2022:
  - Complete NDA submission for zuranolone in MDD and PPD (2H 2022).
  - Present additional zuranolone data throughout 2022.

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 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 people 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 people. 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 people with MCI due to PD over 42 days, followed by a controlled follow-up period.

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

- Late 2022:
  - Phase 3 Study in HD (CIH-301): Initiate a Phase 3 safety 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 mild cognitive impairment and mild dementia due to AD.
  - Present additional SAGE-718 data 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 recently initiated a Phase 2 long-term open label safety study with SAGE-324, 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:

- Late 2022:
  - Complete enrollment in KINETIC 2 Study of SAGE-324 in ET.
  - Present additional SAGE-324 data throughout 2022.

Early Development

Sage is progressing its early development programs with IND-enabling work 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.

FINANCIAL RESULTS FOR THE SECOND QUARTER 2022

- **Cash Position**: Cash, cash equivalents and marketable securities as of June 30, 2022 were $1.5 billion compared to $1.6 billion at March 31, 2022.
- **Revenue**: Net revenue from sales of ZULRESSO was $1.5 million in the second quarter of 2022, compared to $1.6 million in the same period of 2021.
- **R&D Expenses:** Research and development expenses were $77.3 million, including $6.5 million of non-cash stock-based compensation expense, in the second quarter of 2022 compared to $66.2 million, including $13.5 million of non-cash stock-based compensation expense, for the same period in 2021. The increase in R&D expenses was primarily due to increased spending on SAGE-324 and Sage's wholly owned pipeline, including SAGE-718 and other programs. The reimbursement from Biogen pursuant to the Sage/Biogen Collaboration and License Agreement was $21.0 million in the second quarter of 2022 compared to $20.1 million in the same period of 2021.

- **SG&A Expenses**: Selling, general and administrative expenses were $52.4 million, including $8.2 million of non-cash stock-based compensation expense, in the second quarter of 2022, compared to $43.3 million, including $14.2 million of non-cash stock-based compensation expense, for the same period in 2021. The increase in SG&A expenses was primarily due to hiring employees to support ongoing activities in anticipation of potential future product launches of our product candidates. The reimbursement from Biogen pursuant to the Sage/Biogen Collaboration and License Agreement was $2.8 million in the second quarter of 2022 compared to $3.5 million in the same period of 2021.
- **Net Loss:** Net loss was $126.3 million for the second quarter of 2022 compared to $107.2 million for 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 anticipates R&D and SG&A spending to increase as it advances planned and ongoing studies for SAGE-718 and SAGE-324 and prepares for the potential launch of zuranolone.
- The Company believes its cash and cash equivalents, anticipated funding from ongoing collaborations, and potential revenue, will support its operations into 2025.

Conference Call Information

Sage will host a conference call and webcast today, Tuesday, August 2, at 8:00 a.m. ET to discuss its second 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 and potential timing for completion of our rolling NDA submission for zuranolone in MDD and PPD; our belief in the regulatory filing pathway for zuranolone in MDD and PPD; 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 zuranolone program; anticipated timelines for commencement of trials, initiation of new activities and other plans for our other programs and early stage 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, funding of future operations and expectations for increases in expenses. 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 PPD and we may not be able to complete the submission on the timeline 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; 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 that negatively impact further development, the potential for approval or the potential for successful commercialization 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 and expense levels 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 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 June 30,		Six Months Ended June 30,	
	2022	2021	2022	2021
Product revenue, net	$ 1,501	$ 1,643	$ 3,082	$ 3,226
Operating costs and expenses:				
Cost of goods sold	200	148	486	335
Research and development	77,297	66,170	155,315	124,226
Selling, general and administrative	52,411	43,346	98,888	83,193
Total operating costs and expenses	129,908	109,664	254,689	207,754
Loss from operations	(128,407)	(108,021)	(251,607)	(204,528)
Interest income, net	2,102	732	3,270	1,440
Other income, net	45	44	22	79
Net loss	$ (126,260)	$ (107,245)	$ (248,315)	$ (203,009)
Net loss per share - basic and diluted	$ (2.13)	$ (1.83)	$ (4.20)	$ (3.47)
Weighted average shares outstanding - basic and diluted	59,266,322	58,582,569	59,148,246	58,478,970

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

	June 30, 2022	December 31, 2021
Cash, cash equivalents and marketable securities	$1,513,707	$1,742,296
Total assets	$1,601,377	$1,825,288
Total liabilities	$ 97,141	$ 96,257
Total stockholders' equity	$1,504,236	$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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