Sage Therapeutics and Shionogi & Co., Ltd., Enter Strategic Collaboration to Develop and Commercialize SAGE-217 for MDD and Other Indications in Japan, Taiwan and South Korea

Collaboration intended to accelerate development of SAGE-217 in key Asian markets and supports Sage's mission to bring transformational medicines to patients around the world

Collaboration supports Shionogi's vision of creating a more vigorous society by exploring the potential to provide relief from the psychological uncertainty of depression with a novel treatment paradigm.

CAMBRIDGE, Mass. and OSAKA, Japan, June 13, 2018 – Sage Therapeutics (NASDAQ: SAGE), a clinical-stage biopharmaceutical company developing novel medicines to treat life-altering central nervous system (CNS) disorders, and Shionogi & Co., Ltd., today announced they have entered into a strategic collaboration for the clinical development and commercialization of SAGE-217 for the treatment of major depressive disorder (MDD) and other indications in Japan, Taiwan and South Korea. Sage received Breakthrough Therapy Designation from the U.S. Food and Drug Administration (FDA) for SAGE-217 in MDD in February 2018, and recently announced an expedited development plan for SAGE-217 in the U.S. with a pivotal Phase 3 placebo-controlled trial in patients with MDD expected to commence this year, and an ongoing placebo-controlled trial in women with PPD, now also designated a pivotal trial. The goal of the collaboration is to accelerate development of a potentially groundbreaking medicine to patients in key Asian markets.

Under the terms of the agreement, Shionogi will be responsible for all clinical development, regulatory filings and commercialization of SAGE-217 for MDD, and potentially other indications, in Japan, Taiwan and South Korea. Shionogi will make an upfront payment to Sage of $90 million, and Sage will be eligible to receive additional development and commercial milestones of up to $485 million. Sage will receive tiered royalties on sales of SAGE-217 in Japan, Taiwan and South Korea, if development efforts are successful, with tiers averaging in the greater than 20 percent range, subject to other terms of the agreement. Shionogi has also granted Sage certain rights to co-promote SAGE-217 in Japan across all indications. Sage maintains exclusive rights to develop and commercialize SAGE-217 outside of Japan, Taiwan and South Korea.

"We are pleased to collaborate with Shionogi, a company that shares our excitement at the opportunity to work together to accelerate development and broaden geographic access to a potentially paradigm-shifting treatment for depression," said Jeff Jonas, M.D., chief executive officer of Sage.

"Shionogi is a well-regarded commercial leader in mood disorders in the Asian market. By working together, we believe we can expand the global footprint for SAGE-217 alongside our ongoing efforts in the U.S. and E.U. As we have always said, our goal is to build a fully-integrated, multi-national biopharmaceutical company and this collaboration moves us another step closer to achieving the goal."

"This collaboration, if successful, will enable us to move one step closer in realizing a more vigorous society in which patients in need are provided the potential for relief from the psychological uncertainty of depression allowing the possibility of fulfillment of one's innate ability. In addition, the compound will allow us to build up and strenghthen the psychiatry presence that we have built through Cymbalta and Intuniv." said Dr. Isao Teshirogi, President and Chief Executive Officer, Shionogi & Co., Ltd.

About SAGE-217

SAGE-217 is a next generation positive allosteric modulator that has been optimized for selectivity to synaptic and extrasynaptic GABAA receptors and a pharmacokinetic profile intended for daily oral dosing. The GABA system is the major inhibitory signaling pathway of the brain and CNS, and contributes significantly to regulating CNS function. SAGE-217 is currently being developed for MDD and certain other mood and movement disorders.

Sage received Breakthrough Therapy Designation from the FDA for SAGE-217 in MDD in February 2018. The Breakthrough Therapy Designation is intended to offer a potentially expedited development path and review in the U.S. for promising drug candidates, which includes increased interaction and guidance from the FDA. This regulatory decision was based primarily on the positive results from the Phase 2, placebo-controlled trial of SAGE-217 in 89 adult patients with moderate to severe MDD. In the trial, SAGE-217 met the primary endpoint with a statistically significant mean reduction in the Hamilton Rating Scale for Depression (HAM-D) 17-item total score from baseline at Day 15 in the SAGE-217 group, compared to placebo ($p<0.0001$). Statistically significant improvements were observed in the HAM-D score compared to placebo by the morning following the first dose through Week 4 and the effects of SAGE-217 remained numerically greater than placebo through the end of follow-up at Week 6. SAGE-217 was generally well-tolerated. The most common adverse events in the SAGE-217 group were headache, dizziness, nausea, and somnolence.

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 CNS disorders. Sage has a portfolio of novel product candidates targeting critical CNS receptor systems, $GABA_A$ and NMDA. Sage's lead program, a proprietary IV formulation of brexanolone (SAGE-547), has completed Phase 3 clinical

development for postpartum depression and a New Drug Application is currently under review with the U.S. Food and Drug Administration. Sage is developing its next generation modulators, including SAGE-217 and SAGE-718, in various CNS disorders. For more information, please visit www.sagerx.com.

About Shionogi & Co., Ltd.

Shionogi & Co., Ltd. is a major research-driven pharmaceutical company dedicated to bringing benefits to patients based on its corporate philosophy of "supplying the best possible medicine to protect the health and wellbeing of the patients we serve." Shionogi's research and development currently targets two therapeutic areas: infectious diseases, and pain/CNS disorders. For over 50 years, Shionogi has developed and commercialized innovative oral and parenteral anti-infectives. In addition, Shionogi is engaged in new research areas, such as obesity/geriatric metabolic diseases and oncology/immunology. Contributing to the health and QOL of patients around the world through development in these therapeutic areas is Shionogi's primary goal. For more details, please visit www.shionogi.co.jp/en/.

Forward-Looking Statements

Various statements in this release are "forward-looking" statements, including without limitation, statements as to: the potential for expedited development of SAGE-217 in MDD and PPD; the timing of planned clinical activities related to SAGE-217; the potential of SAGE-217 to be a paradigm shift in the treatment of depression; the potential for successful development and commercialization of SAGE-217 in the U.S. and in the Shionogi markets; and expectations for future milestones and royalties under the collaboration. These forward-looking statements are neither promises nor guarantees of future performance, and are subject to a variety of risks and uncertainties which could cause actual results to differ materially from those contemplated in these forward-looking statements, including the risks that: expedited development and review of SAGE-217 may not be achieved in any market; regulatory authorities in the U.S. or in the Shionogi markets may decide that the design or results of the SAGE-217 clinical program are not sufficient for regulatory approval in MDD, PPD or any other indication; development of SAGE-217 may not be successful in any indication; success in non-clinical studies or in earlier stage clinical trials may not be repeated or observed in ongoing or future studies which may not support further development or be sufficient to gain regulatory approval to market the product; adverse events may be encountered at any stage of development that negatively impact further development; and even if development efforts are successful there may be events that limit market potential or trigger reductions in milestones or royalties. Other risks and uncertainties include, but are not limited to, issues relatd to: adverse outcome of important litigation; domestic and foreign healthcare reforms and changes of laws and regulations; general industry and market

conditions; changes in interest rates and currency exchange rates; manufacturing and marketing risks, which include, but are not limited to, inability to build production capacity to meet demand and unavailability of raw materials; entry of competitive products; and other technical and other unexpected hurdles in the development and manufacture of SAGE-217 as well as those risks more fully discussed in the section entitled "Risk Factors" in Sage's most recent Quarterly Report on Form 10-Q, as well as discussions of potential risks, uncertainties, and other important factors in either company's other filings with the Securities and Exchange Commission. In addition, any forward-looking statements represent the companies views only as of today, and should not be relied upon as representing their views as of any subsequent date. The companies explicitly disclaim any obligation to update any forward-looking statements.

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