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Eisai, Biogen present Clinical study of Elenbecestat for Alzheimer's at AAIC 2018

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Eisai Co., Ltd. and Biogen Inc. announced detailed results from a Phase II clinical study (Study 202) of the investigational oral BACE (beta amyloid cleaving enzyme) inhibitor elenbecestat (development code: E2609) at the Alzheimer's Association International Conference (AAIC) 2018 being held in Chicago, Illinois, United States, from July 22 to 26, 2018. This poster presentation was accepted as a Late Breaking Abstract for AAIC.

Study 202 (ClinicalTrials.gov identifier NCT02322021) is a multicenter, randomized, double-blind, placebo- controlled parallel-group 18-month Phase II clinical study, conducted in the United States in patients with mild cognitive impairment (MCI) due to Alzheimer's disease, or mild to moderate dementia due to Alzheimer's disease (AD) with confirmed amyloid pathology by positron emission tomography (PET).

Seventy patients were randomized to four treatment arms receiving elenbecestat (5, 15, or 50 mg) or placebo daily. During the study period, more than half the patients in the elenbecestat 5 mg and 15 mg arms were switched to the 50 mg arm. These patients received elenbecestat 50 mg for three months or longer.

Analysis was carried out on the combination of patients in the initial 50 mg treatment arm plus the patients switched to the 50 mg arm, referred to collectively as the "50 mg total group arm" (38 patients). In addition to the primary safety objective, the study assessed amyloid pathology in the brain at 18 months as measured by amyloid PET as well as efficacy in terms of clinical symptoms, which were exploratory objectives in this study.

The primary objective of the study was to assess the safety and tolerability of elenbecestat after 18 months of treatment. The

incidence of treatment-emergent adverse events was similar between elenbecestat and placebo, and no dose-dependent response was observed for adverse events.

The six most common adverse events reported were upper respiratory tract infection, abnormal dreams and nightmares, contact dermatitis, headache, diarrhea, and falls. No adverse reactions suggestive of hepatic toxicity were observed in this study.

Regarding the accumulation of amyloid in the brain at 18 months as measured by PET via quantitative evaluation of Standard Uptake Value Ratio (SUVr) using the florbetaben PET tracer (n=28), a statistically significant reduction of brain amyloid load as compared to placebo was observed in the 50 mg total group arm with a reduction in SUVr of 0.104 (p=0.011).

Although a small sample size, using the florbetapir PET tracer (n=7) demonstrated a statistically significant decrease in brain amyloid load compared to placebo for the 50 mg total group arm (reduction in SUVr of 0.227) at 18 months (p=0.024).

Clinical efficacy was evaluated using the Clinical Dementia Rating Sum of Boxes (CDR-SB) rating scale. After 18 months of treatment, clinical assessment using CDR-SB demonstrated a mean treatment difference of -0.5 based off of an increase of 1.1 for the elenbecestat 50 mg total group arm (29 patients) versus an increase of 1.6 for the placebo group (12 patients). This represented a 31% slowing in rate of decline for the elenbecestat arm which is potentially considered to be clinically important.

Furthermore, based on information obtained from analyses of changes in CDR-SB and amyloid PET SUVr values from ADNI data, in a sub-population analysis of patients with baseline SUVr range between 1.4 and 1.9 who were identified in this study as being expected to have a higher rate of disease progression, there was 72% less decline in CDR-SB for patients in the 50 mg total group arm (n=10) versus placebo (n=5). While the study was not powered to show statistical significance compared to placebo on clinical symptoms, the results suggest that elenbecestat could slow decline in cognitive function of patients with MCI due to Alzheimer's disease, or mild to moderate dementia due to Alzheimer's disease.

Elenbecestat, discovered by Eisai, has been jointly developed by Eisai and Biogen since March 2014. The two companies are currently conducting two global Phase III clinical studies (MISSION AD1/2) in early Alzheimer's disease.

This release discusses investigational uses of agents in development and is not intended to convey conclusions about efficacy or safety. There is no guarantee that such investigational agent will successfully complete clinical development or gain health authority approval.