August 9, 2016

Sage Therapeutics Announces Second Quarter 2016 Financial Results and Provides Corporate Update

Portfolio Expansion Underway Based on Recent Positive Data from SAGE-547 and SAGE-217

Top-line Data Readout of Phase 3 STATUS Trial in SRSE Now Expected in 1H 2017

Dosing Commenced in Expanded Phase 2 Program for SAGE-547 in Moderate and Severe Postpartum Depression

Phase 2 Initiations Planned for SAGE-217 in Essential Tremor and Postpartum Depression in 2H 2016

Proof-of-Concept Study Initiations Planned with SAGE-547 in Major Depressive Disorder and SAGE-217 in Parkinson's Disease in 2H 2016

Conference Call Today at 8:00 AM ET

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Sage Therapeutics, Inc. (NASDAQ: SAGE) today reported business highlights and financial results for the second quarter ended June 30, 2016, and provided an update on corporate strategy and financial guidance.

"The successful completion of our recent clinical studies has allowed us to begin a portfolio transformation at Sage. While it is commonly understood that GABA dysfunction is at the core of many CNS conditions, Sage is pursuing development of compounds that modulate GABA in a more complex and tailored manner, and we're executing a new approach to drug development," said Jeff Jonas, M.D., Chief Executive Officer of Sage. "Sage's growing pipeline of drug candidates impacting GABA provides us with an industry-leading opportunity to develop medicines leveraging this mechanism of action."

"We have recently expanded our Phase 2 development program exploring SAGE-547 for postpartum depression with the initiation of two clinical trials in moderate and severe PPD. This year, we also plan to advance the development of SAGE-217 with a focus on essential tremor and postpartum depression. In considering new indications, Major Depressive Disorder and Parkinson's disease, we expect to continue to exploit small, efficient proof-of-concept studies to guide portfolio strategy. We are also evaluating several additional candidates within our GABA pipeline, such as SAGE-105 and SAGE-324, to explore their potential impact in such CNS disorders as orphan epilepsies. Lastly, while the data readout of the STATUS Trial in SRSE is delayed, we remain confident in our overall assessment of the unmet medical need."

Corporate and Clinical Strategy Update

- **Key findings from the STATUS Trial - evaluating SAGE-547 in Super Refractory Status Epilepticus (SRSE):**
  - Overall, the number of patients presenting at STATUS Trial sites for evaluation is tracking ahead of expectations. The number of patients enrolling after screening, identified in a blinded analysis by the Company, was less than expected based on several factors.
  - The operational metrics relating to the number of patients presenting to trial sites proved to be in line with expectations. However, other factors relating to patient evaluation and pre-treatment prior to enrollment have contributed to slower than expected trial enrollment with approximately 16% fewer patients randomized than expected at this time.
  - An evaluation of screening and enrollment patterns provided an opportunity to adjust and refine the enrollment process. For example, moving forward, the criteria for inclusion and exclusion has been clarified for new patients believed to be suffering from anoxic brain injury, to prevent exclusion of patients who could benefit from therapy. In addition, trial sites will now be permitted to use a more typical standard of care approach, seizure suppression, as a diagnostic screen, instead of requiring burst suppression. The study's screening approach was more restrictive than the clinical practice at several sites, limiting enrollment. This modification of the initial screen has no impact on the primary endpoint.
  - Clarifications to the enrollment procedures are intended to bring enrollment trends in line with the Sage's operating assumptions, with top-line results from the Phase 3 STATUS Trial now anticipated in the first half of

2017, with an anticipated 2018 commercial launch of SAGE-547 in SRSE, if successfully developed and approved.

- **Expansion of GABA Pipeline and Clinical Programs**
  - **SAGE-547:** Based on the positive results from the Phase 2 clinical trial in severe PPD, Sage is broadening its SAGE-547 PPD clinical program and continuing to use SAGE-547 as a probe to guide development in other mood and affective disorders:
    - **Postpartum depression (PPD):** Sage has initiated an expansion of the Phase 2 clinical program in PPD and recently commenced dosing in separate clinical trials evaluating moderate and severe patients. The multicenter, placebo-controlled trials will explore dose-ranging of SAGE-547 in severe PPD patients and SAGE-547 efficacy in moderate PPD patients.
    - **Major Depressive Disorder (MDD):** Sage plans to initiate a small proof-of-concept Phase 2 clinical trial using SAGE-547 in MDD to guide future clinical development for SAGE-217.
  - **SAGE-217:** Sage plans to focus initial clinical development for SAGE-217 on essential tremor and PPD. Pending results of our probe studies with SAGE-547 in MDD and SAGE-217 in Parkinson's disease, the Company will decide on further development options for SAGE-217 in 1H 2017.
    - Sage presented positive Phase 1 clinical results for SAGE-217, a novel, internally-developed orally active next generation GABA modulator, at the 13th Eilat Conference on New Antiepileptic Drugs and Devices in June 2016.
    - **Essential tremor:** In July 2016, Sage announced that safety, tolerability and pharmacokinetics of SAGE-217 were studied in a small open-label Phase 1 cohort of essential tremor patients (n=6). While not designed to demonstrate efficacy, preliminary data show that single doses of SAGE-217 resulted in a similar reduction in tremor symptoms as achieved with a single 12 hour infusion of SAGE-547 in the Company's previous placebo-controlled probe study (n=25). Based on these data, Sage plans to initiate a Phase 2 clinical trial for SAGE-217 in essential tremor during 2H 2016.
    - **PPD:** Sage plans to develop SAGE-217 for PPD based on the recent positive results from the Phase 2 clinical trial of SAGE-547 in severe PPD. SAGE-217 will initially be studied in severe PPD, with a Phase 2 clinical trial planned for initiation in 2H 2016.
    - **Parkinson's disease:** Given the potential role of GABA in reducing tremor and the associated symptoms of Parkinson's disease, Sage plans to initiate a proof-of-concept Phase 2 clinical trial of SAGE-217 in Parkinson's disease in 2H 2016.
  - **Other GABA programs:** Sage also plans to prioritize advancement of a novel GABA candidate, such as SAGE-105 or SAGE-324, into IND-enabling studies for development in other GABA-related indications, such as orphan epilepsies.
- **Updated Financial Guidance**
  - Sage is currently undertaking a full portfolio review of its GABA-based candidates, as well as expanding its research efforts to identify additional indications with a biological rationale for treatment with the Company's differentiated GABA compounds. This effort will include extended research into other mood and affective disorders such as depression, panic and mania.
  - Sage plans to provide additional public updates on this initiative by the end of the year, including potential new development candidates.
  - The Company expects that its cash, cash equivalents and marketable securities will be sufficient to fund its operating expenses and capital expenditure requirements, based on its current operating plans, into late 2017.

Recent and Expected Near-Term Clinical Milestones

- **2H 2016**
  - Reported top-line data from Phase 2 trial of SAGE-547 in severe PPD
  - Recently initiated Phase 2 dose-ranging expansion trial for SAGE-547 in severe PPD and Phase 2 trial of SAGE-547 in moderate PPD
  - Present Phase 2 results from SAGE-547 severe PPD trial at medical congress
  - Initiate Phase 2 trial of SAGE-217 in severe PPD
  - Initiate Phase 2 trial of SAGE-217 in essential tremor
  - Initiate Phase 2 proof-of-concept trial of SAGE-547 in Major Depressive Disorder
  - Initiate Phase 2 proof-of-concept trial of SAGE-217 in Parkinson's disease

- Initiate Phase 1 trial of SAGE-689, subject to successfully addressing FDA data request

- **1H 2017**
  - Top-line data from Phase 3 STATUS Trial of SAGE-547 in SRSE
  - Top-line data from Phase 2 proof-of-concept trial of SAGE-547 in Major Depressive Disorder
  - Top-line data from Phase 2 proof-of-concept trial of SAGE-217 in Parkinson's disease
  - Initiate Phase 1 trial of first NMDA candidate, SAGE-718

Second Quarter 2016 Financial Results

- **Cash Position:** Cash, cash equivalents and marketable securities as of June 30, 2016 were $272.3 million, compared with $186.8 million at December 31, 2015.
- **R&D Expenses:** Research and development expenses were $26.1 million, including $2.0 million of non-cash stock-based compensation expense, in the second quarter of 2016, compared to $18.6 million, including $2.3 million of non-cash stock-based compensation expense, for the same period of 2015. The increase in R&D expense was primarily due to the continued advancement of our SAGE-547 and SAGE-217 clinical programs.
- **G&A Expenses:** General and administrative expenses were $8.9 million, including $2.4 million of non-cash stock-based compensation expense, in the second quarter of 2016, compared to $6.5 million, including $3.1 million of non-cash stock-based compensation expense, for the same period of 2015. The increase in G&A expenses was primarily due to personnel-related costs and expanding commercial operations in preparation for the potential launch of SAGE-547.
- **Net Loss:** Net loss was $34.7 million for the second quarter of 2016 compared to net loss of $25.0 million for the same period of 2015.

Conference Call Information

Sage will host a conference call and webcast today at 8:00 AM ET to discuss its second quarter 2016 financial results and recent business updates. The live webcast can be accessed on the investor page of Sage's website at investor.sagerx.com. The conference call can be accessed by dialing 1-866-450-8683 (toll-free domestic) or 1-281-542-4847 (international) and using the conference ID 57731355. 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 clinical-stage biopharmaceutical company committed to developing novel medicines to transform the lives of patients with life-altering central nervous system (CNS) disorders. Sage has a portfolio of novel product candidates targeting critical CNS receptor systems, GABA and NMDA. Sage's lead program, SAGE-547, is in Phase 3 clinical development for super-refractory status epilepticus, a rare and severe seizure disorder, and is being developed for severe postpartum depression. Sage is developing its next generation modulators, including SAGE-217, SAGE-689 and SAGE-718, with a focus on acute and chronic CNS disorders. 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 expectations regarding development of our product candidates and their potential in the treatment of various CNS disorders; the expected timing of clinical trials and IND-enabling activities; the anticipated availability and announcement of data and results from clinical trials of our product candidates; our plans for evaluation of new indications and new compounds; our expectations regarding enrollment trends in the STATUS trial; our belief in the unmet need in SRSE, and our estimates as to the potential number of patients with SRSE; our expectations regarding timing of a potential launch of SAGE-547 in SRSE, if successfully developed and approved; and our expectations with respect to the sufficiency of our cash, cash equivalents and marketable securities. 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 continue to experience slower than expected enrollment and randomization of evaluable patients in the STATUS trial or slower than expected clinical site initiation and enrollment in our other clinical trials, or the potential need for additional analysis or data or the need to enroll additional patients, leading to possible delays in completion of trials or in the availability of data; we may not be able to generate supportive non-clinical data or to successfully demonstrate the efficacy and safety of our product candidates at each stage of development; success in our non-clinical studies or in earlier stage clinical trials may not be repeated or observed in ongoing or future studies involving the same compound or other product candidates, and ongoing and future pre-clinical and clinical results may not support further development of product

candidates or be sufficient to gain regulatory approval to market any product; decisions or actions of regulatory agencies may affect the initiation, timing, progress and cost of clinical trials, and our ability to proceed with further clinical studies of a product candidate or to obtain marketing approval; the actual size of the patient populations associated with the diseases for which we are developing our product candidates may be significantly lower than our estimates; the internal and external costs required for our activities, and to build our organization in connection with such activities, and the resulting use of cash, may be higher than expected, or we may conduct additional clinical trials or pre-clinical studies or engage in new activities, requiring additional expenditures and using cash more quickly than anticipated; and we may encounter technical and other unexpected hurdles in the development and manufacture of our products which may delay our timing or increase our expenses and use of cash, 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 Balance Sheets
(in thousands)
(unaudited)

	June 30, 2016	December 31, 2015
Assets		
Current Assets:		
Cash and cash equivalents	$ 189,003	$ 186,753
Marketable securities	83,292	-
Prepaid expenses and other current assets	1,812	1,738
Total current assets	274,107	188,491
Property and equipment and other long-term assets	1,523	525
Total assets	$ 275,630	$ 189,016
Liabilities and Stockholders' Equity		
Current Liabilities:		
Accounts payable	$ 5,957	$ 5,159
Accrued expenses	12,382	10,148
Total current liabilities	18,339	15,307
Other liabilities	82	14
Total liabilities	18,421	15,321
Total stockholders' equity	257,209	173,695
Total liabilities and stockholders' equity	$ 275,630	$ 189,016

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,	
	2016	2015	2016	2015
Operating expenses:				
Research and development	26,096	18,603	49,677	31,503
General and administrative	8,910	6,456	16,044	10,453
Total operating expenses	35,006	25,059	65,721	41,956
Loss from operations	(35,006)	(25,059)	(65,721)	(41,956)
Interest income, net	266	41	442	62
Other expense, net	(7)	(9)	(11)	(4)
Net loss	$ (34,747)	$ (25,027)	$ (65,290)	$ (41,898)

Net loss per share - basic and diluted	$ (1.08)	$ (0.90)	$ (2.05)	$ (1.57)
Weighted-average shares outstanding - basic and diluted	32,062,298	27,860,332	31,835,194	26,765,705

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