Eisai Presented New Analyses of ARIA and QOL on Lecanemab in Clarity AD at the AD/PD™ 2023 Annual Meeting

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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 Eisai presented new analyses on amyloid-related imaging abnormalities (ARIA) with the use of antiplatelet and anticoagulant medications, isolated ARIA-H, and caregiver burden and health-related quality of life (QOL), from the results of Eisai's Phase 3 Clarity AD study of lecanemab (generic name, U.S. brand name: LEQEMBI™), an anti-amyloid-β (Aβ) protofibril* antibody, at the 2023 International Conference on Alzheimer's and Parkinson's Diseases annual meeting AD/PD™.

Clarity AD was a global confirmatory Phase 3 placebo-controlled, double-blind, parallel-group, randomized study in 1,795 people with early Alzheimer's disease (AD) (lecanemab group: 10 mg/kg bi-weekly IV treatment: 898, placebo group: 897). Lecanemab met the primary endpoint and all key secondary endpoints with highly statistically significant results. In November 2022, results of the 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*.

1. **Lecanemab Phase 3 Clarity AD Trial: ARIA With the Use of Antiplatelets or Anticoagulants in Early Alzheimer's Disease**

   In the Clarity AD study, ARIA rates were higher for patients receiving lecanemab compared to those on placebo. The objective of this analysis was to evaluate antiplatelet and anticoagulant medication use in participants who experienced either ARIA-E (edema) or ARIA-H (combined cerebral microhemorrhages, superficial siderosis, and intracerebral hemorrhages >1 cm in diameter).

   The risks of ARIA appear slightly higher in the placebo group with antiplatelet or with anticoagulants relative to placebo subjects not on anticoagulants (no antiplatelet or anticoagulation: 8.9%, antiplatelet: 9.7%, anticoagulation (anticoagulation alone or with antiplatelet): 10.8%). ARIA rates may be slightly lower in those on lecanemab treated with antiplatelet or with anticoagulation, relative to lecanemab treated subjects not with antiplatelet or with anticoagulation (no antiplatelet or anticoagulation: 21.8%, antiplatelet: 17.9%, anticoagulation: 13.3%).

   The incidence of ARIA-E was 13.1% in the lecanemab group and 1.5% in the placebo group when no antiplatelet or anticoagulant medication was used, 10.4% in the lecanemab group and 0.84% in the placebo group when antiplatelet medication was used, and 4.8% in the lecanemab group and 2.7% in the placebo group when anticoagulant medication was used.

   Because intracerebral hemorrhage >1cm have been observed in patients taking lecanemab, additional caution should be exercised when considering administration of antithrombotics or a thrombolytic agent.

   In Clarity AD, ARIA did not occur more frequently in lecanemab-treated participants on antiplatelet or anticoagulant drugs compared to lecanemab-treated participants that were not on either.

2. **Isolated ARIA-H in Patients Treated with Lecanemab in the Phase 3 Clarity AD Study in Early Alzheimer's Disease**

   The objective of this analysis was to describe the occurrences and timing of isolated ARIA-H events (i.e., those events not occurring temporally concurrent with ARIA-E). The incidence of overall ARIA-H was 17.3% in the lecanemab group and 9.0% in the placebo group, and the incidence of isolated ARIA-H was similar in the lecanemab (8.9%) and placebo (7.8%) groups in Clarity AD. While ARIA-H concurrent with ARIA-E occurred early in the treatment as expected given timing of ARIA-E, isolated ARIA-H in both the placebo and lecanemab groups were infrequent and occurred at a steady rate over 18 months of treatment. The incidence of isolated ARIA-H increased with number of ApoEε4 alleles in both placebo (noncarriers: 3.8%; heterozygotes: 7.3%; homozygotes: 18.0%), and lecanemab group (noncarriers: 8.3%; heterozygotes: 8.4%; homozygotes: 12.1%). On the other hand, it was found that the ApoEε4 carrier status did not impact the timing of overall occurrence of ARIA-H.

   In Clarity AD, the pattern of occurrence of isolated ARIA-H in lecanemab group was similar to that in placebo group.

3. **Lecanemab Clarity AD: Quality-of-Life Results from a Randomized, Double-Blind Phase 3 Trial in Early Alzheimer's Disease**

   The objective of this analysis was to describe the health-related quality-of-life (HRQoL) pre-specified exploratory results from Clarity AD. HRQoL by subject was measured using the European Quality of Life–5 Dimensions (EQ-5D-5L**) and

Quality of Life in AD (QOL-AD***) scales at baseline and every 6 months post-baseline. QOL-AD was also assessed for the subject by the care partner. Additionally, care partners were administered the Zarit Burden Interview**** every 6 months to assess care partner burden associated with dementia.

At month 18, adjusted mean change from baseline in EQ-5D-5L and QOL-AD of subject showed 49% and 56% less decline, respectively. Care partner burden measured Zarit Burden Interview and QOL-AD by partner resulted in 38% and 23% less decline at 18 months, respectively. Assessment results were consistent across ApoE genotypes.

The results of the Clarity AD Health-related QoL measures presented additional evidence for meaningful benefits of lecanemab treatment to patients and care partners.

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.

* Protofibrils are large Aβ aggregated soluble species of 75-5000 Kd.[1]
** The European Quality of Life-5 Dimensions (EQ-5D-5L) is used as a patient-reported measure of quality of life and consists of five domains (degree of mobility, personal care, daily living, pain/discomfort and anxiety/blushing).
*** Quality of Life in AD (QOL-AD) is a quality-of-life index specific to dementia.
**** The Zarit Burden Interview is a scale to measure caregiver burden.

References

[1] Söderberg, L., Johannesson, M., Nygren, P. et al. Lecanemab, Aducanumab, and Gantenerumab — Binding Profiles to Different Forms of Amyloid-Beta Might Explain Efficacy and Side Effects in Clinical Trials for Alzheimer's Disease. *Neurotherapeutics* (2022). https://doi.org/10.1007/s13311-022-01308-6. Accessed March 23, 2023

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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). In the U.S., LEQEMBI was granted accelerated approval by the U.S. Food and Drug Administration (FDA) on January 6, 2023. LEQEMBI is indicated for the treatment of Alzheimer's disease (AD) in the U.S. 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 in the U.S. 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.

Please see full Prescribing Information in the United States.

The Clarity AD study of lecanemab met its primary endpoint and all key secondary endpoints with highly statistically

significant results. 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 LEQEMBI 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, and 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 lecanemab subcutaneous bioavailability study, and subcutaneous dosing is currently being evaluated in the Clarity AD (Study 301) 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, 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.

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 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.

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, LinkedIn, Facebook, YouTube.

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.