AAN 74th ANNUAL MEETING ABSTRACT

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Abstract Title: SAGE-718 in Patients With Mild Cognitive Impairment or Mild Dementia Due to Alzheimer's Disease: Results From the Phase 2 LUMINARY Study

Press Release Title: Preliminary Study: New Drug May Be Safe for People with Mild Cognitive Impairment

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Objective: To evaluate the safety/tolerability of SAGE-718 and its effects on cognitive symptoms in patients with Alzheimer's disease (AD).

Background: Cognitive impairment has a deleterious impact on patients with AD and their caregivers; new therapies are needed. SAGE-718, a novel N-methyl-D-aspartate receptor positive allosteric modulator, is being investigated for the treatment of cognitive impairment in patients with neurodegenerative diseases such as AD.

Design/Methods: LUMINARY (NCT04602624) is an open-label, Phase 2 study evaluating SAGE-718 (3mg QD for 14 days) in patients with AD. Patients (aged 50–80 years) with Montreal Cognitive Assessment (MoCA) scores of 15-24 were included. Treatment-emergent adverse event (TEAE) incidence through Day 28 (primary endpoint), other safety outcomes (secondary endpoints), and cognitive and functional assessments were analyzed.

Results: Twenty-six patients (69.2% female; mean age 67 years), with a mean±SD MoCA of 20.7±2.61 were enrolled. Most patients (23/26) had a global Clinical Dementia Rating score of 0.5. Eight TEAEs were reported in 7 (26.9%) patients; all were mild/moderate; 6 were treatment related. No serious adverse events or deaths were reported. At Day 14, improvements from baseline were observed on multiple tests of executive functioning (Digit Symbol Substitution, Multitasking, One Touch Stockings, Spatial Working Memory, and 2-Back tests) and learning and memory (Pattern Recognition Memory and Verbal Recognition Memory tests). Statistically significant MoCA improvement (+2.3 points vs baseline) was observed at Day 28. No changes in attention/psychomotor speed were observed. Functional assessments also captured notable improvement in some patients (Clinical Global Impressions Scales and Amsterdam Instrumental Activities of Daily Living Questionnaire), particularly on items measuring aspects of complex/higher order activities.

Conclusions: In this study, SAGE-718 was generally well tolerated and associated with cognitive and functional improvements in patients with AD. These results support further investigation of SAGE-718 for the treatment of cognitive impairment associated with AD and other neurodegenerative diseases.

Study Support: Sage Therapeutics, Inc.