BIOARCTIC

Press Release

Long-term health outcomes for lecanemab using simulation model and Phase 3 Clarity AD data published

Stockholm, April 4, 2023 – BioArctic AB (publ) (Nasdaq Stockholm: BIOA B) today announced that its partner Eisai has published an article about long-term health outcomes of anti-amyloid-beta (Aβ) protofibril[1] 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 a disease simulation model 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. 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. A subgroup analysis suggested that earlier initiation of treatment with lecanemab may have a greater impact on disease progression.

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, 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)[2] 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 model[3]) 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. Treatment with lecanemab 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. Moreover, the use of lecanemab allowed approximately 5% of patients to avoid institutional care.

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[1] Protofibrils are large Aβ aggregated soluble species of 75-5000 Kd.

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

[3] 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

The study findings demonstrate the potential clinical value of lecanemab for individuals with early AD by slowing down disease progression and prolonging time in earlier stages of disease, which significantly benefits not only patients and caregivers but also society overall.

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 2b data that demonstrated that lecanemab reduced the accumulation of Aβ 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. 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 Priority Review was granted on February 27, 2023.

Eisai serves as the lead of lecanemab development and regulatory submissions globally with both Eisai and Biogen co-commercializing and co-promoting the product and Eisai having final decision-making authority. BioArctic has the right to commercialize lecanemab in the Nordic region and currently Eisai and BioArctic are preparing for a joint commercialization in the region.

The information was released for public disclosure, through the agency of the contact person below, on April 4, 2023, at 01.30 a.m. CET.

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About lecanemab
Lecanemab (Brand Name in the U.S.: LEQEMBI™) is the result of a strategic research alliance between BioArctic and Eisai. Lecanemab is a humanized immunoglobulin gamma 1 (IgG1) monoclonal antibody directed against aggregated soluble and insoluble forms of amyloid-beta (Aβ). In the US, LEQEMBI was granted accelerated approval by the US 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 LEQEMBI US Prescribing Information.

Eisai has completed a lecanemab subcutaneous bioavailability study, and subcutaneous dosing is currently being evaluated in the Clarity AD open label extension study. Since July 2020 Eisai's 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 and Eisai. Since January 2022, the Tau NexGen clinical study for Dominantly Inherited AD (DIAD) is ongoing, where lecanemab is given as a background anti-amyloid treatment when exploring combination therapies with anti-tau treatments. The study is conducted by Dominantly Inherited Alzheimer Network Trials Unit (DIAN-TU), led by Washington University School of Medicine in St. Louis.

About the collaboration between BioArctic and Eisai
Since 2005, BioArctic has a long-term collaboration with Eisai regarding the development and commercialization of drugs for the treatment of Alzheimer's disease. The most important agreements are the Development and Commercialization Agreement for the lecanemab antibody, which was signed in December 2007, and the Development and Commercialization agreement for the antibody BAN2401 back-up for Alzheimer's disease, which was signed in May 2015. In March 2014, Eisai and Biogen entered into a joint development and commercialization agreement for lecanemab. Eisai is responsible for the clinical development, application for market approval and commercialization of the products for Alzheimer's disease. BioArctic has the right to commercialize lecanemab in the Nordic region and currently Eisai and BioArctic are preparing for a joint commercialization in the region. BioArctic has no development costs for lecanemab in Alzheimer's disease and is entitled to payments in connection with regulatory approvals, and sales milestones as well as royalties on global sales.

About BioArctic AB

BioArctic AB (publ) is a Swedish research-based biopharma company focusing on disease-modifying treatments for neurodegenerative diseases, such as Alzheimer's disease, Parkinson's disease and ALS. BioArctic focuses on innovative treatments in areas with high unmet medical needs. The company was founded in 2003 based on innovative research from Uppsala University, Sweden. Collaborations with universities are of great importance to the company together with its strategically important global partner Eisai in Alzheimer disease. The project portfolio is a combination of fully funded projects run in partnership with global pharmaceutical companies and innovative in-house projects with significant market and out-licensing potential. BioArctic's Class B share is listed on Nasdaq Stockholm Large Cap (ticker: BIOA B). For more information about BioArctic, please visit www.bioarctic.com.