No.21-84

November 9, 2021
Eisai Co., Ltd.

DIAN-TU SELECTS LECANEMAB AS BACKGROUND ANTI-AMYLOID THERAPY IN CLINICAL TRIAL EVALUATING INVESTIGATIONAL THERAPY TARGETING TAU FOR DOMINANTLY INHERITED ALZHEIMER'S DISEASE

Eisai's anti-microtubule binding region (MTBR) tau antibody E2814 previously selected as the first investigational therapy among anti-tau drugs for the DIAN-TU Tau Next Generation trial

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") announced today that the Dominantly Inherited Alzheimer Network Trials Unit (DIAN-TU), led by Washington University School of Medicine in St. Louis, has an agreement with the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) to amend the clinical study (Tau NexGen) design to include a background anti-amyloid agent. The Tau NexGen clinical study was originally designed to focus on therapies that target tau. With increasing evidence from clinical studies showing that targeting amyloid can reduce biomarkers of Alzheimer's disease (AD), the Tau NexGen clinical trial leaders selected Eisai's investigational anti-amyloid beta (Aβ) protofibril antibody lecanemab as the background anti-amyloid agent.

The purpose of the Tau NexGen study is to assess the safety, tolerability, biomarker and cognitive efficacy of investigational therapies in people who have an Alzheimer's disease-causing gene mutation. The study will evaluate if treatment with study drug slows the rate of progression of cognitive impairment and improves disease-related biomarkers.

People who have this genetic mutation of dominantly inherited Alzheimer's disease (DIAD) are known to develop AD and will likely develop symptoms at around the same age their affected parents did, often in their 50s, 40s or even 30s. In March 2021, the DIAN-TU selected anti-microtubule binding region (MTBR) tau antibody E2814, which was created from collaboration research between Eisai and University College London, as the first investigational medicine among anti-tau drugs for the DIAN-TU tau study.

In the amended Tau NexGen study, symptomatic participants will be administered lecanemab for six months before being randomly assigned to also receive the anti-tau drug or a placebo. Since amyloid plaques accumulate before tau tangles in AD, this study design allows the researchers to assess whether amyloid removal clears the way for the anti-tau drug to function most effectively. Pre-symptomatic participants will be randomly assigned to receive the anti-tau drug or a placebo for a year before beginning lecanemab administration. By staggering the drugs in this way, the researchers will be able to evaluate the effects of the anti-tau drug alone before assessing the effects of the two drugs together. The primary endpoint is a slowing of tau accumulation in the brain in symptomatic participants, as seen on PET brain scans. As a secondary endpoint, the researchers will evaluate whether the investigational therapies affect levels of a specific kind of tau — phosphorylated tau 217 — in the cerebrospinal fluid of pre-symptomatic participants. If these primary and secondary endpoints are positive in the analysis two years after the start of study, the study will be extended for another two years to assess whether the drug slows cognitive

decline and has further effects on tau pathology.

“With growing evidence that removing amyloid plaques has biologically beneficial effects on amyloid and tau, we believe that targeting both Alzheimer’s disease pathologies — amyloid plaques and tau tangles — at the same time can provide the highest chance of success,” said principal investigator Randall J. Bateman, M.D., director of DIAN-TU and the Charles F. and Joanne Knight Distinguished Professor of Neurology at Washington University.

“Eisai’s anti-MTBR tau antibody E2814 was chosen as the first investigational therapy among anti-tau drugs for the groundbreaking Dominantly Inherited Alzheimer Network Trials Unit Tau NexGen, which was originally designed to target tau proteins. The growing body of evidence suggesting the removal of amyloid plaque slows cognitive decline is creating new possibilities to potentially fight this devastating disease. Eisai is proud that our investigational anti-amyloid beta protofibril antibody lecanemab has been selected as the background anti-amyloid agent in this arm of the study,” said Lynn Kramer, M.D., FAAN, Chief Clinical Officer, Neurology Business Group, Eisai Co., Ltd. “In our Phase 2b study, lecanemab 10 mg/kg biweekly dosing without titration, demonstrated robust clearance of the brain amyloid plaques from early stage of administration and slowed cognitive decline in people living with early AD. Encouragingly, the rate of amyloid-related imaging abnormalities-edema/effusion for this same dosing was 9.9% with less than 2% being symptomatic.”

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. Our vision is clear: a world free of neurodegeneration.

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[Notes to editors]

1. About Dominantly Inherited Alzheimer Network (DIAN)

The DIAN is an international research effort focused on dominantly inherited Alzheimer’s disease. Dominantly Inherited Alzheimer’s disease (DIAD) is a rare form of AD that causes memory loss and dementia in individuals — typically while they are in their 30s to 50s. The disease affects less than 1% of the total population of people with Alzheimer’s. The aim of the Dominantly Inherited Alzheimer Network

Trials Unit (DIAN-TU) is to find solutions to treat or prevent this disease and, potentially, all forms of Alzheimer's. The DIAN-TU is an international public-private partnership dedicated to designing and managing interventional therapeutic trials for individuals with and at risk of DIAD.

2. About Lecanemab (BAN2401)

Lecanemab is an investigational humanized monoclonal antibody for Alzheimer's disease (AD) that is the result of a strategic research alliance between Eisai and BioArctic. Lecanemab selectively binds to neutralize and eliminate soluble, toxic amyloid-beta (Aβ) aggregates (protofibrils) that are thought to contribute to the neurodegenerative process in AD. As such, lecanemab may have the potential to have an effect on disease pathology and to slow down the progression of the disease. With regard to the results from pre-specified analysis at 18 months of treatment, Study 201 demonstrated reduction of brain Aβ accumulation ($P<0.0001$) and slowing of disease progression measured by ADCOMS* ($P<0.05$) in early AD subjects. The study did not achieve its primary outcome measure** at 12 months of treatment. The Study 201 open-label extension was initiated after completion of the Core period and a Gap period off treatment (average of 24 months) to evaluate safety and efficacy, and is underway.

Eisai obtained the global rights to study, develop, manufacture and market lecanemab for the treatment of AD pursuant to an agreement concluded with BioArctic in December 2007. In March 2014, Eisai and Biogen entered into a joint development and commercialization agreement for lecanemab and the parties amended that agreement in October 2017. Currently, lecanemab is being studied in a pivotal Phase 3 clinical study in symptomatic early AD (Clarity AD), following the outcome of the Phase 2 clinical study (Study 201). In July 2020 the Phase 3 clinical study (AHEAD 3-45) for individuals with preclinical AD, meaning they are clinically normal and have intermediate or elevated levels of amyloid in their brains, was initiated. AHEAD 3-45 is conducted as a public-private partnership between the Alzheimer's Clinical Trial Consortium that provides the infrastructure for academic clinical trials in Alzheimer's Disease and related dementias in the U.S., funded by the National Institute on Aging, part of the National Institutes of Health, and Eisai.

In September 2021, a rolling submission to the FDA of a Biologics License Application (BLA) for the treatment of early AD under the accelerated approval pathway was initiated. Lecanemab was granted Breakthrough Therapy designation in June 2021, a U.S. Food and Drug Administration (FDA) program intended to expedite the development and review of medicines for serious or life-threatening conditions.

* Developed by Eisai, ADCOMS (AD Composite Score) combines items from the ADAS-Cog (Alzheimer's Disease Assessment Scale-cognitive subscale), CDR (Clinical Dementia Rating) and the MMSE (Mini-Mental State Examination) scales to enable a sensitive detection of changes in clinical functions of early AD symptoms and changes in memory.
** An 80% or higher estimated probability of demonstrating 25% or greater slowing in clinical decline at 12 months treatment measured by ADCOMS from baseline compared to placebo

3. About E2814

An investigational anti-microtubule binding region (MTBR) tau antibody, E2814 is being developed as a disease modifying agent for tauopathies including sporadic 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.