BIOARCTIC

Press release

Results from lecanemab confirmatory phase 3 Clarity AD study to be presented at 15th Clinical Trials on Alzheimer's Disease (CTAD) conference

Stockholm, November 21, 2022 – BioArctic AB's (publ) (Nasdaq Stockholm: BIOA B) partner Eisai will present the efficacy, safety and biomarker results from the Phase 3 confirmatory Clarity AD clinical trial for lecanemab[1] (development code: BAN2401), at the 15th Clinical Trials on Alzheimer's Disease (CTAD) conference, held in San Francisco, CA and virtually from November 29 to December 2. The data will be presented by Eisai and distinguished faculty members in a scientific session on the first day of the meeting (November 29 at 4:50 p.m. PT). Additionally, BioArctic will present a poster on Aβ protofibrils and binding properties of lecanemab and Eisai will present other important research from the lecanemab clinical development program in several oral and poster presentations.

Topline results from Clarity AD were announced in late September and showed that lecanemab met the primary endpoint and all key secondary endpoints with highly statistically significant results, and the profile of Amyloid-Related Imaging Abnormalities (ARIA) incidence was within expectations.

Key lecanemab CTAD presentations

- Clarity AD: Results from the Phase 3 confirmatory Clarity AD clinical trial of lecanemab in patients with early AD will be presented in a scientific session on November 29 at 4:50 p.m. PT. Eisai will host a live webcast of presentations in the session and can be viewed live on the investors section of the Eisai Co., Ltd. website.
- Aβ protofibrils and lecanemab ninding properties: Research studying the characterization of Aβ protofibrils and the unique binding properties and mechanisms of Aβ clearance of lecanemab (Poster #P029)
- AHEAD 3-45 Study:
    - An evaluation of tau PET screening data from the Phase 3 AHEAD 3-45 study of lecanemab for associations with plasma p-tau217 and cognitive testing (Late Breaker Oral #LB1)
    - A study exploring increased accuracy of amyloid PET prediction in preclinical AD using plasma levels for Aβ42/40 and p-tau217 ratios from screening data from the Phase 3 study AHEAD 3-45 (Late Breaker Oral #LB2)

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. 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

[1] Lecanemab is an investigational anti-amyloid beta (Aβ) protofibril antibody for the potential 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.

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.

CTAD 2022 presentations relating to lecanemab

Scientific Session:

Clarity AD: A Phase 3 Placebo-Controlled, Double-Blind, Parallel-Group, 18-Month Study Evaluating Lecanemab in Early Alzheimer's Disease Tues, Nov 29, 4:50 – 6:05 p.m. PT	
Chairman: Takeshi Iwatsubo, University of Tokyo	
Clarity AD: Clinical Trial Background and Study Design Overview	Michael Irizarry Eisai Inc.
Lecanemab for the Treatment of Early Alzheimer's Disease: Topline Efficacy Results from Clarity AD	Christopher van Dyck Yale School of Medicine
Safety Profile of Lecanemab in Early Alzheimer's Disease	Marwan Sabbagh Barrow Neurological Institute
Imaging, Plasma and CSF Biomarkers Assessments from Clarity AD	Randall Bateman Washington University
Context of Clarity AD Results	Sharon Cohen Toronto Memory Program
Panel Discussion / Q&A	

Oral presentations

Asset in Development, Session, Time (Pacific Time)	**Presentation Title, Presenter/Authors**
Lecanemab Session: Late Breaking Oral Communications: #LB1 Wed, Nov 30 Session Time: 10:30 – 11:00 a.m. Presentation Time: 10:30 – 10:45 a.m.	Tau PET Associated with Plasma P-Tau217 and Cognitive Testing in Preclinical AD: Screening Data from the AHEAD Study A3 and A45 Trials Presenter: K Johnson Authors: K Johnson, et al
Lecanemab Session: Late Breaking Oral Communications: #LB2 Wed, Nov 30 Session Time: 10:30 – 11:00 a.m. Presentation Time: 10:45 – 11:00 a.m.	Plasma Levels of Abeta42/40 and P-Tau217 Ratios Increase Accuracy of Amyloid PET Prediction in Preclinical AD Presenter: R Rissman Authors: R Rissman, et al

Poster presentations

Asset in Development, Session, Time (Pacific Time)	Presentation Title, Authors
Lecanemab Session: Clinical Trials Methodology: #P012 Tues, Nov 29, 4:00 p.m. – Wed, Nov 30, 6:00 p.m.	Development and Feasibility of a Data-Driven Approach to Preclinical Alzheimer's Disease Clinical Trial Recruitment through Centralized Pre-Screening Data Collection Authors: D Kirn, et al
Lecanemab Session: New Therapies and Clinical Trials: #P029 Tues, Nov 29, 4:00 p.m. – Wed, Nov 30, 6:00 p.m.	Characterization of Amyloid-Beta Protofibrils in Alzheimer's Disease Brain and the Unique Binding Properties of Lecanemab Authors: L Lannfelt, et al

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This release discusses investigational uses of agents in development and is not intended to convey conclusions about efficacy or safety. There is no guarantee that such investigational agents will successfully complete clinical development or gain health authority approval.

The information was released for public disclosure, through the agency of the contact persons below, on November 21, 2022, at 08:00 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)[2] at 18 months
Key secondary endpoints	Change From Baseline at 18 months in: Amyloid Positron Emission Tomography (PET) using Centiloids Alzheimer Disease Assessment Scale - Cognitive Subscale 14 (ADAS-cog14[3]) Alzheimer's Disease Composite Score (ADCOMS[4]) Alzheimer's Disease Cooperative Study-Activities of Daily Living Scale for Mild Cognitive Impairment (ADCS MCI-ADL[5])

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.

In the global Phase 3 confirmatory Clarity AD study, lecanemab treatment met the primary endpoint and reduced clinical decline on the global cognitive and functional scale, 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 are 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

[2] 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.

[3] 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.

[4] 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

[5] 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.

placebo of treatment in amyloid levels in the brain measured by amyloid positron emission tomography (PET), the AD Assessment Scale-cognitive subscale14 (ADAS-cog14), 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 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, lecanemab's ARIA incidence profile was within expectations.

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 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 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.