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Eisai Co., Ltd.

EISAI PUBLISHES LONG-TERM HEALTH OUTCOMES USING SIMULATION MODEL OF LECANEMAB USING PHASE 3 CLARITY AD DATA IN PEER-REVIEWED NEUROLOGY AND THERAPY JOURNAL

Treatment with Lecanemab Resulted in a Delay of 2 to 3 Years in the Mean Time to Progression to More Severe Stages of Alzheimer's Disease, Compared with Standard of Care Alone

Subgroup Analysis Suggested that Earlier Initiation of Treatment with Lecanemab May Have a Greater Impact on Disease Progression

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") today announced an article about long-term health outcomes of anti-amyloid-beta (A β) protofibril* antibody lecanemab in people living with mild cognitive impairment (MCI) due to Alzheimer's disease (AD) and mild AD (collectively known as early AD) using simulation modeling was published in the peer-reviewed journal [Neurology and Therapy](#). In this simulation, lecanemab treatment is estimated to potentially slow the rate of disease progression, maintaining treated patients for a longer duration in earlier stages of early AD and improving patients' quality of life.

This paper has been revised to incorporate data from the Phase 3 Clarity AD clinical trial, replacing the previous simulation of long-term health outcomes which relied on results from the Phase 2b clinical trial (Study 201), published in April 2022.

The article compares the long-term clinical outcomes of individuals with early AD and amyloid pathology who received standard of care (SoC) alone (including stable use of acetylcholinesterase inhibitor or memantine) with those who received lecanemab plus SoC (lecanemab+SoC). The analysis is based on a disease simulation model (AD ACE model¹) that used data from the Phase 3 Clarity AD clinical trial, which evaluated the efficacy and safety of lecanemab, and published literature to simulate the natural progression of AD. The study showed that the estimated lifetime risk of disease progression to mild, moderate, and severe AD dementia could potentially be reduced by 7.5%, 13.7% and 8.8%, respectively, in patients who received lecanemab+SoC, compared to those who received SoC alone. Moreover, the use of lecanemab allowed approximately 5% of patients to avoid institutional care. Treatment with lecanemab also resulted in a delay of 2 to 3 years in the mean time to progression to more severe stages of AD, compared with SoC alone. The model showed that the mean time to progression to mild, moderate, and severe AD dementia was longer for patients in the lecanemab-treated group compared to those in the SoC group, by 2.71 years (SoC vs. lecanemab+SoC: 2.35 vs.5.06 years), 2.95 (5.69 vs. 8.64 years) and 2.24 (8.46 vs.10.79 years), respectively. In addition, admission to institutional care was delayed by 0.60 years in the lecanemab-treated group compared to SoC alone (SoC vs. lecanemab+SoC: 6.25 years vs. 6.85 years). In terms of quality-adjusted life-years (QALYs)^{***}, patients treated with lecanemab experienced an increase of 0.71 QALYs compared to those receiving SoC, with QALYs for lecanemab-treated patients amounting to 4.39 years. Furthermore, a subgroup analysis by age and disease severity at baseline suggested that earlier initiation of treatment with lecanemab may have a greater impact on disease progression. The incremental mean

times for transition to mild and moderate AD dementia were 2.55 and 3.15 years, respectively, when treating MCI due to AD in a subgroup analysis compared to SoC.

“The outcomes of this simulation quantitatively demonstrate the long-term health outcomes of lecanemab and support the results of the simulation from Study 201. These predicted and simulated long-term health outcomes provide insights for healthcare decision-makers regarding the potential clinical and socioeconomic value of lecanemab. Treatment with lecanemab may potentially provide a benefit over the current standard of care by delaying the progression of AD and potentially allowing people taking lecanemab to live independently longer, and improve their quality of life,” said Ivan Cheung, Senior Vice President, and Global Alzheimer’s Disease Officer, Eisai Co., Ltd., Chairman and CEO, Eisai Inc. “Eisai will continue to transparently and expeditiously publish data and information about lecanemab to foster meaningful discussions about its clinical and societal value for people and countries around the globe.”

Lecanemab was approved under the accelerated approval pathway in the U.S. and was launched in the U.S. on January 18, 2023. The accelerated approval was based on Phase 2 data that demonstrated that lecanemab reduced the accumulation of A β plaque in the brain, a defining feature of AD, and its continued approval may be contingent upon verification of lecanemab’s clinical benefit in a confirmatory trial. The U.S. Food and Drug Administration (FDA) determined that the results of Clarity AD can serve as the confirmatory study to verify the clinical benefit of lecanemab.

In the U.S., Eisai submitted a supplemental Biologics License Application (sBLA) to the FDA for approval under the traditional pathway on January 6, 2023. On March 3, 2023, the FDA accepted Eisai’s sBLA based on the Clarity AD clinical data, and the lecanemab application has been granted Priority Review, with a Prescription Drug User Fee Act (PDUFA) action date of July 6, 2023. The FDA is currently planning to hold an Advisory Committee to discuss this application but has not yet publicly announced the date of the meeting. Eisai submitted an application for manufacturing and marketing approval to the Pharmaceuticals and Medical Devices Agency (PMDA) on January 16, 2023, in Japan. The Priority Review was granted by the Ministry of Health, Labour and Welfare (MHLW) on January 26, 2023. Eisai utilized the prior assessment consultation system of PMDA, with the aim of shortening the review period for lecanemab. In Europe, Eisai submitted a marketing authorization application (MAA) to the European Medicines Agency (EMA) on January 9, 2023, which was accepted on January 26, 2023. In China, Eisai initiated submission of data for a BLA to the National Medical Products Administration (NMPA) of China in December 2022, and the Priority Review was granted on February 27, 2023.

Eisai serves as the lead of LEQEMBI development and regulatory submissions globally with both Eisai and Biogen Inc. co-commercializing and co-promoting the product and Eisai having final decision-making authority.

* Protofibrils are large A β aggregated soluble species of 75-5000 Kd.²

** Standard of Care (SoC) for AD currently consists of lifestyle modifications and pharmacologic treatment of symptoms.

*** The quality-adjusted life year (QALY) is a measure of the value of health outcomes. Since health is a function of length of life (i.e., quantity) and quality of life (QOL), the QALY was developed as an attempt to combine the value of these attributes into a single index number. One QALY equates to one year in perfect health. QOL scores range from 1 (full health) to 0 (dead). For example, if a new treatment and an existing treatment both increase survival years by 3 years, but the new treatment maintains a QOL of 0.7 (QALY=2.1), while the existing treatment has a lower QOL of 0.5 (QALY=1.5), the incremental QALY for the new treatment would be 0.6 (QALY = QOL score x survival years).

¹ Kansal AR, Tafazzoli A, Ishak KJ, Krotneva S. Alzheimer's disease Archimedes condition-event simulator: Development and validation. *Alzheimers & Dementia: Translational Research & Clinical Interventions*. 2018;4:76-88. Published 2018 Feb 16. doi:10.1016/j.trci.2018.01.001

² Söderberg, L., Johannesson, M., Nygren, P. et al. Lecanemab, Aducanumab, and Gantenerumab — Binding Profiles to Different Forms of Amyloid-Beta Might Explain Efficacy and Side Effects in Clinical Trials for Alzheimer's Disease. *Neurotherapeutics* (2022). <https://doi.org/10.1007/s13311-022-01308-6>. Accessed February 9, 2023

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[Notes to editors]

1. About Lecanemab

Lecanemab (Brand Name in the U.S.: LEQEMBI™) is the result of a strategic research alliance between Eisai and BioArctic. Lecanemab is a humanized immunoglobulin gamma 1 (IgG1) monoclonal antibody directed against aggregated soluble (protofibril) and insoluble forms of amyloid-beta (Aβ). In the U.S., LEQEMBI was granted accelerated approval by the U.S. Food and Drug Administration (FDA) on January 6, 2023. LEQEMBI is indicated for the treatment of Alzheimer's disease (AD) in the U.S. Treatment with LEQEMBI should be initiated in patients with mild cognitive impairment or mild dementia stage of disease, the population in which treatment was initiated in clinical trials. There are no safety or effectiveness data on initiating treatment at earlier or later stages of the disease than were studied. This indication is approved under accelerated approval based on reduction in Aβ plaques observed in patients treated with LEQEMBI. Continued approval for this indication may be contingent upon verification of clinical benefit in a confirmatory trial.

Please see full [Prescribing Information](#) in the United States.

Eisai has completed lecanemab subcutaneous bioavailability study, and subcutaneous dosing is currently being evaluated in the Clarity AD (Study 301) OLE.

Since 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, is ongoing. 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 AD and related dementias in the U.S, funded by the National Institute on Aging, part of the National Institutes of Health, Eisai and Biogen.

Since January 2022, the Tau NexGen clinical study for Dominantly Inherited AD (DIAD), that is conducted by Dominantly Inherited Alzheimer Network Trials Unit (DIAN-TU), led by Washington University School of Medicine in St. Louis, is ongoing.

2. About the Collaboration between Eisai and Biogen for AD

Eisai and Biogen have been collaborating on the joint development and commercialization of AD treatments since 2014. Eisai serves as the lead of lecanemab development and regulatory submissions globally with both companies co-commercializing and co-promoting the product and Eisai having final decision-making authority.

3. About the Collaboration between Eisai and BioArctic for AD

Since 2005, Eisai and BioArctic have had a long-term collaboration regarding the development and commercialization of AD treatments. Eisai obtained the global rights to study, develop, manufacture and market lecanemab for the treatment of AD pursuant to an agreement with BioArctic in December 2007. The development and commercialization agreement on the antibody lecanemab back-up was signed in May 2015.