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SAGE Therapeutics Presents New Preclinical Data on SAGE-217 at Eilat Conference on New Anti-Epileptic Drugs

Data Highlight Potential of SAGE-217 to Address Acute and Chronic Forms of Epilepsy and Seizure Disorders

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- SAGE Therapeutics (NASDAQ: SAGE) today presented preclinical data on its second-generation neuroactive steroid, SAGE-217, at the Twelfth Eilat Conference on New Anti-Epileptic Drugs in Madrid, Spain. The data suggest improved activity for this compound versus other first-generation neuroactive steroids in development, as well as favorable selectivity and pharmacokinetic profile of the drug.

"SAGE has developed a proprietary chemistry platform that we believe allows us to efficiently identify and design selective neuroactive molecules that impact two important, validated nervous system targets - $GABA_A$ and NMDA receptors," said Albert Robichaud, Ph.D., chief scientific officer of SAGE Therapeutics. "The data presented suggest the potential for high potency and selectivity of SAGE-217 and its potential efficacy in well-validated, preclinical seizure models. This promising compound is the second of several we plan to develop in our seizure franchise targeting a range of disorders from status epilepticus to orphan genetic epilepsies, such as Dravet syndrome."

SAGE-217 is a GABA-potentiating, second-generation neuroactive steroid that has demonstrated favorable CNS exposure (rodent brain to plasma ratio > 1.3-3.2), an attractive pharmacokinetic profile and the potential for IV, IM and oral administration. Preclinical data generated through *in vitro* electrophysiology studies utilizing mammalian cell lines showed that SAGE-217 was more efficacious in *in vitro* assays of $GABA_A$ modulation than either allopregnanolone or ganaxolone at both synaptic $\alpha_1\beta_2\gamma_2$-containing $GABA_A$ receptors and extra-synaptic $\alpha_4\beta_3\delta$-containing $GABA_A$ receptors. SAGE-217 also exhibited reduced off-target activities compared to the known first-generation analogs. In addition, in comparison to first-generation neurosteroids, SAGE-217 demonstrated efficacy at reduced levels of plasma and brain exposure in models of benzodiazepine-resistant seizure.

The company also presented data previously reported on SAGE-547, an allosteric modulator of $GABA_A$ receptors currently in clinical development for super-refractory status epilepticus (SRSE).

"We continue to make good progress on our portfolio of seizure product candidates," said Steve Kanes, M.D., chief medical officer of SAGE. "SAGE-547 is advancing on track as an acute therapy in our Phase 1/2 clinical trial in patients with SRSE. We look forward to initiating development of SAGE-217 as a potential maintenance or chronic treatment for status epilepticus, as well as for other orphan genetic seizure disorders."

About SAGE-217

SAGE-217 is a novel neuroactive steroid that acts as a positive allosteric modulator of synaptic and extra-synaptic $GABA_A$ receptor subtypes. Unlike many of the naturally occurring neuroactive steroids, SAGE-217 has a pharmacokinetic profile to potentially support once-daily oral dosing and a selectivity profile that minimizes potential off-target side effects. SAGE-217 is currently in preclinical development for a range of seizure conditions, including orphan genetic epilepsy disorders, such as Rett syndrome and Dravet syndrome.

About SAGE-547

SAGE-547 is an allosteric modulator of both synaptic and extra-synaptic $GABA_A$ receptors. $GABA_A$ receptors are widely regarded as validated drug targets for a variety of CNS disorders, with decades of research and multiple approved drugs targeting these receptor systems. SAGE-547 is an intravenous agent in Phase 1/2 clinical development as an adjunctive therapy, a therapy combined with current therapeutic approaches, for the treatment of SRSE.

About SAGE Therapeutics

SAGE Therapeutics is a clinical-stage biopharmaceutical company committed to developing and commercializing novel medicines to treat life-threatening, rare central nervous system, or CNS disorders. SAGE's lead program, SAGE-547, is in

clinical development for super-refractory status epilepticus, or SRSE, and is the first of several compounds the company is developing in its portfolio of potential seizure medicines. SAGE's proprietary chemistry platform has generated multiple new compounds that target $GABA_A$ and NMDA receptors, which are broadly accepted as impacting many psychiatric and neurological disorders. For more information, please visit www.sagerx.com.

Forward-Looking Statements

This release contains forward-looking statements and information, including statements concerning SAGE's expectations regarding the potential safety, pharmacological effect and efficacy of SAGE-547 and SAGE-217, the expected development pathway for these and other product candidates and its expectations with respect to the timing and success of its clinical trials concerning. These and other statements concerning SAGE's future expectations, plans and prospects constitute forward-looking statements for the purposes of the safe harbor provisions under The Private Securities Litigation Reform Act of 1995 and other federal securities laws. In particular it should be noted that the initial data reported from the ongoing Phase 1/2 clinical trial of SAGE-547 are preliminary in nature and that the SAGE-547 clinical trial has not been completed. The preliminary data may change as additional data is released and such preliminary data may not be repeated or observed in ongoing or future studies involving SAGE-547 or our other product candidates. It should also be noted that the SAGE-217 data presented are from pre-clinical studies and have not been validated in human clinical trials. Actual results may differ materially from those indicated by these forward-looking statements as a result of various important factors, including, without limitation, SAGE's ability to successfully demonstrate the efficacy and safety of its product candidates, the pre-clinical and clinical results for its product candidates, which may not support further development of product candidates, actions of regulatory agencies, which may affect the initiation, timing and progress of clinical trials, obtaining, maintaining and protecting intellectual property, SAGE's ability to enforce its patents against infringers and defend its patent portfolio against challenges from third parties, competition from others developing products for similar uses, SAGE's ability to manage operating expenses, SAGE's ability to obtain additional funding to support its business activities and establish and maintain strategic business alliances and new business initiatives, SAGE's dependence on third parties for development, manufacture, marketing, sales and distribution of products, the outcome of litigation, and unexpected expenditures, as well as discussions of potential risks, uncertainties, and other important factors in SAGE's most recent quarterly report on Form 10-Q filed with the Securities and Exchange Commission, as well any subsequent filings with the Securities and Exchange Commission. In addition, any forward-looking statements represent SAGE's views only as of today and should not be relied upon as representing its views as of any subsequent date. SAGE explicitly disclaims any obligation to update any forward-looking statements.

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