FDA Approves LEQEMBI® (lecanemab-irmb) IV Maintenance Dosing for the Treatment of Early Alzheimer's Disease

Once every four weeks maintenance dosing may be easier for patients and care partners to continue treatment

Alzheimer's disease progression does not stop after plaque clearance; ongoing treatment with LEQEMBI can slow disease progression and prolong the benefits of therapy

TOKYO and CAMBRIDGE, Mass., Jan. 26, 2025 (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 that the U.S. Food and Drug Administration (FDA) has approved the Supplemental Biologics License Application (sBLA) for once every four weeks lecanemab-irmb (U.S. brand name: LEQEMBI®) intravenous (IV) maintenance dosing. LEQEMBI is indicated for the treatment of Alzheimer's disease (AD) in patients with mild cognitive impairment (MCI) or mild dementia stage of disease (collectively referred to as early AD) in the U.S. After 18 months of once every two weeks initiation phase, a transition to the maintenance dosing regimen of 10 mg/kg once every four weeks may be considered or the regimen of 10 mg/kg once every two weeks may be continued.

The sBLA is based on modeling of observed data from the Phase 2 study (Study 201) and its long-term extension (LTE) as well as the Clarity AD study (Study 301) and its LTE study. Modeling simulations predict that transitioning to once every four weeks maintenance dosing after 18 months of once every two weeks treatment will maintain clinical and biomarker benefits of therapy. AD is a progressive, relentless disease caused by a continuous underlying neurotoxic process that begins before and continues after plaque removal.[1,2,3] Only LEQEMBI works to fight AD in two ways: continuously clearing protofibrils and rapidly clearing plaque. This is important because with continuous administration, LEQEMBI clears highly toxic protofibrils* which can continue to cause neuronal injury even after the amyloid-beta (Aβ) plaque has been cleared from the brain.

Importance of Ongoing Treatment

- Data from the off-treatment period between the Study 201 (Phase 2) core study and LTE showed that discontinuation of treatment is associated with reaccumulation of amyloid PET and plasma and CSF biomarkers, and reversion to placebo rate of clinical decline.[4]
- For maintenance treatment, once every four weeks dosing regimen may be easier than once every two weeks dosing for patients and care partners to continue treatment for early AD.
- Ongoing treatment can slow disease progression and prolong the benefit of therapy,[4] with the goal of helping patients maintain who they are for longer.
- In the Clarity AD core study (18 months), the mean change from baseline between the once every two weeks lecanemab treated group and the placebo group was -0.45 ($P<0.0001$) on

the primary endpoint of the Clinical Dementia Rating-Sum of Boxes (CDR-SB) global cognitive and functional scale.

- Over three years of treatment across the Clarity AD core study and LTE, LEQEMBI reduced cognitive decline on the CDR-SB by -0.95** relative to a matched natural history cohort - showing clinically meaningful benefit for early AD patients.
    - A change from 0.5 to 1 on the CDR score domains of Memory, Community Affairs and Home/Hobbies is the difference between slight impairment and loss of independence, such as people's ability to be left alone, remember recent events, participate in daily activities, complete household chores, function independently and engage in hobbies and intellectual interests.

LEQEMBI is approved in the U.S., Japan, China, South Korea, Hong Kong, Israel, UAE, Great Britain, Mexico and Macau. In November 2024, the treatment received a positive opinion from the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) recommending approval. Eisai has submitted applications for approval of lecanemab in 17 countries and regions. Additionally, the FDA accepted Eisai's Supplemental Biologics License (BLA) for the LEQEMBI subcutaneous autoinjector for weekly maintenance dosing in January 2025 and set a PDUFA action date for August 31, 2025.

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.

*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 associated with this progressive, debilitating condition.[5] Protofibrils cause injury to neurons in the brain, which in turn, can negatively impact cognitive function via multiple mechanisms, 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 prevent the progression of AD by reducing damage to neurons in the brain and cognitive dysfunction.[6]

**The lecanemab group was compared to the expected decline based on the Alzheimer's Disease Neuroimaging Initiative (ADNI) group. ADNI is a clinical research project launched in 2005 to develop methods to predict the onset of AD and to confirm the effectiveness of treatments. The ADNI observational cohort represents the exact population of those in Clarity AD study; matched ADNI participants show similar degree of decline to placebo group out to 18 months, supporting the appropriateness of the matching.

INDICATION

LEQEMBI® [(lecanemab-irmb) 100 mg/mL injection for intravenous use] is indicated for the treatment of Alzheimer's disease (AD). Treatment with LEQEMBI should be initiated in patients

with mild cognitive impairment (MCI) or mild dementia stage of disease, the population in which treatment was initiated in clinical trials.

Please see full Prescribing Information for LEQEMBI, including Boxed WARNING.

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Notes to Editors

1. **About lecanemab (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 is approved in the U.S.,[7] Japan,[8] China,[9] South Korea,[10] Hong Kong,[11] Israel,[12] the United Arab Emirates,[13] the United Kingdom,[14] Mexico,[15] and Macau. In November 2024, the treatment received a positive opinion from the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) recommending approval. Eisai has submitted applications for approval of lecanemab in 17 countries and regions.

LEQEMBI's approvals in these countries was 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. The primary endpoint was the global cognitive and functional scale, Clinical Dementia Rating Sum of Boxes (CDR-SB). In the Clarity AD clinical trial, treatment with lecanemab reduced clinical decline on CDR-SB by 27% at 18 months compared

to placebo.[16,17] The mean CDR-SB score at baseline was approximately 3.2 in both groups. The adjusted least-squares mean change from baseline at 18 months was 1.21 with lecanemab and 1.66 with placebo (difference, −0.45; 95% confidence interval [CI], −0.67 to −0.23; P<0.001). 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 a statistically significant benefit of 37% compared to placebo. The adjusted mean change from baseline at 18 months in the ADCS-MCI-ADL score was −3.5 in the lecanemab group and −5.5 in the placebo group (difference, 2.0; 95% CI, 1.2 to 2.8; P<0.001). The ADCS MCI-ADL assesses the ability of patients to function independently, including being able to dress, feed themselves and participate in community activities. The most common adverse events (>10%) in the lecanemab group were infusion reactions, ARIA-H (combined cerebral microhemorrhages, cerebral macrohemorrhages, and superficial siderosis), ARIA-E (edema/effusion), headache, and fall.

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 patients' 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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