Eisai Receives Positive Opinion from the CHMP in the European Union for Lecanemab in Early Alzheimer's Disease

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TOKYO and CAMBRIDGE, Mass., Nov. 14, 2024 (GLOBE NEWSWIRE) -- 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 a positive opinion has been received from the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) recommending approval of the amyloid-beta (Aβ) monoclonal antibody lecanemab as a treatment of adult patients with a clinical diagnosis of mild cognitive impairment and mild dementia due to Alzheimer's disease (Early Alzheimer's disease) who are apolipoprotein E ε4 (ApoE ε4)* non-carriers or heterozygotes with confirmed amyloid pathology.[1] Eisai had requested a re-examination of the prior negative opinion adopted by the CHMP in July 2024. In accordance with European Medicines Agency regulatory process, the European Commission is expected to make a final decision on the marketing authorization application (MAA) of lecanemab based on the CHMP recommendation within 67 days of receipt of CHMP opinion.[2]

Lecanemab selectively binds to soluble Aβ aggregates (protofibrils**), as well as insoluble Aβ aggregates (fibrils) which are a major component of Aβ plaques in AD, thereby reducing both Aβ protofibrils and Aβ plaques in the brain.[3,4,5]

AD currently affects an estimated 6.9 million people in Europe,[6] and this figure is expected to nearly double by 2050 as aging populations increase.[7] AD progresses in stages that increase in severity over time, and each stage of the disease presents different challenges for those living with AD and their care partners. There is a significant unmet need for new treatment options that slow down the progression of early AD and reduce the overall burden on people affected by AD and society.

Eisai serves as the lead for lecanemab's development and regulatory submissions globally with both Eisai and Biogen co-commercializing and co-promoting the product and Eisai having final decision-making authority.

* Apolipoprotein E is a protein involved in the metabolism of fats in humans. It is implicated in AD.
** Protofibrils are believed to contribute to the brain injury that occurs with AD and are considered to be the most toxic form of Aβ, having a primary role in the cognitive decline of this progressive, debilitating condition.[8] Protofibrils cause injury to neurons in the brain which, in turn, can negatively impact cognitive function via multiple mechanisms,[8] not only increasing the development of insoluble Aβ plaques but also increasing direct damage to brain cell membranes and the connections that transmit signals between nerve cells or nerve cells and other cells. It is believed the reduction of protofibrils may slow the progression of AD by reducing damage to neurons in the brain and cognitive dysfunction.[9]

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Notes to Editors

1. **About lecanemab (generic name, brand name: Leqembi®)**
Lecanemab is the result of a strategic research alliance between Eisai and BioArctic. It is a humanized immunoglobulin gamma 1 (IgG1) monoclonal antibody directed against aggregated soluble (protofibril) and insoluble forms of amyloid-beta (Aβ).

Lecanemab's Positive Opinion from the CHMP in the European Union was primarily based on Phase 3 data from Eisai's global Clarity AD clinical trial, in which it met its primary endpoint and all key secondary endpoints with statistically significant results.[1,3] Clarity AD was a Phase 3 global, placebo-controlled, double-blind, parallel-group, randomized study in 1,795 patients with early AD (MCI or mild dementia due to AD, with confirmed presence of amyloid pathology), of which 1,521 were in the recommended indicated population (ApoE ε4 non-carriers or heterozygotes). 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 for 18 months.[1]

The primary endpoint was the global cognitive and functional scale, CDR-SB.[1] In the Clarity AD clinical trial, treatment with lecanemab, in the

recommended indicated population (ApoE ε4 non-carriers or heterozygotes), reduced clinical decline on CDR-SB by 31% at 18 months compared to placebo based on conservative control based imputation.[1] The mean CDR-SB score at baseline was approximately 3.2 in both groups.[1] The adjusted least-squares mean change from baseline at 18 months was 1.217 with lecanemab and 1.752 with placebo (difference, −0.535; 95% confidence interval [CI], −0.778 to −0.293; P=0.00001).[1] CDR-SB is a global cognitive and functional scale that measures six domains of functioning, including memory, orientation, judgement and problem solving, community affairs, home and hobbies, and personal care.[10]

In addition, the secondary endpoint from the AD Cooperative Study-Activities of Daily Living Scale for Mild Cognitive Impairment (ADCS-MCI-ADL), which measures information provided by people caring for patients with AD, noted 33% less decline compared to placebo at 18 months.[1] The adjusted mean change from baseline at 18 months in the ADCS-MCI-ADL score was −3.873 in the lecanemab group and −5.809 in the placebo group (difference, 1.936; 95% CI, 1.029 to 2.844; P=0.00002).[1] The ADCS-MCI-ADL assesses the ability of patients to function independently, including being able to dress, feed themselves and participate in community activities.

In the ApoE ε4 heterozygotes or non-carriers population, the most common adverse reactions were infusion-related reaction (26%), ARIA-H (13%), headache (11%) and ARIA-E (9%).[1]

Lecanemab has been approved in the U.S., Japan, China, South Korea, Hong Kong, Israel, the United Arab Emirates and Great Britain and is under regulatory review in 17 countries. A supplemental Biologics License Application (sBLA) for intravenous maintenance dosing was submitted to the U.S. Food and Drug Administration (FDA) in March 2024, which was accepted in June 2024. In May 2024, the rolling submission of a Biologics License Application (BLA) for maintenance dosing of a subcutaneous injection formulation, which is being developed to enhance convenience for patients, was initiated in the U.S. under Fast Track status, with the rolling submission and completed in October 2024.

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 and includes lecanemab as the backbone anti-amyloid therapy.

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 lecanemab 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 lecanemab for the treatment of AD pursuant to an agreement with BioArctic in December 2007. The development and commercialization agreement on the antibody lecanemab 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 www.eisai.com (for global headquarters: Eisai Co., Ltd.), and connect with us on X, LinkedIn and Facebook. The website and social media channels are intended for audiences outside of the UK and Europe. For audiences based in the UK and Europe, please visit www.eisai.eu and Eisai EMEA LinkedIn.

5. **About Biogen**
Founded in 1978, Biogen is a leading biotechnology company that pioneers innovative science to deliver new medicines to transform patient's lives and to create value for shareholders and our communities. We apply deep understanding of human biology and leverage different modalities to advance first-in-class treatments or therapies that deliver superior outcomes. Our approach is to take bold risks, balanced with return on investment to deliver long-term growth.

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

Biogen Safe Harbor
This news release contains forward-looking statements, including about the potential clinical effects of lecanemab; the potential benefits, safety and efficacy of lecanemab; 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 lecanemab; 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.

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 lecanemab; actual timing and content of submissions to and decisions made by the regulatory authorities regarding lecanemab; uncertainty of success in the development and potential commercialization of lecanemab; 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; and third party collaboration risks, 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.

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*This release was updated on November 14, 2024 to correctly note that the number of people in the indicated population from the Clarity AD trial is 1,521.