BIOARCTIC

Press release

Lecanemab phase 3 Clarity AD study in early Alzheimer's disease meets primary and all key secondary endpoints with high statistical significance

Stockholm, September 28, 2022 – BioArctic AB's (publ) (Nasdaq Stockholm: BIOA B) partner Eisai today announced positive topline results for the large global Phase 3 confirmatory Clarity AD study in 1,795 subjects. The study met the primary endpoint (CDR-SB[1]: Clinical Dementia Rating-Sum of Boxes) showing a highly statistically significant reduction of clinical decline. All key secondary endpoints were also met demonstrating highly statistically significant results. Clarity AD is a clinical trial of lecanemab (development code: BAN2401), an investigational anti-amyloid beta (Aβ) protofibril antibody for the treatment of mild cognitive impairment (MCI) due to Alzheimer's disease (AD) and mild AD (collectively known as early AD), with confirmed presence of amyloid pathology in the brain. The relative risk in Clarity AD of the main side effect associated with anti-amyloid therapies, ARIA, was within expectations. Eisai will discuss this data with regulatory authorities in the U.S., Japan and Europe with the aim to file for traditional approval in the US and for marketing authorization applications in Japan and Europe by the end of the first quarter of 2023. Additionally, Eisai will present the Clarity AD study results on November 29, 2022, at the Clinical Trials on Alzheimer's Disease conference (CTAD) and publish the findings in a peer-reviewed medical journal.

Lecanemab treatment met the primary endpoint and reduced clinical decline on the global cognitive and functional scale, Clinical Dementia Rating-Sum of Boxes (CDR-SB) compared with placebo at 18 months by 27%, which represents a treatment difference in the score change of -0.45 (p=0.00005) in the analysis of Intent-to-treat (ITT) population. Starting as early as six months, across all time points, the treatment showed highly statistically significant changes in CDR-SB from baseline compared to placebo (all p-values were less than 0.01). All key secondary endpoints were also met with highly statistically significant results compared with placebo ($p<0.01$). Key secondary endpoints were the change from baseline at 18 months compared with placebo of treatment in amyloid levels in the brain measured by amyloid positron emission tomography (PET), the AD Assessment Scale-cognitive subscale14 (ADAS-cog 14), AD Composite Score (ADCOMS) and the AD Cooperative Study-Activities of Daily Living Scale for Mild Cognitive Impairment (ADCS MCI-ADL).

The incidence of amyloid-related imaging abnormalities-edema/effusion (ARIA-E), an adverse event associated with anti-amyloid antibodies, was 12.5% in the lecanemab group and 1.7% in the placebo

[1] CDR-SB is a numeric scale used to quantify the various severity of symptoms of dementia. Based on interviews of people living with AD and family/caregivers, qualified healthcare professionals assess a cognitive and functional performance in six areas: memory, orientation, judgment and problem solving, community affairs, home and hobbies, and personal care. The total score of the six areas is the score of CDR-SB, and CDR-SB is also used as an appropriate item for evaluating the effectiveness of therapeutic drugs targeting early stages of AD.

group. The incidence of symptomatic ARIA-E was 2.8% in the lecanemab group and 0.0% in the placebo group. The ARIA-H (ARIA cerebral microhemorrhages, cerebral macrohemorrhages, and superficial siderosis) rate was 17.0% in the lecanemab group and 8.7% in the placebo group. The incidence of symptomatic ARIA-H was 0.7% in the lecanemab group and 0.2% in the placebo group. There was no imbalance in isolated ARIA-H (i.e., ARIA-H in patients who did not also experience ARIA-E) between lecanemab (8.8%) and placebo (7.6%). The total incidence of ARIA (ARIA-E and/or ARIA-H) was 21.3% in the lecanemab group and 9.3% in the placebo group. Overall, the relative risk profile of ARIA for lecanemab was within expectations

Clarity AD was a global confirmatory Phase 3 placebo-controlled, double-blind, parallel-group, randomized study in 1,795 people with early AD. The treatment group was administered lecanemab 10 mg/kg bi-weekly, with participants allocated in a 1:1 ratio to receive either placebo or lecanemab. The baseline characteristics of both placebo and lecanemab groups was similar and well balanced. Eligibility criteria allowed patients with a broad range of comorbidities/comedications: hypertension, diabetes, heart disease, obesity, renal disease, anti-coagulants, etc. Eisai's recruitment strategy for the Clarity AD clinical trial ensured greater inclusion of ethnic and racial populations in the U.S., resulting in approximately 25% of the total U.S. enrollment including Hispanic and African American persons living with early AD. Due to the inclusive eligibility criteria and the successful recruitment of diverse ethnic and racial populations in the U.S., Clarity AD's population is generally comparable to the country's Medicare population.

"We are very excited about the great lecanemab Phase 3 results in early Alzheimer's disease announced by our partner Eisai today. It brings hope to millions of people around the world who are fighting Alzheimer's disease every day. The Clarity AD results fully meet all our expectations, both in terms of highly statistical significance and in the consistency over primary and all key secondary endpoints. This is a huge accomplishment by our employees and our partner Eisai who have worked tirelessly for almost two decades to make this project a success. We are proud that our founder Lars Lannfelt's discoveries has the potential to fundamentally improve the treatment of Alzheimer's disease, where there currently are very limited options," said BioArctic's CEO Gunilla Osswald. "The results are also a confirmation of our technology platform and strengthens our hope to also be able to help improve the treatment of other neurodegenerative diseases such as Parkinson's disease, ALS and others."

In July 2022, the U.S. Food and Drug Administration (FDA) accepted Eisai's Biologics License Application (BLA) for lecanemab under the Accelerated Approval Pathway and granted Priority Review. The Prescription Drugs User Fee Act action date (PDUFA) is set for January 6, 2023. The FDA has agreed that the results of Clarity AD can serve as the confirmatory study to verify the clinical benefit of lecanemab. In an effort to secure traditional FDA approval for lecanemab as soon as possible, Eisai submitted the BLA through the FDA's Accelerated Approval Pathway so that the agency could complete its review of all lecanemab data with the exception of the data from the confirmatory Clarity AD study.

In March 2022, Eisai began submitting application data, with the exception of Clarity AD data, to Japan's Pharmaceuticals and Medical Devices Agency (PMDA) under the prior assessment

consultation system with the aim of obtaining early approval for lecanemab so that people living with early AD may have access to the therapy as soon as possible.

Eisai aims to file for traditional approval in the U.S., and to submit marketing authorization applications in Japan and Europe by the end of the first quarter 2023.

This release discusses investigational uses of an agent in development. There is no guarantee that any investigational uses of such product will successfully gain health authority approval.

This information is information that BioArctic AB (publ) is obliged to disclose pursuant to the EU Market Abuse Regulation. The information was released for public disclosure, through the agency of the contact persons above, on September 28, 2022, at 01:30 a.m. CET.

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About Clarity AD

Study title	A Study to Confirm Safety and Efficacy of Lecanemab in Participants With Early Alzheimer's Disease (Clarity AD)
Study population	1,795 participants of mild cognitive impairment (MCI) due to Alzheimer's disease (AD) and mild AD (collectively known as early AD) with confirmed presence of amyloid pathology in the brain in the global study, and an additional 111 subjects ongoing in China.
Treatment administered	10 mg/kg bi-weekly of lecanemab or placebo
Duration of treatment	18 months
Study locations	Japan, the U.S., Europe and China
Primary endpoint	Change from baseline in the Clinical Dementia Rating-Sum of Boxes (CDR-SB) at 18 months
Key secondary endpoints	Change From Baseline in: Amyloid Positron Emission Tomography (PET) using Centiloids Alzheimer Disease Assessment Scale - Cognitive Subscale 14 (ADAS-cog14[2]) Alzheimer's Disease Composite Score (ADCOMS[3]) Alzheimer's Disease Cooperative Study-Activities of Daily Living Scale for Mild Cognitive Impairment (ADCS MCI-ADL[4]) at 18 months

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 BioArctic and Eisai. Lecanemab selectively binds to neutralize and eliminate soluble toxic 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. Currently, lecanemab is being developed as the only late-stage anti-Aβ antibody that can be used for the treatment of early AD without the need for titration, enabling full treatment effect from day one.

The Clarity AD open-label extension is underway with treatment initiated after completion of the Core period to further evaluate the safety and efficacy of lecanemab. In addition, the lecanemab Phase 3 clinical study AHEAD 3-45 is ongoing for individuals with preclinical (asymptomatic) AD, meaning they are clinically normal and have intermediate or elevated levels of brain amyloid. AHEAD 3-45 is conducted as a public-private partnership between the Alzheimer's Clinical Trial Consortium, funded by the National Institute on Aging, part of the National Institutes of Health, and Eisai. In 2021, lecanemab was selected for the Tau NexGen clinical study for Dominantly Inherited Alzheimer's disease (DIAD), as a background anti-amyloid treatment when exploring combination therapies with anti-tau treatments. The study, which is ongoing, is conducted by

[2] ADAS-cog is the most common cognitive assessment instrument used in Alzheimer's disease clinical trials all over the world. ADAS-cog14 consists of 14 competencies: word recall, commands, constructional praxis, object and finger naming, ideational praxis, orientation, word recognition, remembering word recognition instructions, comprehension of spoken language, word finding difficulty, spoken language ability, delayed word recall, number cancellation, and maze task. ADAS-cog has been used in trials for earlier stages of AD including MCI.

[3] Developed by Eisai, combines items from the ADAS-cog scale for assessing cognitive functions, MMSE and the CDR scale for evaluating the severity of dementia to enable highly sensitive detection of changes in clinical functions of early AD symptoms and changes in memory

[4] ADCS-MCI-ADL assesses the competence of patients with MCI in activities of daily living (ADLs), based on 24 questions to the patient's partner about actual recent activities of daily living.

Dominantly Inherited Alzheimer Network Trials Unit (DIAN-TU), led by Washington University School of Medicine in St. Louis. Furthermore, Eisai has performed a lecanemab subcutaneous dosing Phase 1 study and the subcutaneous formulation is currently being evaluated in the Clarity AD open label extension study.

About Amyloid Related Imaging Abnormalities (ARIA)
ARIA is an important adverse event of amyloid-lowering therapies that is critical to monitor and manage during treatment. ARIA is most commonly seen as temporary swelling/effusion (ARIA-E) in areas of the brain that usually resolves over time. Some people may also have small spots of bleeding in or on the surface of the brain (ARIA-H; cerebral microhemorrhages, cerebral macrohemorrhages, and superficial siderosis) in isolation or with the swelling. Although most people with ARIA do not have symptoms, some people may have symptoms such as: headache, confusion, dizziness, vision changes, and nausea.

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 right to commercialize lecanemab in the Nordic under certain conditions and is currently preparing for commercialization in the Nordics together with Eisai. BioArctic has no development costs for lecanemab in Alzheimer's disease and is entitled to payments in connection with regulatory filings, 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 Mid Cap (ticker: BIOA B). For more information about BioArctic, please visit www.bioarctic.com.