Sage Therapeutics Inc Logo

Sage Therapeutics Announces Second Quarter 2020 Financial Results and Highlights Pipeline and Business Progress

August 10, 2020

Pipeline progress continues with first patient dosed and ongoing enrollment in multiple clinical trials across the depression and neurology franchises

Durability of response was observed in patients with MDD who responded to a 2-week treatment with zuranolone in MOUNTAIN Study six-month follow-up period

Conference call today at 8:30 a.m. ET

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Aug. 10, 2020-- 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 second quarter ended June 30, 2020.

During the quarter, Sage initiated enrollment and dosing in two new trials with zuranolone 50 mg:

- Phase 3 SKYLARK Study (PPD-301) in postpartum depression (PPD)
- Phase 3 WATERFALL Study (MDD-301B) in major depressive disorder (MDD)
    - Based on strong enrollment to date, topline data from this study is now anticipated in first half of 2021

In addition, Sage initiated dosing in the 50 mg cohort of the open-label Phase 3 SHORELINE Study and is on-track to initiate dosing in 2H 2020 in the Phase 3 CORAL Study (MDD-305) investigating zuranolone 50 mg as an acute rapid response therapy (RRT) in patients with MDD when co-initiated with a newly administered standard antidepressant therapy. The Company also initiated dosing in the Phase 2 KINETIC Study evaluating SAGE-324 in patients with essential tremor and is on-track to initiate the Phase 2 PARADIGM Study in the second half of 2020 evaluating SAGE-718 in patients with Parkinson’s disease (PD) with impaired cognitive function.

Sage also reported results from the 6-month follow-up cohort with zuranolone 30 mg from the MOUNTAIN study. There were no symptoms of withdrawal observed after discontinuation of zuranolone (Day 14) and 74.5% of patients who responded to zuranolone maintained their response at the last follow-up at Day 182. Zuranolone was generally well-tolerated and showed a similar safety profile as seen in earlier studies.

“We have created a novel drug company successfully able to convert our chemical equity into a rich pipeline of clinical assets that are new chemical entities, not repurposed molecules,” said Jeff Jonas, M.D., chief executive officer at Sage Therapeutics. “Even in the face of the difficulties currently challenging the world, I’m pleased to report that the team at Sage is executing across all three brain health franchises and we expect to report on numerous catalysts in the next 18 months.”

Portfolio Updates
Sage is advancing a portfolio of novel, new 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 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 Administration (FDA) as the first treatment specifically indicated for PPD. Zuranolone received breakthrough therapy designation from the U.S. FDA for the treatment of MDD.

- **Zuranolone ongoing studies:** Sage is evaluating the potential of zuranolone as a rapid-acting, short-course treatment for PPD and MDD. Sage recently initiated three new short-term clinical studies in 2020, with the potential, if successful, for three distinct indications: PPD, acute rapid response therapy (RRT) in MDD when co-initiated with a new standard antidepressant, and as-needed, or episodic, treatment of MDD. Enrollment and dosing are now ongoing in two of these trials:
    - SKYLARK (PPD-301) Study investigating zuranolone as an oral therapy in women with PPD:
        - Placebo-controlled trial evaluating a two-week course of zuranolone 50 mg in women with PPD, with additional short-term follow-up.
        - *Topline data from this study is anticipated in 2021.*
    - WATERFALL (MDD-301B) Study investigating zuranolone for as-needed, or episodic, treatment in MDD:
        - Placebo-controlled trial evaluating a two-week course of zuranolone 50 mg in patients with MDD, with additional short-term follow-up.
        - *Based on strong enrollment to date, with more than 50% enrolled, topline data from this study is now anticipated in the first half of 2021.*

Sage is on-track to commence dosing of the third new zuranolone Phase 3 trial in 2020:

- CORAL (MDD-305) Study investigating zuranolone for acute RRT in patients with MDD when co-initiated with a newly administered standard antidepressant therapy:
    - Placebo-controlled trial evaluating a two-week course of zuranolone 50 mg, when co-initiated with an open-label antidepressant, in patients with MDD, with additional short-term follow-up.
    - *Topline data from this study is anticipated in 2021.*

Additional study updates:

- SHORELINE Study (MDD-303): The Company is on track to report topline data in the second half of 2020 from patients with MDD who received zuranolone 30 mg in the SHORELINE Study, designed to evaluate safety and tolerability of as-needed repeat treatment over a 1-year period.
    - Patient dosing has begun in a new 50 mg cohort of patients with MDD; enrollment is ongoing.

- **MOUNTAIN Study 6-month follow-up data:** As part of the MOUNTAIN Study, subjects were offered the opportunity to participate in a 6-month, blinded follow-up to assess durability of response. The study was not powered to detect statistical significance beyond the Day 15 endpoint. More detailed data will be prepared for presentation and publication.
    - Of the subjects who were dosed in the MOUNTAIN Study, approximately 50% agreed to join the 6-month follow-up period and nearly 75% of patients who responded to zuranolone 30 mg at Day 15 maintained their response rate at the last follow-up on Day 182.

Safety:

- No drug-related adverse events, changes in laboratories, ECG measures, vital signs, or suicidality ratings were present over the long-term following exposure to zuranolone. Zuranolone was generally well-tolerated and showed a similar safety profile as seen in earlier studies.
- There were no signals of withdrawal or rebound after treatment with zuranolone was completed.

Durability of treatment:

- In subjects with response after the 14-day treatment period (Day 15), a large majority maintained this response throughout the 6-month follow-up regardless of arm.
    - Out of responders to zuranolone 30 mg at Day 15 (N=77), a large majority (74.5%) maintained their response rate at the last follow up at Day 182.
    - This continued benefit was seen with all efficacy measures over the 6-month follow-up period: (17-item Hamilton Rating Scale for Depression (HAM-D), Clinician Global Impression – Improvement (CGI-I), Clinician Global Impression – Severity (CGI-S).

- Sage's collaboration with Shionogi & Co., Ltd. is progressing, with Shionogi initiating a Phase 2 trial with zuranolone in Japan for the treatment of MDD. Under terms of collaboration, Shionogi is responsible for all clinical development, regulatory filings and commercialization of zuranolone for MDD, and potentially other indications, in Japan, Taiwan and South Korea.

- Sage is also currently evaluating the ongoing zuranolone clinical pharmacology and safety program and plans to finalize requirements to support a potential future NDA with the FDA.

- **ZULRESSO™ (brexanolone) CIV injection:**
    - Revenue in the second quarter of 2020 from sales of ZULRESSO was $1.1 million, compared to $2.3 million in the first quarter of 2020. In April 2020, as a part of the Company's restructuring, Sage downsized commercial efforts, including elimination of its entire salesforce. The Company now has a small commercial team with a primary focus on working with healthcare providers and supporting women with PPD in geographies with active, ZULRESSO treating sites.
    - The rapid spread of COVID-19 in the U.S. resulted in multiple sites of care pausing treatment of new patients with ZULRESSO during the quarter. Concerns about exposure to the virus have also caused a significant reduction in the number of women with PPD seeking treatment with ZULRESSO and in physicians willing to prescribe it. Given the ongoing surge in the number of cases of COVID-19 in the U.S. and continuing concerns about the pandemic across the country, the Company expects the significant adverse impact of the pandemic on ZULRESSO revenues to continue. The Company does not plan to provide revenue guidance for the balance of 2020.
    - The Company has received clearance from the U.S. FDA, under the Coronavirus Treatment Acceleration Program (CTAP), to initiate a Phase 3 study with brexanolone in patients with advanced COVID-19 related acute respiratory distress syndrome (ARDS).
        - Additional information about this program will be provided during Sage's upcoming FutureCast investor day planned for September.

Neurology Franchise
SAGE-324, a next-generation PAM of $GABA_A$ receptors and Sage's lead neurology asset, is in development as a potential oral therapy for neurological conditions, such as essential tremor (ET), epilepsy and Parkinson's disease.

- **SAGE-324:** Sage initiated enrollment and dosing in the KINETIC Study (324-ETD-201), a placebo-controlled Phase 2 study evaluating the safety and efficacy of SAGE-324 in patients with ET. Patients will receive a once-daily, four-week course of SAGE-324 60 mg or placebo.
    - *Topline data from this study is anticipated in 4Q 2020/1Q 2021.*

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), Parkinson's disease (PD) and Alzheimer's disease (AD).

- **SAGE-718:** The Company is on-track to initiate the PARADIGM Study (718-CNP-201), a Phase 2a open-label study in 2020 evaluating SAGE-718 in patients with PD cognitive dysfunction.
    - Results from this study will inform potential advancement of SAGE-718 into further

development.
    - *Topline data from this study is anticipated in 2H 2020.*

Anticipated Upcoming Milestones

2H 2020

- Zuranolone:
    - Initiate dosing in Phase 3 CORAL (MDD-305) Study evaluating a two-week course of zuranolone 50 mg, when co-initiated with an open-label anti-depressant, as an acute rapid response therapy in patients with MDD.
    - Report topline data from Phase 3 SHORELINE (MDD-303 – 30 mg) Study.
- Brexanolone:
    - Initiate Phase 3 study in patients with advanced COVID-19 related acute respiratory distress syndrome (ARDS).
- SAGE-718:
    - Report topline data from Phase 2a study in patients with Parkinson's disease cognitive dysfunction.
- SAGE-324:
    - Report topline data from Phase 2 placebo-controlled study in ET (4Q 2020/1Q 2021).

2021

- Zuranolone:
    - Report topline data from Phase 3 WATERFALL Study (1H 21).
    - 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).

Financial Results for the Second Quarter 2020

- **Revenue**: Sage recorded $1.1 million in net revenue in the second quarter of 2020 from sales of ZULRESSO, compared to $0.5 million for the same period in 2019. Sage recorded no collaboration revenue in the second quarter of 2020 compared to $0.4 million in collaboration revenue from Shionogi & Co., Ltd. related to reimbursement of product expense for the same period in 2019.
- **Cash Position**: Cash, cash equivalents, restricted cash, and marketable securities as of June 30, 2020 were $759 million compared to $875 million at March 31, 2020.
- **R&D Expenses**: Research and development expenses were $73.3 million, including $10.1 million of non-cash stock-based compensation expense, in the second quarter of 2020 compared to $89.1 million, including $13.7 million of non-cash stock-based compensation expense, for the same period in 2019. The decrease in R&D expenses was primarily related to the completion of the MOUNTAIN Study, a Phase 3 clinical trial of zuranolone in MDD and the decrease in non-cash stock-based compensation expense.
- **SG&A Expenses**: Selling, general and administrative expenses were $38.2 million, including $12.1 million of non-cash stock-based compensation expense, in the second quarter of 2020 compared to $88.2 million, including $21.1 million of non-cash stock-based compensation expense, for the same period in 2019. The decrease in SG&A expenses was primarily due to the restructuring that the Company announced during the second quarter of 2020.
- **Restructuring Expenses**: Restructuring expenses were $28.4 million in the second quarter of 2020 compared to none for the same period in 2019.
- **Net Loss**: Net loss was $136.3 million for the second quarter of 2020, compared to $168.2 million for the same period in 2019.

Financial Guidance

- Sage anticipates a cash balance of at least $550 million at end of 2020, which the Company anticipates will support operations into 2022 based on current operating plans.

Conference Call Information
Sage will host a conference call and webcast today, Monday, August 10, 2020, at 8:30 a.m. ET to discuss its second quarter 2020 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 revenues from sales of ZULRESSO and the expected continuing impact of the COVID-19 pandemic on ZULRESSO revenues; our clinical development plans and expected timelines; our expectations with respect to 2020 operating expenses and year-end cash; our belief that existing cash will support operations into 2022; our belief in the potential of our product candidates in various indications; the potential profile and benefit of our product candidates; and the goals, opportunity and potential for our business. These statements constitute forward-looking statements as that term is defined in the Private Securities Litigation Reform Act of 1995. These forward-looking statements are neither promises nor guarantees of future performance, and are subject to a variety of risks and uncertainties, many of which are beyond our control, which could cause actual results to differ materially from those contemplated in these forward-looking statements, including the risks that: we may never be able to generate meaningful revenues from sales of ZULRESSO or to generate revenues at levels necessary to justify our investment; the impact of the COVID-19 pandemic on sales of ZULRESSO may last longer than we expect or may reoccur in waves; our post-restructuring focus on geographies where there are existing, active ZULRESSO treating sites may not be sufficient for us to achieve success from the sale of ZULRESSO or to generate revenues at meaningful levels or at levels necessary to justify our investment even after the impact of the COVID-19 pandemic lessens; we may not be able to overcome the barriers to treatment with ZULRESSO or we may continue to encounter other issues or challenges in commercializing ZULRESSO which could further limit the potential of ZULRESSO and the timing and amount of future revenues; results achieved with use of ZULRESSO in the treatment of PPD in commercial use may be different than observed in clinical trials, and may vary among patients; the number of women with PPD or the unmet need for additional treatment options may be significantly smaller than we expect; we may encounter delays in initiation or conduct of our ongoing and planned clinical trials, including slower than expected site initiation or enrollment, that may impact our ability to meet our expected time-lines and increase our costs; we may not be able to mitigate the impact of COVID-19 on our clinical development timelines and the impact may be more significant than we expect and may negatively impact expected site initiation, enrollment or conduct in our clinical trials, or cause us to pause trials or not be able to use data, in each case which may significantly impact our ability to meet our expected time-lines or may significantly impact the integrity or sufficiency of the data from our trials or increase our costs or cause us to have to change our plans; the 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; our expectations as to expenses, year-end cash and cash needs 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; 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; success in our non-clinical studies or in earlier clinical trials may not be repeated or observed in ongoing or future studies, and ongoing and future non-clinical and clinical results may not meet their primary or key secondary endpoints or be sufficient to file for or gain regulatory approval to market 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 planning to study in new trials; we may encounter issues with the efficacy or durability of short-term treatment, or co-initiated treatment with zuranolone or safety and efficacy concerns with respect to retreatment that require additional studies be conducted; the FDA may ultimately decide that the design or results of our completed and planned clinical trials for any of our product candidates, even if positive, are not sufficient for regulatory approval in the indications that are the focus of our development plan; other decisions or actions of the FDA or other regulatory agencies may affect the initiation, timing, design, size, progress and cost of clinical trials and our ability to proceed with further development; we may encounter technical and other unexpected hurdles in the development and manufacture of our product candidates which may delay our timing or change our plans or increase our costs; as well as those risks more fully discussed in the section entitled "Risk Factors" in our most recent Quarterly Report on Form 10-Q, as well as discussions of potential risks, uncertainties, and other important factors in our subsequent filings with the Securities and Exchange Commission. In addition, any forward-looking statements represent our views only as of today, and should not be relied upon as representing our views as of any subsequent date. We explicitly disclaim any obligation to update any forward-looking statements.

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

	Three Months Ended March 31,		Six Months Ended June 30,	
	2020	**2019**	**2020**	**2019**
Product revenue, net	$ 1,089	$ 519	$ 3,375	$ 519
Collaboration revenue	-	354	-	819
Total revenue	1,089	873	3,375	1,338
Operating costs and expenses:				
Cost of goods sold	110	44	280	44

Research and development	73,320	89,059	136,930	175,457
Selling, general and administrative	38,224	88,227	108,355	172,146
Restructuring	28,402	-	28,402	-
Total operating costs and expenses	140,056	177,330	273,967	347,647
Loss from operations	(138,967)	(176,457)	(270,592)	(346,309)
Interest income, net	2,686	8,220	7,416	14,662
Other income (expense), net	(66)	16	89	20
Net loss	$ (136,347)	$ (168,221)	$ (263,087)	$ (331,627)
Net loss per share - basic and diluted	$ (2.63)	$ (3.28)	$ (5.07)	$ (6.65)
Weighted average shares outstanding - basic and diluted	51,926,074	51,257,640	51,917,417	49,882,377

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

	June 30, 2020	December 31, 2019
Cash, cash equivalents, restricted cash and investments	$ 758,889	$ 1,010,760
Total assets	$ 827,242	$ 1,084,150

Total liabilities	$	87,327	$	139,495
Total stockholders' equity	$	739,915	$	944,655

About ZULRESSO™ (brexanolone) CIV injection
ZULRESSO, the first medicine specifically approved by the U.S. Food and Drug Administration (FDA) for the treatment of postpartum depression (PPD) in adults, is a positive allosteric modulator of both synaptic and extrasynaptic $GABA_A$ receptors. Allosteric modulation of neurotransmitter receptor activity results in varying degrees of desired activity rather than complete activation or inhibition of the receptor.

SELECT IMPORTANT SAFETY INFORMATION
These are not all the side effects of ZULRESSO.

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 untilyour 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/20200810005142/en/

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