BIOARCTIC

Press release

Eisai publishes additional detailed analyses from lecanemab phase 2b study

Stockholm, March 31, 2023 – BioArctic AB's (publ) (Nasdaq Stockholm: BIOA B) partner Eisai announced today the publication of additional detailed analyses from the phase 2b clinical study (Study 201), evaluating the efficacy and safety of lecanemab for mild cognitive impairment (MCI) due to Alzheimer's disease (AD) and mild AD (collectively known as early AD). Lecanemab is a humanized immunoglobulin gamma 1 (IgG1) monoclonal antibody directed against aggregated soluble (protofibrils) and insoluble forms of amyloid beta (Aβ). The data was published in three articles in peer-reviewed journals;

1. **Detailed results on biomarker, cognitive, and clinical effects from phase 2b core to OLE (open-label extension): *Alzheimer's Research and Therapy***
2. **Consistency of efficacy results across various clinical measures and statistical methods in phase 2b: *Alzheimer's Research and Therapy***
3. **ARIA (amyloid-related imaging abnormality) profile in phase 2b: *Alzheimer's & Dementia: Translational Research and Clinical Interventions***

The phase 2b study of lecanemab was a multicenter, double-blind, placebo-controlled, trial conducted in 856 patients with early AD. Its core study evaluated key efficacy assessments, including clinical change on the AD Composite Score (ADCOMS) as the primary endpoint at 12 months and as key secondary endpoints, ADCOMS, Clinical Dementia Rating-Sum-of-Boxes (CDR-SB) and AD Assessment Scale-Cognitive Subscale 14 (ADAS-Cog14) at 18 months. Following analysis of the 18-month core phase, an intervening off-treatment period (gap period) ranging from 9-59 months (mean 24 months) was taken, which was followed by an OLE with 10 mg/kg IV bi-weekly lecanemab dosing to assess long-term safety and tolerability. The results of primary analysis in the core study including clinical efficacy and biomarkers have already been published in *Alzheimer's Research & Therapy*, showing a consistent reduction in clinical decline across several clinical and biomarker endpoints with lecanemab 10 mg/kg bi-weekly dosing.

1. Detailed results on biomarker, cognitive, and clinical effects from the phase 2b study.
"Lecanemab in patients with early Alzheimer's disease: detailed results on biomarker, cognitive, and clinical effects from the randomized and open-label extension of the phase 2 proof-of-concept study"
Lecanemab treatment resulted in significant reduction in amyloid plaques and a slowing of clinical decline. The potential for disease modification with lecanemab is supported by an increasing drug-

placebo difference over time on clinical measures, a durable drug effect during the gap in dosing with the placebo group not catching up to the treatment group during the OLE, and an impact on biological measures that reflect key pathophysiological changes in AD. Clinical progression and gradual re-accumulation of pathological biomarkers supports the need for continued dosing, even after the observed clearance of brain amyloid measured with Positron Emission Tomography (PET). Data also suggest the potential to use plasma biomarkers to monitor for lecanemab treatment effects and potentially track individual patient responses to treatment.

2. Consistency of efficacy results across various clinical measures and statistical methods in phase 2b.

"Consistency of efficacy results across various clinical measures and statistical methods in the lecanemab phase 2 trial of early Alzheimer's disease"

The robustness of lecanemab's efficacy in phase 2b, was assessed by sensitivity analyses using several statistical models for the three key clinical endpoints ADCOMS, CDR-SB, and ADAS-Cog14. The sensitivity analyses consistently showed positive lecanemab treatment effects for all endpoints and all statistical models examined, with analyses of the three key endpoints showing slowing of declines ranging from 26.5 to 55.9%. The conclusion of the primary analysis of the lecanemab phase 2b study is strengthened by the consistently positive observations across multiple statistical models, efficacy endpoints, and time-points assessed.

3. ARIA profile in phase 2b

"ARIA in patients treated with lecanemab (BAN2401) in a phase 2 study in early Alzheimer's disease"

In the phase 2b core and OLE study, there was a low dose-dependent incidence (<10%) of ARIA-E (amyloid-related imaging abnormalities-edema), with <3% symptomatic cases at the highest dose (10 mg/kg bi-weekly). ARIA-E was generally asymptomatic, mild-to-moderate in severity, and occurred early (<3 months). ARIA-E was correlated with maximum lecanemab serum concentration and incidence was higher in apolipoprotein E4 (ApoE4) homozygous carriers. ARIA-H and ARIA-E occurred with similar frequency at the relevant dose in the core and OLE studies. Based on the fact that lecanemab was well tolerated at the highest dose in this study, the Phase 3 Clarity AD study was conducted at this dose and without dose titration. A subcutaneous formulation that may reduce the maximum serum concentration of lecanemab is being evaluated to determine if this could reduce incidence of ARIA-E compared to intravenous formulation.

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.

To learn more, visit www.LEQEMBI.com.

The information was released for public disclosure, through the agency of the contact person below, on March 31, 2023, at 08:00 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). Lecanemab selectively binds and eliminates Aβ protofibrils that are thought to contribute to the neurotoxicity 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. LEQEMBI is indicated for the treatment of Alzheimer's disease (AD) in the U.S. under an accelerated approval by the U.S. Food and Drug Administration (FDA). 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. The Clarity AD study of lecanemab met its primary endpoint and all key secondary endpoints with highly statistically significant results.

Please see LEQEMBI US Prescribing Information.

Lecanemab-irmb 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 FDA determined that the results of the Phase 3 Clarity AD study can serve as the confirmatory study to verify the clinical benefit of lecanemab. In November 2022, the results of Clarity AD study were presented at the Clinical Trials on Alzheimer's Disease (CTAD) conference and simultaneously published in the peer-reviewed medical journal, *The New England Journal of Medicine*.

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. 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 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.