# Sage Therapeutics Announces First Quarter 2021 Financial Results and Highlights Pipeline and Business Progress

May 4, 2021

*Company on-track to initiate placebo-controlled Phase 2 trial with SAGE-718 in Huntington's disease in late 2021, as the target for the first indication for SAGE-718, following encouraging signals in Phase 1 data*

*PARADIGM Study with SAGE-718 showed improved performance from baseline on multiple tests of executive function over 14 days of treatment in patients with Parkinson's disease cognitive impairment, further supporting development in disorders associated with cognitive dysfunction*

*Positive topline data from Phase 2 KINETIC Study showed statistically significant reduction in tremor score with SAGE-324 compared to placebo at Day 29 in adults with essential tremor*

*Continued positive data demonstrated for the 30 and 50 mg doses of zuranolone in open-label SHORELINE Study of zuranolone in patients with major depressive disorder*

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

CAMBRIDGE, Mass.--(BUSINESS WIRE)--May 4, 2021-- Today, Sage Therapeutics, Inc. (NASDAQ: SAGE), a biopharmaceutical company committed to developing novel therapies with the potential to transform the lives of people with debilitating disorders of the brain, reported business highlights and financial results for the first quarter ended March 31, 2021.

"Sage started 2021 with significant advances across our depression, neurology and neuropsychiatry franchises, and the progress we've made so far this year sets us up for near-, medium- and long-term value creation opportunities as we further advance our deep organic pipeline," said Barry Greene, chief executive officer at Sage Therapeutics. "In the first quarter alone, we demonstrated the significant potential of our innovative development-stage therapeutics that modulate the GABA and NMDA pathways, through the positive clinical data demonstrated in studies of zuranolone, SAGE-324 and now SAGE-718. We are making great progress toward our goal of becoming the leading brain health company and a top-tier biopharmaceutical company, with multiple upcoming catalysts that I believe represent important steps on our mission of delivering medicines that matter to address the ongoing crisis in brain health."

**First Quarter 2021 and Recent 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 $GABA_A$ and NMDA receptor systems. Dysfunction in these systems is thought to be at the core of numerous brain health 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 Administration (FDA) as the first treatment specifically indicated for postpartum depression (PPD). Zuranolone has received breakthrough therapy designation from the FDA for the treatment of major depressive disorder (MDD). Sage is jointly developing zuranolone in the U.S. with Biogen.*

Zuranolone is being evaluated as a potential rapid-acting, short-course treatment for PPD and MDD in the NEST and LANDSCAPE clinical trial programs. Four Phase 3 clinical studies with zuranolone are ongoing. If successful, these programs may support paths to approval with three distinct opportunities to address patient needs: PPD, acute rapid response therapy (RRT) in MDD when co-initiated with a new standard antidepressant, and as-needed treatment of MDD.

- In March 2021, Sage reported complete, topline 12-month data from the 30 mg cohort and interim topline data from the 50 mg cohort of the ongoing Phase 3 open-label SHORELINE Study. The SHORELINE Study is designed to evaluate the safety and tolerability of zuranolone in adults for up to one year. Data reported showed:
  - After the initial 2-week zuranolone treatment, more than 70% of patients who received 30 mg and 80% of patients who received 50 mg achieved positive response at Day 15.
  - In the 30 mg zuranolone cohort, approximately 70% of participants with positive response to an initial 2-week treatment required at most one additional zuranolone treatment during the 12-month study.
    - Of the 489 patients continuing in the study, 210 (42.9%) patients used only the single initial zuranolone course, while 125 (25.6%) used a total of two courses, 58 (11.9%) used a total of three courses, 53 (10.8%) used a total of four courses, and 43 (8.8%) used a total of five courses.
  - In the 199 patients who received zuranolone 50 mg only, approximately 80% achieved response and 43.2% achieved remission after the initial 2-week treatment period.
    - In this cohort the adverse event (AE) profile was similar to that seen in patients who received 30 mg zuranolone.

- In both 30 mg and 50 mg cohorts, zuranolone was generally well-tolerated with an AE profile consistent with data reported earlier.
    - **30 mg cohort:** 368 (51%) patients reported at least one adverse event. The most common treatment emergent adverse events (TEAEs) (reported ≥5%) were somnolence (86; 11.9%), headache (103; 14.2%), and dizziness (54; 7.4%). Most adverse events were mild or moderate.
    - **Retreatment:** The overall incidence rates of TEAEs during the second, third, fourth, and fifth treatment courses were, 42% (120/286), 28.6% (45/157), 29% (28/96), and 27.9% (12/43), respectively. The incidence of TEAEs in the first treatment course was 51% (368/725). The safety profile on treatment, off-treatment, and in between treatments has shown a consistent pattern to date in AE presentation across treatment courses.
    - **50 mg cohort:** 62.8% (125/199) subjects reported at least one AE. Events ≥5% of somnolence, dizziness, and sedation 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.
- The Company plans to reopen enrollment in the 50 mg cohort of the open-label SHORELINE Study, increasing the target enrollment to 500 patients. Additionally, the Company plans to offer patients from the CORAL Study the ability to roll-over into the SHORELINE Study following completion of the CORAL Study. These extensions of the SHORELINE Study will allow Sage to collect additional long-term data on patients treated with zuranolone 50 mg.

The Company expects the following zuranolone data readouts in 2021:

- 1H 2021:
    - WATERFALL (MDD-301B) Study: A placebo-controlled Phase 3 trial evaluating a two-week course of zuranolone 50 mg in patients with MDD, with additional short-term follow-up. In February 2021 the Company announced the WATERFALL Study was closed to enrollment.
- Late 2021:
    - CORAL (MDD-305) Study: A placebo-controlled Phase 3 trial evaluating a two-week course of zuranolone 50 mg, when co-initiated with a new antidepressant, in patients with MDD, with additional short-term follow-up.
    - SHORELINE (MDD-303) Study 50 mg Cohort (1-year data): An open-label Phase 3 trial designed to naturalistically follow patients with MDD and evaluate the safety and tolerability of zuranolone 50 mg in adults for up to one year.
    - SKYLARK (PPD-301) Study: A placebo-controlled Phase 3 trial evaluating a two-week course of zuranolone 50 mg in women with PPD, with additional short-term follow-up.

Sage plans to align with the FDA on data to support a potential future new drug application (NDA). Additional development plans for zuranolone in indications beyond MDD and PPD will be determined as part of the Company's strategic collaboration with Biogen.

**Neurology Franchise**

*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 Parkinson's disease (PD). Sage is jointly developing SAGE-324 in the U.S. with Biogen.*

- In April 2021, Sage reported topline data from the KINETIC Study evaluating SAGE-324 in the treatment of people with ET. The KINETIC Study is a Phase 2 study that evaluated the efficacy, safety, and tolerability of SAGE-324 60 mg in patients with ET aged 18 to 80 years old.
    - **In the full analysis set (ITT),** patients receiving SAGE-324 experienced a statistically significant reduction from baseline in TETRAS Performance Subscale Item 4 compared to placebo at Day 29 (P=0.049), corresponding to a 36% reduction in upper limb tremor amplitude from baseline in the SAGE-324 group compared to a 21% reduction in the placebo group.
    - In a pre-specified subgroup analysis, patients with a more severe tremor at baseline (TETRAS ≥12) demonstrated a statistically significant reduction from baseline in the TETRAS Item 4 upper limb tremor score at Day 29 (p=0.007) which corresponded to a 41% reduction in upper limb tremor amplitude compared to an 18% reduction for placebo.
    - **Safety and Tolerability:** Patients were randomized 1:1 to receive SAGE-324 (60 mg) or matched placebo once daily in the morning. The trial evaluated treatment of SAGE-324 at the higher end of the dose range and the daily dose could be down-titrated to 45 mg or 30 mg if 60 mg was not well tolerated. Down-titration of dose occurred in 62% of patients who received SAGE-324 and discontinuations were noted in 38% of patients receiving SAGE-324. AEs were generally consistent with the safety profile of SAGE-324 seen to date. The most common TEAEs that occurred in ≥10% of patients in the SAGE-324 treatment group and at a rate at least twice as high as that of patients in the placebo group were: somnolence 68%; dizziness 38%; balance disorder 15%; diplopia 12%; dysarthria 12%; and gait disturbance 12%.
    - **Activities of Daily Living (ADL) Scores:** ADL scores showed a statistically significant correlation with upper limb tremor score at all timepoints. While not powered to fully examine TETRAS ADL, SAGE-324 was also numerically superior to placebo at all time points during treatment.

The following milestones are expected for the neurology franchise in late 2021:

- Sage anticipates initiating a dose-ranging Phase 2 clinical trial with SAGE-324.

Additional development plans for SAGE-324 will be determined as part of the Company's strategic collaboration with Biogen.

**Neuropsychiatry Franchise**
*SAGE-718, Sage's first-in-class NMDA receptor PAM and lead neuropsychiatric drug candidate, is in development as a potential oral therapy for cognitive disorders associated with NMDA receptor dysfunction, potentially including Huntington's disease (HD), PD and Alzheimer's disease (AD).*

In the Phase 2a open-label PARADIGM Study, eight patients aged 50 to 75 years old with mild cognitive impairment due to PD received SAGE-718 3 mg daily for two-weeks.

- Patients showed performance improvements from baseline on multiple tests in the cognitive domain of executive function during the 14 days of treatment.
- Emerging signals on several measures also suggested improved performance from baseline on additional cognitive tests in the domains of learning and memory over a similar timeframe.
- SAGE-718 was generally well tolerated; there were no serious AEs and no TEAEs were determined to be related to SAGE-718.
- As expected, and due to its potentially unique profile, in certain tests of attention and psychomotor speed, SAGE-718 demonstrated neutral results. Other classes of medicines, including amphetamines, have been shown to alter simple attention or reaction time but not improve cognitive attributes.

Findings from the PARADIGM Study extend Sage's understanding of the potential impact of SAGE-718 on multiple domains of cognition. To date, SAGE-718 has demonstrated improvements in executive function in phase 1 and phase 2a studies and these findings add to the Company's confidence in the potential for SAGE-718 to become an important treatment for disorders associated with cognitive dysfunction, including HD, PD and AD.

Based on data generated with SAGE-718 to date, the Company intends to pursue several paths forward for SAGE-718 in parallel:

- HD
  - Initiate a placebo-controlled Phase 2 trial with SAGE-718 in early to moderate HD in late 2021. If the overall HD development program is successful, the Company believes HD could be the lead indication pursued for SAGE-718.
- PD
  - Activate a new 4-week dosing cohort in the PARADIGM Study to gather additional data in the PD patient population.

The following milestones are expected for the neuropsychiatry franchise in late 2021:

- LUMINARY (718-CNA-201) Study**:** The Company anticipates topline data from the LUMINARY Study, a Phase 2a open-label trial evaluating SAGE-718 in patients with AD mild cognitive impairment and mild dementia. The Company initiated enrollment and dosing in this study in early 2021.
- Phase 2 Study in HD: The Company expects to initiate a placebo-controlled Phase 2 trial with SAGE-718 in early to moderate HD.

**Early Development**
Sage expects to complete certain Phase 1 clinical studies for two programs in its early development pipeline in 2021, SAGE-689 (single ascending dose) and SAGE-904 (single ascending dose and multiple ascending dose).

- **SAGE-689:** is an intramuscular $GABA_A$ receptor PAM in development as a potential therapy for disorders associated with acute GABA hypofunction.
- **SAGE-904:** is Sage's second NMDA receptor PAM product candidate in development as a potential oral therapy for disorders associated with NMDA hypofunction.

Results from the planned Phase 1 studies will inform further development of these programs.

Additionally, the Company recently announced plans to advance SAGE-319 and SAGE-421 to preclinical studies.

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

**Other Development Opportunities**
Sage's Phase 3 trial with brexanolone in patients with advanced COVID-19 related acute respiratory distress syndrome (ARDS) is ongoing. The Company expects data from this trial in 2021.

**ANTICIPATED 2021 MILESTONES**

1H21:

- Zuranolone:
  - Report topline data from Phase 3 WATERFALL Study

Late 2021:

- Zuranolone:
  - Report topline data from Phase 3 SKYLARK Study
  - Report topline data from Phase 3 CORAL Study
  - Report topline data from Phase 3 SHORELINE Study 50 mg cohort
- SAGE-324:
  - Initiate Phase 2 dose-ranging study in ET
- SAGE-718:
  - Report topline data from Phase 2a LUMINARY open-label, signal finding study in patients with AD mild cognitive impairment and mild dementia
  - Initiate placebo-controlled Phase 2 study in early to moderate HD
- Brexanolone:
  - Report data from Phase 3 study in patients with advanced COVID-19 related ARDS
- SAGE-689 & SAGE-904:
  - Complete planned Phase 1 studies (SAD for SAGE-689 and SAD/MAD for SAGE-904)

**FINANCIAL RESULTS FOR THE FIRST QUARTER 2021**

- **Cash Position:** Cash, cash equivalents and marketable securities as of March 31, 2021 were $2.0 billion compared to $2.1 billion at December 31, 2020.
- **Revenue:** Net revenue from sales of ZULRESSO was $1.6 million in the first quarter of 2021 compared to $2.3 million in the same period of 2020.
- **R&D Expenses:** Research and development expenses were $58.1 million, including $9.3 million of non-cash stock-based compensation expense, in the first quarter of 2021 compared to $63.6 million, including $12.2 million of non-cash stock-based compensation expense, for the same period in 2020, a decrease of $5.5 million. The amount for the first quarter of 2021 reflects an increase in expenses of $16.6 million and a reduction in expenses of $22.1 million due to reimbursement from Biogen pursuant to the Biogen Collaboration and License Agreement. The primary reasons for the increase in expenses were spending on the WATERFALL Study and the CORAL Study.
- **SG&A Expenses:** Selling, general and administrative expenses were $39.8 million, including $12.7 million of non-cash stock-based compensation expense, in the first quarter of 2021 compared to $70.1 million, including $18.9 million of non-cash stock-based compensation expense, for the same period in 2020, a decrease of $30.3 million. The amount for the first quarter of 2021 reflects a decrease in expenses of $27.6 million, and a reduction in expenses of $2.7 million due to reimbursement from Biogen pursuant to the Biogen Collaboration and License Agreement. The primary reason for the decrease in expenses was the impact of the restructuring that the Company announced during the second quarter of 2020.
- **Net Loss:** Net loss was $95.8 million for the first quarter of 2021 compared to a net loss of $126.7 million for the same period in 2020.

**FINANCIAL GUIDANCE**

- Sage anticipates cash, cash equivalents, and marketable securities of more than $1.7 billion at end of 2021.
- The Company does not anticipate receipt of any milestone payments from collaborations in 2021.

**Conference Call Information**
Sage will host a conference call and webcast today, Tuesday, May 4, at 8:00 a.m. ET to discuss its first quarter 2021 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 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 planned research and development activities and related timelines, including plans for reporting data, initiation of new activities, and advancement of our pipeline; our belief in the potential profile and benefit of our product candidates, and the opportunity to help patients in various indications; the potential regulatory pathways for our product candidates and potential lead indications; our goal to deliver medicines that we hope will help patients; our mission to become the leading brain health company and top-tier bio-pharmaceutical company; our statements regarding the vision, opportunity and potential for our business and potential value creation opportunities; and our expectations with respect to 2021 year-end cash. 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: success in non-clinical studies or in earlier clinical trials or at interim time periods 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 the product without further development work or may not support further development at all; 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 different or more severe adverse events at the higher doses we are studying in our ongoing 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; the impact of the COVID-19 pandemic on our clinical development timelines 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 timelines 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; we may encounter other 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; 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 plans; 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 anticipated benefits of our ongoing collaborations may never be achieved and 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 development of any of our product candidates in any indication we are currently pursuing or may in the future pursue; our expectations as to year-end cash may prove not to be correct for 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; the number of patients with the diseases or disorders for which our products are developed or the unmet need for additional treatment options may be significantly smaller than we expect; 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 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.*

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

| | Three Months Ended March 31, | |
|---|---|---|
| | **2021** | **2020** |
| Product revenue, net | $ 1,583 | $ 2,286 |
| Operating costs and expenses: | | |
| Cost of goods sold | 187 | 170 |
| Research and development | 58,056 | 63,610 |
| Selling, general and administrative | 39,847 | 70,130 |
| Total operating costs and expenses | 98,090 | 133,910 |
| Loss from operations | (96,507) | (131,624) |
| Interest income, net | 708 | 4,729 |
| Other income, net | 35 | 155 |
| Net loss | $ (95,764) | $ (126,740) |
| Net loss per share - basic and diluted | $ (1.64) | $ (2.44) |
| Weighted average shares outstanding - basic and diluted | 58,374,219 | 51,908,760 |

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

| | **March 31, 2021** | **December 31, 2020** |
|---|---|---|

| | | | | |
|---|---|---|---|---|
| Cash, cash equivalents and marketable securities | $ | 2,004,017 | $ | 2,099,549 |
| Total assets | $ | 2,080,698 | $ | 2,159,246 |
| Total liabilities | $ | 77,422 | $ | 86,912 |
| Total stockholders' equity | $ | 2,003,276 | $ | 2,072,334 |

**ZULRESSO can cause serious side effects, including:**

- **Excessive sedation and sudden loss of consciousness.** ZULRESSO may cause you to feel very sleepy (excessive sedation) or pass out (loss of consciousness). Your healthcare provider should check you for symptoms of excessive sleepiness every 2 hours while you are awake.
  - During your infusion, tell your healthcare provider right away if you feel like you cannot stay awake during the time you are normally awake or if you feel like you are going to pass out. Your healthcare provider may lower your dose or stop the infusion until symptoms go away.
  - You must have a caregiver or family member with you to help care for your child(ren) during your infusion.
- Because of the risk of serious harm resulting from excessive sedation or sudden loss of consciousness, ZULRESSO is only available through a restricted program called the ZULRESSO REMS.

**ZULRESSO can cause other serious side effects, including:**

- **Increased risk of suicidal thoughts or actions.** ZULRESSO and other antidepressant medicines may increase suicidal thoughts and actions in some people 24 years of age and younger. **Pay close attention to and tell your healthcare provider right away if you have any of the following symptoms, especially if they are new, worse, or worry you:**
  - Attempts to commit suicide, thoughts about suicide or dying, new or worse depression, other unusual or sudden changes in behavior or mood.
  - Keep all follow-up visits and call your healthcare provider between visits as needed, especially if you have concerns about symptoms.

**The most common side effects of ZULRESSO include:**

- Sleepiness, dry mouth, passing out, flushing of the skin or face.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

**Before receiving ZULRESSO, tell your healthcare provider about all your medical conditions** including if you drink alcohol, have kidney problems, are pregnant or think you may be pregnant, or are breastfeeding or plan to breastfeed. It is not known if ZULRESSO will harm your unborn baby. If you become pregnant during treatment, talk with your healthcare provider about enrolling with the National Pregnancy Registry for Antidepressants at 1-844-405-6185.

**While receiving ZULRESSO, avoid the following:**

- Driving a car or doing other dangerous activities after your ZULRESSO infusion until your feeling of sleepiness has completely gone away.
- Do not drink alcohol.

**Tell your healthcare provider about all the medicines you take,** including prescription and over-the-counter medicines, vitamins, and herbal supplements. ZULRESSO and some medicines may interact with each other and cause serious side effects.

**Especially tell your healthcare provider if you take** other antidepressants, opioids, or Central Nervous System (CNS) depressants (such as benzodiazepines).

**Please see the patient Medication Guide, including information about serious side effects, for ZULRESSO in the full Prescribing Information.**

View source version on businesswire.com: https://www.businesswire.com/news/home/20210504005397/en/

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