# Eisai Presents New Analysis of Lecanemab Clinical Efficacy Results from Phase 2B Study at Clinical Trials on Alzheimer's Disease (CTAD) Conference

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***Consistency of Efficacy Assessments Evaluated Across Various Statistical Methods***

TOKYO and CAMBRIDGE, Mass., Nov.11, 2021 – Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") and Biogen Inc. (Nasdaq: BIIB, Corporate headquarters: Cambridge, Massachusetts, CEO: Michel Vounatsos, "Biogen") announced today results of sensitivity analyses evaluating the consistency of lecanemab efficacy results across multiple statistical models in patients with Mild Cognitive Impairment (MCI) due to Alzheimer's disease (AD) and mild AD (collectively known as early AD). This presentation was made by Eisai at the 2021 Clinical Trials on Alzheimer's Disease (CTAD) conference, November 9-12, 2021 in Boston, Massachusetts and virtually.

In September 2021, Eisai initiated a rolling submission of a Biologics License Application (BLA) for lecanemab, an investigational anti-amyloid beta protofibril antibody, for the treatment of early AD, to the U.S. Food and Drug Administration (FDA) under the accelerated approval pathway.

Study 201, a multicenter, double-blind, placebo-controlled, Phase 2b trial conducted in 856 patients with early AD, evaluated key efficacy assessments, including clinical change on the Alzheimer's Disease Composite Score (ADCOMS) at the primary endpoint of 12 months and at select key secondary endpoints, Clinical Dementia Rating-Sum-of-Boxes (CDR-SB) and Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog14) at 18 months. Six sensitivity analyses across four statistical models (mixed model for repeated measures, disease progression model, natural cubic spline model, and quadratic mixed model) showed consistent positive lecanemab treatment effects for ADCOMS, CDR-SB and ADAS-Cog14 at 18 months.

The primary endpoint was Bayesian analysis of 12-month clinical change on ADCOMS with the goal to identify the most efficacious dose (ED90 dose). Primary analysis was super-superiority over placebo by ≥25%: goal was 80% probability of ≥25% reduction in decline versus placebo. Study achieved the goal of identifying smallest dose that achieved ≥90% of maximum treatment effect (10 mg/kg biweekly), i.e., the ED90 dose. At 12 months, ED90 dose had 64% probability of being super-superior to placebo by 25% reduction. At 12 months, ED90 dose had 98% probability superior to placebo. Consistent treatment effect was observed at 18 months for ADCOMS (29% to 37%), CDR-SB (26.5% to 35%), and ADAS-Cog (47% to 56%), with separation from placebo observed by six months for the top dose (10mg/kg biweekly) across all analyses.

"In Study 201, lecanemab showed robust clearance of brain amyloid and slowing of clinical decline across several clinical and biomarker endpoints. This sensitivity analysis shows lecanemab clinical efficacy results across statistical models are consistent, reliable and further enhances our confidence in the clinical potential of this investigational therapy," said Michael Irizarry, M.D., Vice President, Deputy Chief Clinical Officer, Neurology Business Group, Eisai Inc. "Through our comprehensive research program, we will continue to advance the understanding of how this anti-amyloid beta protofibril antibody may play a role in the treatment of early and preclinical AD. In March 2021, Eisai completed enrollment of 1,795 patients with early Alzheimer's disease in our confirmatory Phase 3 Clarity AD clinical study. The Phase 3 clinical study, AHEAD 3-45, is currently exploring lecanemab's safety and efficacy in individuals with preclinical AD."

This release discusses investigational uses of an agent in development and is not intended to convey conclusions about efficacy or safety. There is no guarantee that such investigational agent will successfully complete clinical development or gain health authority approval.

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[Notes to editors]

**1. About Lecanemab (BAN2401)**

Lecanemab is an investigational humanized monoclonal antibody for Alzheimer's disease (AD) that is the result of a strategic research alliance between Eisai and BioArctic. Lecanemab selectively binds to neutralize and eliminate soluble, toxic amyloid-beta (Aβ) aggregates (protofibrils) that are thought to contribute to the neurodegenerative process 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. With regard to the results from pre-specified analysis at 18 months of treatment, Study 201 demonstrated reduction of brain Aβ accumulation ($P<0.0001$) and slowing of disease progression measured by ADCOMS* ($P<0.05$) in early AD subjects. The study did not achieve its primary outcome measure** at 12 months of treatment. The Study 201 open-label extension was initiated after completion of the Core period and a Gap period off treatment (average of 24 months) to evaluate safety and efficacy, and is underway.

Eisai obtained the global rights to study, develop, manufacture and market lecanemab for the treatment of AD pursuant to an agreement concluded with BioArctic in December 2007. In March 2014, Eisai and Biogen entered into a joint development and commercialization agreement for lecanemab and the parties amended that agreement in October 2017. Currently, lecanemab is being studied in a pivotal Phase 3 clinical study in symptomatic

early AD (Clarity-AD), following the outcome of the Phase 2 clinical study (Study 201). In 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, was initiated. 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 Alzheimer's Disease and related dementias in the U.S., funded by the National Institute on Aging, part of the National Institutes of Health, Eisai and Biogen.

* Developed by Eisai, ADCOMS (AD Composite Score) combines items from the ADAS-Cog (Alzheimer's Disease Assessment Scale-cognitive subscale), CDR (Clinical Dementia Rating) and the MMSE (Mini-Mental State Examination) scales to enable a sensitive detection of changes in clinical functions of early AD symptoms and changes in memory.
** An 80% or higher estimated probability of demonstrating 25% or greater slowing in clinical decline at 12 months treatment measured by ADCOMS from baseline compared to placebo.

**2. About the Collaboration between Eisai and Biogen for Alzheimer's Disease**
Eisai and Biogen are collaborating on the joint development and commercialization of AD treatments. Eisai serves as the lead in the co-development of lecanemab.

**3. About the Collaboration between Eisai and BioArctic for Alzheimer's Disease**
Since 2005, BioArctic has had a long-term collaboration with Eisai regarding the development and commercialization of drugs for the treatment of AD. The commercialization agreement on the lecanemab antibody was signed in December 2007, and the development and commercialization agreement on the antibody lecanemab back-up for AD, which was signed in May 2015. Eisai is responsible for the clinical development, application for market approval and commercialization of the products for AD. BioArctic has no development costs for lecanemab in AD.

**4. About Eisai Co., Ltd.**
Eisai Co., Ltd. is a leading global pharmaceutical company headquartered in Japan. Eisai's corporate philosophy is based on the human health care (hhc) concept, which is to give first thought to patients and their families, and to increase the benefits that health care provides to them. With a global network of R&D facilities, manufacturing sites and marketing subsidiaries, we strive to realize our hhc philosophy by delivering innovative products to target diseases with high unmet medical needs, with a particular focus in our strategic areas of Neurology and Oncology.

Leveraging the experience gained from the development and marketing of a treatment for Alzheimer's disease, Eisai aims to establish the "Eisai Dementia Platform." Through this platform, Eisai plans to deliver novel benefits to those living with dementia and their families through constructing a "Dementia Ecosystem," by collaborating with partners such as medical organizations, diagnostic development companies, research organizations, and bio-ventures in addition to private insurance agencies, finance industries, fitness clubs, automobile makers, retailers, and care facilities. For more information about Eisai Co., Ltd., please visit https://www.eisai.com.

**5. About Eisai Inc.**
At Eisai Inc., human health care (hhc) is our goal. We give our first thoughts to patients and their families, and helping to increase the benefits health care provides. As the U.S. pharmaceutical subsidiary of Tokyo-based Eisai Co., Ltd., we have a passionate commitment to patient care that is the driving force behind our efforts to discover and develop innovative therapies to help address unmet medical needs. Eisai is a fully integrated pharmaceutical business that operates in two global business groups: oncology and neurology (dementia-related diseases and neurodegenerative diseases). Our U.S. headquarters, commercial and clinical development organizations are located in New Jersey; our discovery labs are in Massachusetts and Pennsylvania; and our global demand chain organization resides in Maryland and North Carolina. To learn more about Eisai Inc., please visit us at www.eisai.com/US and follow us on Twitter and LinkedIn.

**6. About Biogen**
As pioneers in neuroscience, Biogen discovers, develops, and delivers worldwide innovative therapies for people living with serious neurological diseases as well as related therapeutic adjacencies. One of the world's first global biotechnology companies, Biogen was founded in 1978 by Charles Weissmann, Heinz Schaller, Sir Kenneth Murray, and Nobel Prize winners Walter Gilbert and Phillip Sharp. Today, Biogen has the leading portfolio of medicines to treat multiple sclerosis, has introduced the first approved treatment for spinal muscular atrophy, and is providing the first and only approved treatment to address a defining pathology of Alzheimer's disease. Biogen is also commercializing biosimilars and focusing on advancing the industry's most diversified pipeline in neuroscience that will transform the standard of care for patients in several areas of high unmet need.

In 2020, Biogen launched a bold 20-year, $250 million initiative to address the deeply interrelated issues of climate, health, and equity. Healthy Climate, Healthy Lives™ aims to eliminate fossil fuels across the company's operations, build collaborations with renowned institutions to advance the science to improve human health outcomes, and support underserved communities.

The company routinely posts information that may be important to investors on its website at www.biogen.com. To learn more, please visit www.biogen.com and follow Biogen on social media – Twitter, LinkedIn, Facebook, YouTube.

**7. 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 and ADUHELM; potential regulatory discussions, submissions and approvals and the timing thereof; the expected data readout for the Clarity AD study; 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 ADUHELM; 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 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 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 trials; 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.