



Eisai Presents Latest Analysis of Lecanemab's Effect on Biomarker Changes and Subcutaneous Dosing at The Alzheimer's Association International Conference (AAIC) 2023

Further Phase 3 analysis shows benefits of lecanemab on both amyloid-beta and tau, two underlying pathological hallmarks of Alzheimer's disease

New data on subcutaneous formulation shows promising PK /PD data modeling on efficacy and safety, representing a potential new option for administering therapy

TOKYO and CAMBRIDGE, Mass., July 20, 2023 – Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") and Biogen Inc. (Nasdaq: BIIB, Corporate headquarters: Cambridge, Massachusetts, CEO: Christopher A. Viehbacher, "Biogen") announced today that the results of a detailed analysis of the Phase 3 Clarity AD study demonstrated that lecanemab-irmb (generic name, U.S. brand name: LEQEMBI®) treatment showed reductions in amyloid-beta (A β) pathology and downstream biomarker changes. This analysis, and the latest findings on the lecanemab subcutaneous (SC) formulation currently under development, were presented at the Alzheimer's Association International Conference (AAIC) 2023. The U.S. Food and Drug Administration (FDA) granted traditional approval for LEQEMBI for the treatment of Alzheimer's disease (AD) on July 6, 2023.

Clarity AD was a global confirmatory Phase 3 placebo-controlled, double-blind, parallel-group, randomized study in 1,795 people with early AD (lecanemab group: 10 mg/kg bi-weekly IV treatment: 898, placebo group: 897). Lecanemab met the primary endpoint (change from baseline at 18 months on the global cognitive and functional scale, Clinical Dementia Rating-Sum of Boxes [CDR-SB]) and all key secondary endpoints with statistically significant results. In November 2022, results of the 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](#).

Lecanemab: Amyloid Reduction and Evidence of Downstream Biomarker Modification

In addition to the key secondary endpoint of lecanemab's effect on amyloid accumulation in the brain as measured by amyloid positron emission tomography (PET), the Clarity AD study also measured multiple A/T/N+ (amyloid, tau, neurodegeneration) biomarkers involved in the pathophysiology of AD, such as amyloid (A β 1-42 in CSF, A β 42/40 ratio in plasma), tau (p-Tau181 in cerebral spinal fluid [CSF] and plasma), neurodegeneration (total tau [t-tau] in CSF and neurofilament light [NfL] in CSF and plasma), astrocyte activation (plasma GFAP: glial fibrillary acidic protein) and synaptic dysfunction (neurogranin in CSF).

An increase in plasma A β 42/40 ratio was observed with lecanemab compared to placebo (adjusted mean change from baseline of lecanemab: 0.008, placebo: 0.001, p<0.0001). A reduction in plasma p-Tau181 was observed with lecanemab compared to placebo (adjusted mean change from baseline of lecanemab: -0.575 pg/mL, placebo: 0.201 pg/mL, p<0.0001). The other biomarkers also improved after treatment with lecanemab. These outcomes suggested lecanemab impacts A/T/N+ biomarkers involved in the AD pathophysiology and exerts biological effects that demonstrate slowing of disease progression. Baseline characteristics and initial results were presented from the tau PET substudy of Clarity AD. Lecanemab administration slowed the accumulation of tau pathology in the temporal lobe. Additionally,

lecanemab administration showed a clinical effect in the overall population of the tau PET substudy, and a large effect size was observed in the low tau population* defined in this presentation, which represents the early phase of AD.

Subcutaneous (SC) Lecanemab is Predicted to Achieve Comparable Efficacy and Improved Safety Compared to Lecanemab IV in Early AD

In an exposure/bioavailability and modeling study comparing intravenous (IV) and subcutaneous (SC) dosing of lecanemab, the bioavailability of SC dosing of lecanemab was shown to be approximately 50% of that of IV dosing. Further analysis using the PK/PD model showed that a fixed lecanemab SC dose of 720 mg administered weekly may potentially result in comparable exposure (area under the curve [AUC]) and efficacy as measured by reduction in amyloid PET SUVR to 10 mg/kg IV dose administered bi-weekly. Models developed with data following IV administration show that amyloid-related imaging abnormalities with edema/effusion (ARIA-E) are related to concentrations of lecanemab in the blood, with maximum blood concentrations being the best predictor of ARIA-E. Because SC dosing will have lower maximum blood concentrations than IV dosing, SC dosing is predicted to have a lower incidence of ARIA-E, if the relationship is the same for SC dosing.

The presentation materials of this release will be posted on the [investors section](#) of the Eisai Co., Ltd. website at 19:30 on July 20 in the U.S EDT (8:30 on July 21 in Japan time).

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.

* Using the MK6240 tau PET probe, tau accumulation in the brain was defined as low tau accumulation group (MK6240 cutoff value <1.06, 141 subjects), intermediate accumulation group (MK6240 cutoff value between 1.06 and 2.91, 191 subjects), and high accumulation group (MK6240 cutoff value >2.91, 10 subjects).

Please see full [Prescribing Information](#) for LEQEMBI, including **Boxed WARNING**.

Media Contacts:

Eisai Co., Ltd.

Public Relations Department
TEL: +81 (0) 3-3817-5120

Eisai Inc. (U.S.)

Libby Holman
+ 1-201-753-1945
Libby_Holman@eisai.com

Eisai Europe, Ltd.

(UK, Europe, Australia, New Zealand and Russia)
EMEA Communications Department
+44 (0) 786-601-1272
EMEA-comms@eisai.net

Investor Contacts:

Eisai Co., Ltd.

Investor Relations Department
TEL: +81 (0) 3-3817-5122

Biogen Inc.

Jack Cox
+ 1-781-464-3260
public.affairs@biogen.com

Biogen Inc.

Chuck Triano
+ 1-781-464-2442
IR@biogen.com

Notes to Editors

1. About LEQEMBI® (lecanemab-irmb)

LEQEMBI® (lecanemab-irmb) is the result of a strategic research alliance between Eisai and BioArctic. LEQEMBI is a humanized immunoglobulin gamma 1 (IgG1) monoclonal antibody directed against aggregated soluble (protofibril) and insoluble forms of amyloid-beta (Aβ). LEQEMBI is an amyloid beta-directed antibody indicated as a disease-modifying treatment for Alzheimer's disease (AD) in the U.S. The U.S. Food and Drug Administration (FDA) granted LEQEMBI accelerated approval on January 6, 2023, and Traditional Approval on July 6, 2023. 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.

Eisai has also submitted applications for approval of lecanemab in Japan, EU, China, Canada, Great Britain and South Korea. In Japan and China, the applications have been designated for priority review, and in Great Britain, lecanemab has been designated for the Innovative Licensing and Access Pathway (ILAP), which aims to reduce the time to market for innovative medicines.

Eisai has completed a lecanemab subcutaneous bioavailability study, and subcutaneous dosing is currently being evaluated in the Clarity AD (Study 301) open-label extension (OLE). A maintenance dosing regimen has been evaluated as part of Study 201 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 LEQEMBI 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 LEQEMBI for the treatment of AD pursuant to an agreement with BioArctic in December 2007. The development and commercialization agreement on the antibody LEQEMBI back-up was signed in May 2015.

4. About Eisai Co., Ltd.

Eisai's Corporate Concept is "to give first thought to patients and people in the daily living domain, and to increase the benefits that health care provides." Under this Concept (also known as *human health care (hhc)* Concept), we aim to effectively achieve social good in the form of relieving anxiety over health and reducing health disparities. With a global network of R&D facilities, manufacturing sites and marketing subsidiaries, we strive to create and deliver innovative products to target diseases with high unmet medical needs, with a particular focus in our strategic areas of Neurology and Oncology.

In addition, we demonstrate our commitment to the elimination of neglected tropical diseases (NTDs), which is a target (3.3) of the United Nations Sustainable Development Goals (SDGs), by working on various activities together with global partners.

For more information about Eisai, please visit <http://www.eisai.com/> (for global headquarters: Eisai Co., Ltd.), and connect with us on [Twitter](#), [LinkedIn](#) and [Facebook](#).

5. About Biogen

Founded in 1978, Biogen is a leading global biotechnology company that has pioneered multiple breakthrough innovations including a broad portfolio of medicines to treat multiple sclerosis, the first approved treatment for spinal muscular atrophy, and two co-developed treatments to address a defining pathology of Alzheimer's disease. Biogen is advancing a pipeline of potential novel therapies across neurology, neuropsychiatry, specialized immunology and rare diseases and remains acutely focused on its purpose of serving humanity through science while advancing a healthier, more sustainable and equitable world.

The company routinely posts information that may be important to investors on its website at www.biogen.com. Follow Biogen on social media – [Twitter](#), [LinkedIn](#), [Facebook](#), [YouTube](#).

Biogen Safe Harbor

This news release contains forward-looking statements about the potential benefits, safety and efficacy of LEQEMBI; potential regulatory discussions, submissions and approvals and the timing thereof; the treatment of Alzheimer's disease; the anticipated benefits and potential of Biogen's collaboration arrangements with Eisai; the potential of Biogen's commercial business and pipeline programs, including LEQEMBI; and risks and uncertainties associated with drug development and commercialization. These statements may be identified by words such as "aim," "anticipate," "believe," "could," "estimate," "expect," "forecast," "intend," "may," "plan," "possible," "potential," "will," "would" and other words and terms of similar meaning. Drug development and commercialization involve a high degree of risk, and only a small number of research and development programs result in commercialization of a product. Results in early-stage clinical studies may not be indicative of full results or results from later stage or larger scale clinical studies and do not ensure regulatory approval. You should not place undue reliance on these statements or the scientific data presented.

These statements involve risks and uncertainties that could cause actual results to differ materially from those reflected in such statements, including without limitation unexpected concerns that may arise from additional data, analysis or results obtained during clinical studies; the occurrence of adverse safety events; risks of unexpected costs or delays; the risk of other unexpected hurdles; regulatory submissions may take longer or be more difficult to complete than expected; regulatory authorities may require additional information or further studies, or may fail or refuse to approve or may delay approval of Biogen's drug candidates, including LEQEMBI; actual timing and content of submissions to and decisions made by the regulatory authorities regarding LEQEMBI; uncertainty of success in the development and potential commercialization of LEQEMBI; failure to protect and enforce Biogen's data, intellectual property and other proprietary rights and uncertainties relating to intellectual property claims and challenges; product liability claims; third party collaboration risks; and the direct and indirect impacts of the ongoing COVID-19 pandemic on Biogen's business, results of operations and financial condition. The foregoing sets forth many, but not all, of the factors that could cause actual results to differ from Biogen's expectations in any forward-looking statement. Investors should consider this cautionary statement as well as the risk factors identified in Biogen's most recent annual or quarterly report and in other reports Biogen has filed with the U.S. Securities and Exchange Commission. These statements speak only as of the date of this news release. Biogen does not undertake any obligation to publicly update any forward-looking statements.