FOR EUROPEAN TRADE AND MEDICAL MEDIA

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

The Committee for Medicinal Products for Human Use (CHMP) has adopted a positive opinion for lecanemab as a treatment for adult patients with a clinical diagnosis of mild cognitive impairment and mild dementia due to Alzheimer's disease (AD) (early AD) who are apolipoprotein E ε4 (ApoE ε4) non-carriers or heterozygotes with confirmed amyloid pathology*[1]

Lecanemab becomes the first therapy that targets an underlying cause of AD to be recommended for Marketing Authorisation in the European Union[1,2]

The positive opinion is primarily based on data from the global Phase 3 clinical trial, Clarity AD, which demonstrated that lecanemab slowed disease progression vs placebo at 18 months[1,2,3]

Today's opinion by the CHMP means that a Marketing Authorisation Application decision by the European Commission is expected within 67 days[4]

HATFIELD, HERTFORDSHIRE, UNITED KINGDOM, and CAMBRIDGE, Mass., 14 November, 2024 – Eisai Europe Ltd. and Biogen Inc. announced today that a positive opinion has been received from the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) recommending authorisation of the amyloid-beta (Aβ) monoclonal antibody lecanemab as a treatment for adult patients with a clinical diagnosis of mild cognitive impairment and mild dementia due to Alzheimer's disease (AD) (early AD) who are apolipoprotein E ε4 (ApoE ε4)* non-carriers or heterozygotes with confirmed amyloid pathology.[1] The positive CHMP opinion makes lecanemab the first Aβ monoclonal antibody therapy that targets an underlying cause of AD to be recommended for Marketing Authorisation (MA) in the European Union (EU).[1,2] Eisai had requested a re-examination of the prior negative opinion adopted by the CHMP in July 2024. In accordance with the EMA regulatory process, the European Commission is expected to make a final decision on the Marketing Authorisation Application of lecanemab based on the CHMP recommendation within 67 days of receipt of CHMP opinion.[4]

Lecanemab is an Aβ monoclonal antibody that selectively binds to soluble Aβ aggregates (protofibrils**), as well as insoluble Aβ fibril aggregates, which are a major component of Aβ plaques in early AD, thereby reducing both Aβ protofibrils and Aβ plaques in the brain.[2,5,6,7]

The CHMP's opinion was primarily based on Phase 3 data from Eisai's global, placebo-controlled, double-blind, parallel-group, randomised Clarity AD clinical trial, in which the medicine met its primary endpoint (change from baseline in the Clinical Dementia Rating Sum of Boxes [CDR-SB]† at 18 months) and all key secondary endpoints.[2] In the recommended indicated population, the most common adverse events in the treatment group (n=757) were infusion-related reaction, amyloid-related imaging abnormalities with haemorrhage (small spots of bleeding) (ARIA-H)‡, headache and amyloid-related imaging abnormalities with cerebral oedema (build-up of fluid) (ARIA-E)‡‡.[8,24]

"Today's positive CHMP opinion brings us one step closer to being able to offer a potential treatment option which targets an underlying cause of AD to eligible patients in the EU for the first time," said Gary Hendler, Regional Chairman and CEO, Eisai EMEA, Senior Vice President & Global Corporate Officer, Eisai Co. Ltd, Tokyo. "AD is a progressive neurodegenerative disease that poses significant challenges to human health and wider society – the loss of someone's memory and independence can have a significant impact on not only those living with the disease, but also their family and friends. Eisai is committed to making a meaningful difference to all those affected by AD, and we are pleased that our ongoing work with the CHMP is helping to make this available to eligible patients in the EU."

AD currently affects 6.9 million people in Europe,[9] and this figure is expected to nearly double by 2050 as ageing populations increase.[10] AD progresses in stages that increase in severity over time,[11] and each stage of the disease presents different challenges for those living with AD and their care partners.[12] 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.[13]

"The positive CHMP opinion marks a significant step and recognises the potential of this medicine to make a difference to eligible individuals and their families impacted by this disease. We look forward to the EC's decision and are pleased to be one step closer to offering this medicine in the EU," said Wolfram Schmidt, President, Head of Europe, Biogen. "As a company, we are dedicated to furthering Alzheimer's disease research and treatment, aiming to help address the unmet needs in this devastating condition."

Eisai serves as the lead of lecanemab development and regulatory submissions globally with both Eisai and Biogen co-commercialising 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 a key toxic form of Aβ, having a primary role in the cognitive decline of this progressive, debilitating condition.[14] Protofibrils can cause injury to neurons in the brain which in turn, can negatively impact cognitive function via multiple mechanisms,[14] 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.[15] It is believed the reduction of protofibrils may slow the progression of AD by reducing damage to neurons in the brain and cognitive dysfunction.[15]

†CDR-SB is a disease staging tool used in clinical trials, which can help to stage dementia due to AD.[16] It 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.[16]

‡ARIA-H: amyloid-related imaging abnormalities with haemorrhage (cerebral microhaemorrhages and superficial siderosis).

‡‡ARIA-E: amyloid-related imaging abnormalities with oedema (oedema/effusion).

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Notes to editors:

1. About lecanemab

Lecanemab is the result of a strategic research alliance between Eisai and BioArctic. It is a humanised immunoglobulin gamma 1 (IgG1) monoclonal antibody directed against aggregated soluble (protofibril) and insoluble forms of amyloid-beta (Aβ). The medicine is authorised in the U.S.,[17] Japan,[18] China,[19] South Korea,[20] Hong Kong,[21] Israel,[22] the United Arab Emirates[23] and Great Britain,[8] and is under regulatory review in 17 countries and regions, including the European Union.

The positive CHMP opinion was primarily based on Phase 3 data from Eisai's global Clarity AD clinical trial, in which the medicine met its primary endpoint and all key secondary endpoints.[1,2] Clarity AD was a Phase 3 global, placebo-controlled, double-blind, parallel-group, randomised study in 1,795 patients with early AD (MCI or mild dementia due to AD, with confirmed presence of amyloid pathology).[2] Of the

total number of patients randomised, 31% were non-carriers, 53% of were heterozygotes and 16% were homozygotes, therefore 1,521 were in the recommended indicated population (ApoE ε4 heterozygotes or noncarriers).[3] 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.[2]

The primary endpoint was the global cognitive and functional scale, CDR-SB.[2] In the Clarity AD clinical trial, treatment with lecanemab (n=757), in the CHMP's recommended indicated population (ApoE ε4 heterozygotes or non-carriers), reduced clinical decline on CDR-SB by 31% at 18 months compared to placebo (n=764).[24] The mean CDR-SB score at baseline was approximately 3.2 in both groups.[24] 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% CI, −0.778 to −0.293).[24] 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.[16]

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.[25] 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).[25] The ADCS-MCI-ADL assesses the ability of patients to function independently, including being able to dress, feed themselves and participate in community activities.[26]

In the recommended indicated population (ApoE ε4 heterozygotes or non-carriers) (n=757), the most common adverse reactions were infusion-related reaction (26%), ARIA-H (13%), headache (11%) and ARIA-E (9%).[8,24]

2. About the Collaboration between Eisai and Biogen for AD

Eisai and Biogen have been collaborating on the joint development and commercialisation of AD treatments since 2014. Eisai serves as the lead of lecanemab development and regulatory submissions globally with both companies co-commercialising 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 commercialisation 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 commercialisation agreement on the antibody back-up was signed in May 2015.

4. About Eisai EMEA Neurology

At Eisai, we give our first thought to patients, their care partners and to society, to increase the benefits health care provides them – we call this *human health care* (*hhc*). We focus beyond the realm of health to the value we bring to society. Through the power of collaboration and by using insights to guide our work, we can make a meaningful contribution to people and society, and to improve outcomes and services for all.

In EMEA, we are the European hub of Tokyo-based Eisai Co. Ltd., forming part of a multinational team working across a global network of R&D facilities, manufacturing sites and marketing subsidiaries.

Our collective passion and dedication to patient care is the driving force behind our efforts to discover and develop innovative medicines in a variety of therapeutic areas where a high unmet medical need remains, including oncology and neurology.

Our mission is clear; we strive to make a significant long-lasting contribution to society in an ethical, compliant, and sustainable way by embodying *hhc* in everything we do.

For more information about Eisai in the EMEA region please visit www.eisai.eu.

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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.

Biogen routinely post information that may be important to investors on its website.

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 AD; the anticipated benefits and potential of Biogen's collaboration arrangements with Eisai; the potential of Biogen's commercial business and pipeline programmes; including lecanemab; and risks and uncertainties associated with drug development and commercialisation. 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 commercialisation involve a high degree of risk, and only a small number of research and development programmes result in commercialisation 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 commercialisation of the medicine; 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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