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Eisai presents 4-year Leqembi®▼ (lecanemab) open-label extension data from post-hoc sub-group analysis at German neurology congress

Clarity AD open-label extension data show that after four years of continuous lecanemab treatment in apolipoprotein E ε4 (ApoE ε4) non-carriers and heterozygotes, patients continued to accrue benefit relative to the Alzheimer's Disease Neuroimaging Initiative (ADNI†) cohort, as measured by Clinical Dementia Rating—Sum of Boxes (CDR-SB)[1]*

The treatment also reduced the risk of progression to the next stage of Alzheimer's disease by 32% (95% CI: 0.57, 0.82) over 48 months compared to the ADNI cohort as measured by CDR-SB[1]

HATFIELD, HERTFORDSHIRE, UNITED KINGDOM (UK), and CAMBRIDGE, Mass., 12 November, 2025 – Eisai Europe Ltd. and Biogen Inc. today presented new clinical data from a post-hoc sub-group analysis of the Clarity AD, open-label extension (OLE), demonstrating that treatment with lecanemab in adult patients with early Alzheimer's disease (AD) (mild cognitive impairment [MCI] or mild dementia due to AD, with confirmed amyloid pathology) who are apolipoprotein E ε4 (ApoE ε4) non-carriers or heterozygotes, continued to slow disease progression as measured by CDR-SB compared to matched controls from the Alzheimer's Disease Neuroimaging Initiative (ADNI).[1] The 48-month data was presented at the 98th Congress of the German Society of Neurology (DGN), 2025 in Berlin, Germany.

Clarity AD was a global Phase 3 placebo-controlled, double-blind, parallel-group, randomised study. Of the total number of patients randomised, 1,521 were ApoE ε4 non-carriers or heterozygotes. The primary endpoint was the change in the score of the global cognitive and functional scale, CDR-SB. Clarity AD includes an OLE phase for eligible patients to evaluate the long-term safety profile and tolerability of lecanemab, and whether the effects of the treatment are maintained over time.[1,2]

Participants who received treatment from the start through to 48 months (n=409) as part of the OLE study continued to accrue benefit over time with continued separation through 48 months, relative to the ADNI cohort (n=79), with a 1.53 difference in CDR-SB Adjusted Mean Change from Baseline.[1] Post-hoc slope analysis of CDR-SB results at 48 months presented at the congress showed that the lecanemab cohort had delayed disease progression compared to those in the ADNI cohort (n=79) by 9.8 months.[1]

CDR-SB is a disease staging tool used in clinical trials, which can help to stage dementia due to AD.[3] It is a global cognitive and functional scale that measures six domains, including memory, orientation, judgement and problem solving, community affairs, home and hobbies and personal care.[3] To provide context, a change from 0.5 to 1 on the CDR score domains of Memory, Community Affairs and Home/Hobbies reflects a shift from mild impairment to loss of independence.[3] This can affect a person's ability to be left alone, recall recent events, participate in daily activities, manage household tasks, and engage in hobbies and intellectual interests.[3]

In an analysis of time to worsening of CDR-SB scores, the OLE data at 48 months showed treatment with the medicine reduced the risk of progression to next stage of the disease by 32% vs ADNI, hazard ratio [HR] = 95% CI: 0.57, 0.82) in ApoE ε4 non-carrier or heterozygote patients.[1]

In the Clarity AD core clinical trial in the EU and UK indicated population, the most common adverse reactions in the ApoE ε4 non-carrier or heterozygote population (n=757) were infusion-related reaction (26%), amyloid-related imaging abnormalities with haemosiderin deposition (small spots of brain bleeding) (ARIA-H¶) (13%), fall (11%), headache (11%) and amyloid-related imaging abnormalities with cerebral oedema (build-up of fluid in the brain) (ARIA-E#) (9%).[4,5,6]

No new safety findings have been observed with continuous treatment with lecanemab over 48 months in the ApoE ε4 non-carrier and heterozygote population.[1] The summary of adverse events by 12-month intervals in the UK/EU population is as follows:[1]

Figure 1[7]	<12 months (n=1,366)		12-24 months (n=1,095)		24-36 months (n=850)		36-48 months (n=549)	
Adverse Event (AE)	1115	**81.6%**	794	**72.5%**	582	**68.5%**	320	**58.3%**
Serious Adverse Event (SAE)	150	**11.0%**	99	**9.0%**	64	**7.5%**	36	**6.6%**
Death (Includes all post-treatment events)	7	**0.5%**	8	**0.7%**	4	**0.5%**	1	**0.2%**
AE's Leading to Study Drug Withdrawal	67	**4.9%**	36	**3.3%**	14	**1.6%**	4	**0.7%**
ARIA-E	132	**9.7%**	27	**2.5%**	9	**1.1%**	6	**1.1%**
ARIA-H	154	**11.3%**	125	**11.4%**	66	**7.8%**	47	**8.6%**
Isolated ARIA-H	67	**4.9%**	79	**7.2%**	52	**6.1%**	35	**6.4%**
Headache	102	**7.5%**	58	**5.3%**	26	**3.1%**	19	**3.5%**
Infusion-Related Reaction	309	**22.6%**	50	**4.6%**	24	**2.8%**	11	**2.0%**

Figure 1: As of 31 March 2025[7]

"The presentation of these findings adds to the growing body of evidence demonstrating the potential benefits of lecanemab for eligible patients. As Alzheimer's disease is a progressive and chronic condition, it is crucial to continue generating and analysing long-term data as it deepens our understanding of continuous treatment over time," said Robert Sands, MD, VP, Head of Medical Affairs, Eisai EMEA. "Eisai is committed to investing in research and innovation, with the aim of being a part of the solution for a better future for those impacted by this disease."

"These data show the sustained clinical benefits of lecanemab over four years of treatment, demonstrating the potential to help people living with mild cognitive impairment and mild dementia due to Alzheimer's disease", said Mihaela Vlaicu, Head of Medical, Europe at Biogen. "The findings offer valuable insights to guide evidence-based discussions on the long-term management of early Alzheimer's disease, aiming to slow disease progression."

Lecanemab is an amyloid-beta (Aβ) monoclonal antibody that preferentially binds and clears toxic protofibrils**(soluble Aβ aggregates), in addition to targeting and reducing Aβ plaques (insoluble Aβ aggregates).[2,8,9,10] Aβ protofibrils are a key toxic form of Aβ that accumulate in the brain and cause neuronal injury.[9,11,12]

In the EU and the UK, lecanemab is indicated for the treatment of adult patients with a clinical diagnosis of mild cognitive impairment (MCI) and mild dementia due to AD (early AD) who are ApoE ε4 non-carriers or heterozygotes with confirmed amyloid pathology.[5,6]

Eisai serves as the lead for lecanemab's development and regulatory submissions globally, with both Eisai and Biogen co-commercialising and co-promoting the product, and Eisai having final decision-making authority. In the EU and UK (excluding the Nordic countries), Eisai and Biogen will co-promote the medicine, with Eisai distributing the product as the Marketing Authorisation (MA) Holder. In the Nordic countries, Eisai and BioArctic will co-promote the medicine, with Eisai distributing the product as the MA Holder.

▼: This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. If you get any side effects, talk to your healthcare professional. This includes any possible side effects not listed in the package leaflet. In the UK you can also report side effects directly via Yellow Card Scheme at www.mhra.gov.uk/yellowcard, for EU, via your EU national reporting system. By reporting side effects, you can help provide more information on the safety of this medicine.

*Apolipoprotein E is a protein involved in the metabolism of lipids in humans. It is implicated in AD.[13]

†ADNI is a clinical research project launched in 2004 to develop methods to predict the onset of AD and to confirm the effectiveness of treatments.[14] The project involves a multi-year longitudinal observation targeting healthy elderly individuals as well as patients with MCI and early stages of AD. Patients were prospectively identified in this long-term natural history study prior to initiating Clarity AD to aid in the design of the study. For this reason, ADNI is used as an observational cohort in the OLE portion of Clarity AD as they match the population in the placebo group in the core Clarity AD trial based on multiple characteristics (i.e., age, sex).[1,15,16]

¶ARIA-H: amyloid-related imaging abnormalities with haemosiderin deposition (cerebral microhaemorrhages and superficial siderosis).

[#]ARIA-E: amyloid-related imaging abnormalities with oedema (oedema/effusion).

[**]Protofibrils are believed to contribute to 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.[11] Protofibrils can cause injury to neurons in the brain which in turn, can negatively impact cognitive function via multiple mechanisms,[11] 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.[12] It is believed the reduction of protofibrils may slow the progression of AD by reducing damage to neurons in the brain and cognitive dysfunction.[12]

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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 Aβ.[2,5] The medicine is authorised in 51 countries and is under regulatory review in 10 countries and regions.[5,6,17,18]

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, 1,521 were in the EU indicated population (ApoE ε4 heterozygotes or non-carriers).[1,5] 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 EU indicated population (ApoE ε4 heterozygotes or non-carriers, measured by controlled-based multiple imputation[‡‡]), reduced clinical decline on CDR-SB by 31% at 18 months compared to placebo (n=764). The mean CDR-SB score at baseline was approximately 3.2 in both groups.[4,5] 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).[4,5] CDR-SB is a global cognitive and functional scale that measures six domains, including Memory, Orientation, Judgement and Problem Solving, Community Affairs, Home and Hobbies, and Personal Care.[3]

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.[4,5] 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).[4,5] The ADCS-MCI-ADL assesses the ability of patients to function independently, including being able to participate in community activities, dress and feed themselves.[19]

In the EU and UK indicated population (ApoE ε4 non-carriers or heterozygotes) (n=757), the most common adverse reactions were infusion-related reaction (26%), ARIA-H (13%), fall (11%), headache (11%) and ARIA-E (9%).[4,5,6]

As requested by the regulatory authority, efficacy analyses were conducted for ApoE ε4 non-carriers or heterozygote participants using a control-based multiple imputation method, in which all missing values were imputed with copy-increments (change between visits) using the actual value in the placebo group.[4] This

methodology differs from that used in the Clarity AD primary analysis which used mixed-model repeat measures (MMRM) with missing at random assumption.[2,4]

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

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.

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 with aspirations 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 posts 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 forward-looking statements may be accompanied by such words as "aim," "anticipate," "believe," "contemplate," "continue," "could," "estimate," "expect," "forecast," "goal," "guidance", "hope," "intend," "may," "objective," "plan," "possible," "potential," "predict," "project," "prospect," "should," "target," "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 trials may not be indicative of full results or results from later stage or larger scale clinical trials and do not ensure regulatory approval. You should not place undue reliance on these statements. Given their forward-looking nature, these statements involve substantial risks and uncertainties that may be based on inaccurate assumptions and could cause actual results to differ materially from those reflected in such statements.

These forward-looking statements are based on management's current beliefs and assumptions and on information currently available to management. Given their nature, we cannot assure that any outcome expressed in these forward-looking statements will be realised in whole or in part. We caution that these statements are subject to risks and uncertainties, many of which are outside of our control and could cause future events or results to be materially different from those stated or implied in this document, including, among others, uncertainty of long-term success in developing, licensing, or acquiring other product candidates or additional indications for existing products; expectations, plans and prospects relating to product approvals, approvals of additional indications for our existing products, sales, pricing, growth, reimbursement and launch of our marketed and pipeline products; our ability to effectively implement our corporate strategy; the successful execution of our strategic and growth initiatives, including acquisitions; the risk that positive results in a clinical trial may not be replicated in subsequent or confirmatory trials or success in early stage clinical trials may not be predictive of results in later stage or large scale clinical trials or trials in other potential indications; risks associated with clinical trials, including our ability to adequately manage clinical activities, unexpected concerns that may arise from additional data or analysis obtained during clinical trials, regulatory authorities may require additional information or further studies, or may fail to approve or may delay approval of our drug candidates; the occurrence of adverse safety events, restrictions on use with our products, or product liability claims; and any other risks and uncertainties that are described in other reports we have filed with the U.S. Securities and Exchange Commission.

These statements speak only as of the date of this press release and are based on information and estimates available to us at this time. Should known or unknown risks or uncertainties materialise or should underlying assumptions prove inaccurate, actual results could vary materially from past results and those anticipated, estimated or projected. Investors are cautioned not to put undue reliance on forward-looking statements. A further list and description of risks, uncertainties and other matters can be found in our Annual Report on Form 10-K for the fiscal year ended December 31, 2024 and in our subsequent reports on Form 10-Q and Form 10-K, in each case including in the sections thereof captioned “Note Regarding Forward-Looking Statements” and “Item 1A. Risk Factors,” and in our subsequent reports on Form 8-K. Except as required by law, we do not undertake any obligation to publicly update any forward-looking statements whether as a result of any new information, future events, changed circumstances or otherwise.

Digital Media Disclosures

From time to time, we have used, or expect in the future to use, our investor relations website, the Biogen LinkedIn account and the Biogen X account, as a means of disclosing information to the public in a broad, non-exclusionary manner, including for purposes of the SEC’s Regulation Fair Disclosure (Reg FD). Accordingly, investors should monitor our investor relations website and these social media channels in addition to our press releases, SEC filings, public conference calls and websites, as the information posted on them could be material to investors.

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