Eisai Presents Late-Breaker Updates on Lecanemab Clinical, Biomarker and Safety Data from Phase 2B Study Core and Open-Label Extension Across Five Years at Clinical Trials on Alzheimer's Disease (CTAD) Conference

November 10, 2021

TOKYO and CAMBRIDGE, Mass, Nov. 10, 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 new clinical, biomarker and safety assessments of brain amyloid reduction and five-year clinical status of people living with early Alzheimer's disease (AD) from the lecanemab Phase 2b 201 and the open-label extension (OLE) studies. The findings were presented and discussed in a late-breaking roundtable session with esteemed clinical researchers at the 2021 Clinical Trials on Alzheimer's Disease (CTAD) conference, November 9-12, 2021, in Boston, Massachusetts and virtually. Eisai recently initiated a rolling submission of a Biologics License Application (BLA) for lecanemab, an investigational anti-amyloid beta (Aβ) protofibril antibody, for the treatment of early AD, to the U.S. Food and Drug Administration (FDA) under the accelerated approval pathway.

OLE Study Explores Biomarkers and Clinical Effects Across Five Years
An OLE with 10 mg/kg IV biweekly lecanemab dosing was implemented after analysis of the 18-month, core phase (Study 201, Alz Res Therapy 13;21) with an intervening off-treatment period (gap period) ranging from 9-59 months (mean 24 months). The OLE phase evaluated the effect of lecanemab on amyloid PET over 12 months of treatment, including earlier time points (3 and 6 months) than in the core phase (12 and 18 months). This study design provided the opportunity to explore the biomarker and clinical effects of stopping and restarting lecanemab across five years of disease trajectory.

Amyloid Reduction Correlates with Clinical Benefit
The updated assessment of the OLE phase showed that treatment with lecanemab resulted in reduction of brain amyloid levels in as early as 3 months based on OLE data and robust clearance of amyloid plaque with more than 80% of participants (10/12) achieving amyloid negative status by 12-18 months of treatment as measured by PET (visual read). These results are consistent with core phase results. The 201 study core data suggested that clinical efficacy (ADCOMS) is correlated with amyloid reduction (PET SUVr) at both the population (correlation coefficients=0.832, p-value=0.080) and subject levels (correlation coefficients=0.201, slope=0.199, p=0.036). Amyloid PET levels were significantly reduced by quantitative assessment in newly treated OLE subjects in as early as 3 months after initiation of treatment. Additionally, the core data suggested that clinical efficacy is correlated with plasma Aβ at both the population (correlation coefficients=-0.306, not significant) and subject levels (correlation coefficients=-0.208, slope=-3.957, p-value=0.050).

Potential Slowing of Cognitive Decline May Suggest Disease-Modifying Effect
The clinical treatment difference in study participants between lecanemab treatment and placebo at the end of core period, is maintained after discontinued dosing over the 24-month Gap period. The reduction of clinical decline of participants receiving the highest dose of lecanemab relative to placebo at the end of the 18-month, core period showed a difference of 0.05 in ADCOMS (placebo 0.19, lecanemab 0.14). This treatment difference of 0.10 in subjects who entered OLE was maintained while off-treatment during the gap period up to the beginning of the OLE (placebo 0.28, lecanemab 0.18). Similar findings were observed for CDR-SB and ADAS-Cog, although both groups continued to progress. This pattern of sustained treatment effect after stopping lecanemab, reflected in biomarkers as well amyloid PET, plasma Aβ42/40 and ptau181 is consistent with a disease-modifying effect.

Blood Tests May be Able to Monitor Lecanemab Treatment Effects
New results were presented for two new blood tests that were measured in the Phase 2b and OLE studies: Plasma Aβ 42/40 ratio and Plasma p-tau181. Plasma Aβ 42/40 ratio changes suggested an inverse correlation with amyloid PET changes. Both amyloid PET and blood Aβ show correlation with ADCOMS at the population and individual levels in the core phase (PET correlation coefficients=0.832 population, 0.201 subject level and Aβ plasma correlations coefficients:-0.306 population, -0.208 subject level). Monitoring of treatment effects using plasma biomarkers may allow simple dose modification following robust amyloid removal (e.g., less frequent and/or lower dose).

Safety Profile with Low Incidence of ARIA-E and Symptomatic ARIA Rate in Core and OLE
Consistent with the safety findings in the core period, lecanemab was well-tolerated with <10% incidence of ARIA-E at 10-mg/kg biweekly in the Core and OLE. The incidence of symptomatic ARIA-E was <2% in Core and OLE. This safety profile enables lecanemab to be initiated at the therapeutic dose without titration.

"The latest lecanemab findings provide greater insight into the time course and extent of amyloid reduction observed with lecanemab, and the relationship to clinical outcomes and blood-based biomarkers," said Lynn Kramer, M.D., Chief Clinical Officer, Neurology Business Group, Eisai. "The Clarity AD Phase 3 Study in Early AD, which completed enrollment of 1795 subjects in March, aims to verify these findings."

The presentation video and slides will be available on the investors' section of the Eisai Co., Ltd. Website by 10:00 p.m. US EST on November 11.

This release discusses investigational uses of agents in development and is not intended to convey conclusions about efficacy or safety. There is no guarantee that such investigational agents 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 of 9-59 months (average of 24 months, n=180 from core study enrolled) 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. The ADCOMS scale ranges from a score of 0.00 to 1.97, with higher score indicating greater impairment.

** 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.