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Eisai Co., Ltd

EISAI PRESENTS LATEST CLINICAL FINDINGS SUGGESTING INHIBITION OF TAU PROPAGATION BY ANTI-MTBR TAU ANTIBODY E2814 AT THE 17TH CLINICAL TRIALS ON ALZHEIMER'S DISEASE CONFERENCE (CTAD)

-Eisai Initiates Phase II Clinical Study on Sporadic Early Alzheimer's Disease-

Eisai Co. Ltd (Headquarters: Tokyo, CEO: Haruo Naito, “Eisai”) announced today that the latest findings on anti-MTBR (microtubule binding region) tau antibody E2814 were presented at the 17th annual Clinical Trials on Alzheimer’s Disease (CTAD) conference, held in Madrid, Spain, and virtually. Eisai also announced initiation of a Phase II study (Study 202) on E2814 for sporadic early Alzheimer’s Disease (AD).

Impact of the anti-MTBR tau antibody E2814 on tau pathology biomarkers in Dominantly Inherited Alzheimer’s Disease (DIAD)

E2814 is an investigational anti-MTBR tau antibody designed to target the MTBR of tau. In AD patients, neurofibrillary tangles (NFT) are a pathological hallmark, and they are believed to spread through synaptically connected pathways in the brain, forming the tau propagation hypothesis. It is thought that tau propagation is driven by the specific tau species containing MTBR, tau seeds that spread tau pathology to different brain regions important for cognition and function.

Eisai conducted a Phase I/II clinical study (Study 103, NCT04971733; 7 participants) of the anti-MTBR tau antibody E2814 in patients with Dominantly Inherited Alzheimer’s Disease (DIAD) beginning in June 2021. This study aimed to evaluate the safety and tolerability of E2814 in DIAD patients, with a primary objective of assessing the target engagement of E2814 with MTBR-tau species in their cerebrospinal fluid (CSF). In addition, pharmacodynamic evaluation was performed using multiple biomarkers related to AD tau pathology. In the study, DIAD patients with clinical symptoms were administered E2814 for 12 to 24 months. Data from the Dominantly Inherited Alzheimer Network Observational Study (DIAN-obs), an observational cohort of DIAD, were used as references to evaluate biomarkers changes in E2814 treatment.

Compared to the reference data from DIAN-obs, patients who received E2814 showed approximately 75% and 50% reductions of CSF MTBR-tau243 and p-tau217, respectively, reflecting tau pathophysiology. Additionally, brain tau accumulation observed by tau PET was stabilized or trended toward decrease in DIAD subjects administered E2814. These results suggest that E2814 inhibited tau propagation and suppressed the accumulation of tau aggregates in brains of people living with DIAD. This will be further investigated in the ongoing Phase II/III Tau NexGen study (NCT05269394) with DIAD patients and the Phase II 202 study (NCT06602258) with sporadic early Alzheimer’s disease (AD) patients.

Initiation of Phase II clinical study (Study 202)

In September 2024, Eisai initiated a Phase II clinical study (Study 202) for individuals with early AD in the United States. The study is also scheduled to be conducted in Japan in the future. This study is a placebo-controlled, double-blind, parallel-group, dose exploration study, evaluating the safety, tolerability, and

biomarker efficacy of E2814 in people living with early AD receiving lecanemab as a backbone anti-Aβ therapy.

Eisai positions neurology as a key therapeutic area, and it will continue to create innovation in the development of novel medicines based on cutting-edge neurology research as it seeks to contribute further to improving the benefits of affected individuals and their families in diseases with high unmet needs, such as dementia including AD.

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 agents will successfully complete clinical development or gain health authority approval.

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[Notes to editors]

1. **About E2814**

   An investigational anti-microtubule binding region (MTBR) tau antibody, E2814 is being developed as a disease-modifying agent for tauopathies including sporadic Alzheimer's disease (AD). Phase I clinical studies are underway. E2814 was discovered as part of the research collaboration between Eisai and University College London. E2814 is designed to prevent the spreading of tau seeds within the brains of affected individuals. In addition, E2814 has been selected as an anti-tau therapy in a Phase II/III Tau NexGen study for the treatment of DIAD, conducted by DIAN-TU led by Washington University School of Medicine in St. Louis, is underway.

2. **Biomarkers related to AD tau pathology**

   As fluid biomarkers related to AD tau pathology, tau containing the residue 243 (MTBR-tau243) and tau phosphorylated at the residue 217 (p-tau217) in CSF have been reported.[1] In addition, positron emission tomography (tau PET), which specifically detects tau aggregates, is used as an imaging biomarker. These biomarkers are included in the Revised criteria for diagnosis and staging of Alzheimer's disease published by the National Institute on Aging and the Alzheimer's Association (NIA-AA) in June 2024.[2]

References

1. Horie K, et al. CSF MTBR-tau243 is a specific biomarker of tau tangle pathology in Alzheimer's disease. *Nat Med*. 2023. 29. 1954-1963
2. Jack Jr. CR, et al. Revised criteria for diagnosis and staging of Alzheimer's disease: Alzheimer's Association Workgroup. *Alzheimers Dement*. 2024. 20. 5143-5169