



Additional Detailed Analyses From Phase 2 Study 201 of Lecanemab Published as Three Papers in Peer-Reviewed Journals

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TOKYO and CAMBRIDGE, Mass., March 30, 2023 (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 three additional detailed analyses from the Phase IIb clinical study (Study 201), evaluating the efficacy and safety of lecanemab for mild cognitive impairment (MCI) due to Alzheimer's disease (AD) and mild AD (collectively known as early AD), were published in the peer-reviewed journals.

1. Detailed results on biomarker, cognitive, and clinical effects from Study 201 core to OLE (open-label extension): *Alzheimer's Research and Therapy*
2. Consistency of efficacy results across various clinical measures and statistical methods in Study 201: *Alzheimer's Research and Therapy*
3. ARIA (amyloid-related imaging abnormality) profile in Study 201: *Alzheimer's & Dementia: Translational Research and Clinical Interventions*

Study 201 was a multicenter, double-blind, placebo-controlled, Phase 2b trial conducted in 856 patients with early AD. Its core study evaluated key efficacy assessments, including clinical change on the AD Composite Score (ADCOMS) as the primary endpoint at 12 months and as key secondary endpoints, ADCOMS, Clinical Dementia Rating-Sum-of-Boxes (CDR-SB) and AD Assessment Scale-Cognitive Subscale 14 (ADAS-Cog14) at 18 months. Following analysis of the 18-month core phase, an intervening off-treatment period (gap period) ranging from 9-59 months (mean 24 months) was taken, which was followed by an OLE with 10 mg/kg IV bi-weekly lecanemab dosing to assess long-term safety and tolerability. The results of the primary analysis in the core study including clinical efficacy and biomarkers have already been [published](#), showing a consistent reduction in clinical decline across several clinical and biomarker endpoints with lecanemab 10 mg/kg bi-weekly dosing.

1. Detailed results on biomarker, cognitive, and clinical effects from Study 201.

["Lecanemab in patients with early Alzheimer's disease: detailed results on biomarker, cognitive, and clinical effects from the randomized and open-label extension of the phase 2 proof-of-concept study"](#)

In the core 201 study, lecanemab was shown to reduce brain A β accumulation measured by amyloid PET in a dose- and time-dependent manner after 12 and 18 months of treatment, and corresponding changes in plasma biomarkers and reduction in clinical decline. During the gap period, a trend was observed for plasma A β 42/40 ratio and p-tau181 values to return to the pre-administration levels (re-accumulation) faster than amyloid PET.

In the OLE, lecanemab 10 mg/kg biweekly treatment showed a decrease in brain amyloid beta (A β) accumulation measured by amyloid PET, a decrease in the plasma A β 42/40 ratio, and a decrease in plasma p-tau181.

The potential for disease modification with lecanemab is supported by an increasing difference in clinical measures between the lecanemab group and placebo group in line with time during the core period, differences in clinical progression between subjects who received 10 mg/kg lecanemab and those who received placebo in the core period, which remained persistent throughout the gap period, and an impact on biological measures that reflect key pathophysiological changes in AD. Furthermore, the results showed the potential for monitoring the treatment effects of lecanemab using plasma biomarkers.

2. Consistency of efficacy results across various clinical measures and statistical methods in Study 201.

["Consistency of efficacy results across various clinical measures and statistical methods in the lecanemab phase 2 trial of early Alzheimer's disease"](#)

In order to assess the robustness of lecanemab's efficacy in Study 201, sensitivity analyses were performed using several statistical models for three key clinical endpoints (ADCOMS, CDR-SB, ADAS-Cog14). The sensitivity analysis showed that 18 months of lecanemab treatment consistently reduced the clinical decline in all statistical models examined. The results of all sensitivity analyses for three key clinical endpoints at the highest dose (10 mg/kg bi-weekly) at 18 months were consistent, with a 29.1% to 37.4% reduction in clinical deterioration with lecanemab compared to placebo for ADCOMS, 26.5% to 38.4% for CDR-SB and 37.4% to 55.9% for ADAS-Cog14.

3. ARIA profile in Study 201

["ARIA in patients treated with lecanemab \(BAN2401\) in a phase 2 study in early Alzheimer's disease"](#)

In the core study 201, amyloid-related imaging abnormalities-edema (ARIA-E) was dose dependent, with an incidence 9.9% at the highest doses (10 mg/kg bi-weekly) for the overall population and 14.3% for ApoE4 positive subjects. Most ARIA-E occurred within 30 days after the initial dose and had mild to moderate severity in radiographic severity. Symptomatic ARIA-E occurred in 3% of participants in the 10mg/kg bi-weekly treatment group. ARIA cerebral microhemorrhages, intracerebral hemorrhage >1cm, and superficial siderosis (ARIA-H) occurred in 6.2% of subjects who received 10 mg/kg biweekly lecanemab and those events were mostly mild in severity. There were no symptomatic cases of ARIA-H reported in the core study.

Overall ARIA-E events in the OLE phase were generally consistent with the rate seen in the lecanemab 10 mg/kg biweekly group in the core study (four subjects treated with placebo in the core study had ARIA-E in the OLE (4 of 45: 8.9%). As with the core study, most ARIA-E occurred within 3 months after receiving the initial dose in the OLE and had mostly mild to moderate in radiographic severity. ARIA-H events in the OLE were generally consistent with the rate seen in the lecanemab 10 mg/kg biweekly group in the core study. ARIA-H events were mostly mild or moderate in severity. One symptomatic case of ARIA-H, intracerebral hemorrhage > 1cm, was reported in OLE. This subject did not have concurrent ARIA-E, and the adverse event resolved with residual visual field defect.

PK/PD modeling showed that the incidence of ARIA-E was correlated with C_{max} at steady state. Based on the fact that lecanemab was generally well tolerated at the highest dose in this study, the Phase 3 Clarity AD study was conducted without dose titration. A subcutaneous formulation that may potentially reduce the C_{max} of lecanemab is being developed and evaluated to determine if there is a reduction of the incidence of ARIA-E compared to intravenous formulation.

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.

To learn more, visit www.LEQEMBI.com.

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[Notes to editors]

1. About Lecanemab

Lecanemab (Brand Name in the U.S.: LEQEMBI™) is the result of a strategic research alliance between Eisai and BioArctic. Lecanemab is a humanized immunoglobulin gamma 1 (IgG1) monoclonal antibody directed against aggregated soluble (protofibril) and insoluble forms of amyloid-beta (Aβ). Lecanemab selectively binds and eliminates Aβ protofibrils that are thought to contribute to the neurotoxicity in AD. As such, lecanemab may have the potential to have an effect on disease pathology and to slow down the progression of the disease. LEQEMBI is indicated for the treatment of Alzheimer's disease (AD) in the U.S. under an accelerated approval by the U.S. Food and Drug Administration (FDA). 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. There are no safety or effectiveness data on initiating treatment at earlier or later stages of the disease than were studied. This indication is approved under accelerated approval based on reduction in Aβ plaques observed in patients treated with LEQEMBI. Continued approval for this indication may be contingent upon verification of clinical benefit in a confirmatory trial. The Clarity AD study of lecanemab met its primary endpoint and all key secondary endpoints with highly statistically significant results.

Please see full [Prescribing Information](#) in the United States.

Lecanemab-irnb was approved under the accelerated approval pathway in the U.S. and was launched in the U.S. on January 18, 2023. The accelerated approval was based on Phase 2 data that demonstrated that lecanemab reduced the accumulation of Aβ plaque in the brain, a defining feature of AD, and its continued approval may be contingent upon verification of lecanemab's clinical benefit in a confirmatory trial. The FDA determined that the results of the Phase 3 Clarity AD study can serve as the confirmatory study to verify the clinical benefit of lecanemab. In November 2022, the results of 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*.

In the U.S., Eisai submitted a supplemental Biologics License Application (sBLA) to the FDA for approval under the traditional pathway on January 6, 2023. On March 3, 2023, the FDA accepted Eisai's sBLA based on the Clarity AD clinical data, and the lecanemab application has been granted Priority Review, with a Prescription Drug User Fee Act (PDUFA) action date of July 6, 2023. The FDA is currently planning to hold an Advisory Committee to discuss this application but has not yet publicly announced the date of the meeting. Eisai submitted an application for manufacturing and marketing approval to the Pharmaceuticals and Medical Devices Agency (PMDA) on January 16, 2023, in Japan. The Priority Review was granted by the Ministry of Health, Labour and Welfare (MHLW) on January 26, 2023. Eisai utilized the prior assessment consultation system of PMDA, with the aim of shortening the review period for lecanemab. In Europe, Eisai submitted a marketing authorization application (MAA) to the European Medicines Agency (EMA) on January 9, 2023, which was accepted on January 26, 2023. In China, Eisai initiated submission of data for a BLA to the National Medical Products Administration (NMPA) of China in December 2022, and the Priority Review was granted on February 27, 2023.

Eisai has completed a lecanemab subcutaneous bioavailability study, and subcutaneous dosing is currently being evaluated in the Clarity AD 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, has been 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 the Dominantly Inherited Alzheimer Network Trials Unit (DIAN-TU), led by Washington University School of Medicine in St. Louis, has been 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 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 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 the *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 Twitter [@Eisai_SDGs](https://twitter.com/Eisai_SDGs).

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](https://twitter.com/Biogen), [LinkedIn](https://www.linkedin.com/company/biogen), [Facebook](https://www.facebook.com/biogen), [YouTube](https://www.youtube.com/biogen).

Biogen Safe Harbor

This news release contains forward-looking statements, including statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995, 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 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, including the Clarity AD clinical trial and AHEAD 3-45 study; 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; 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 are based on Biogen's current beliefs and expectations and speak only as of the date of this news release. Biogen does not undertake any obligation to publicly update any forward-looking statements, whether as a result of new information, future developments or otherwise.