Late-Breaking AAIC Presentation Explores Potential Clinical Effects of LECANEMAB (BAN2401)

July 29, 2021

Eisai and Biogen Present Preliminary Assessment of the Clinical Effects of Lecanemab Following 18 Months of Treatment in the Open-Label Extension of the Phase 2 Proof of Concept Study at 2021 Alzheimer's Association International Conference (AAIC)

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") and Biogen Inc. (Nasdaq: BIIB, Corporate headquarters: Cambridge, Massachusetts, CEO: Michel Vounatsos, "Biogen") today announced results of a longitudinal preliminary assessment of the clinical effects of lecanemab (development code: BAN2401) — granted Breakthrough Therapy designation by the U.S. Food and Drug Administration (FDA) in June 2021 — following 18 months of treatment in the open-label extension (OLE) of the Phase 2b proof-of-concept study in subjects with early Alzheimer's disease (AD) (Mild Cognitive Impairment [MCI] due to AD and mild AD) at the Alzheimer's Association International Conference (AAIC) held in Denver, Colo., United States and virtually from July 26 to 30, 2021 (Presentation No.: 57780).

Lecanemab Study 201 and OLE
Lecanemab is an investigational humanized monoclonal antibody that preferentially binds to soluble amyloid-beta (Aβ) aggregates (protofibrils). Lecanemab reduced brain Aβ and slowed clinical decline in an 18-month Phase 2b proof of concept study (Study 201, n=856) in early AD (Alz Res Therapy 13: 2021). After analysis of the core study, there was a long off-treatment gap period of 9-59 months (period of time between the last dose of lecanemab in the core and the OLE baseline; average of 24 months). After this off-treatment gap, the OLE evaluating the 10 mg/kg IV biweekly lecanemab dosing was implemented (n=180 from core study enrolled). The clinical effect of treatment with lecanemab was assessed via the adjusted mean change of the AD Composite Score (ADCOMS), the primary clinical endpoint of the core study. The ADCOMS scale ranges from a score of 0.00 to 1.97, with higher score indicating greater impairment. Additional clinical endpoints included Clinical Dementia Rating-Sum of Boxes (CDR-SB) and AD Assessment Scale – Cognitive Subscale (ADAS-Cog).

May suggest a potential disease-modifying effect
For subjects with early AD at Study 201 OLE baseline, the dose-dependent clinical treatment effect of lecanemab administration relative to placebo during the core phase was maintained. While off-treatment during the gap in the treatment period, people who received 10 mg/kg IV in the core continued to perform better than those who received placebo on ADCOMS. While off-treatment during the gap period, subjects declined at the same rate on key clinical measures in all core treatment group. The increase in adjusted mean change between the three month follow up after the core 18-month and OLE baseline for lecanemab bi-weekly, lecanemab monthly and placebo dosing respectively were 0.11 (0.07 to 0.18), 0.10 (0.12 to 0.22) and 0.09 (0.19 to 0.28) for ADCOMS. Similar results were observed for CDR-SB and ADAS-Cog. This may suggest a potential disease-modifying effect of lecanemab.

Potential relationship between the plasma Aβ42/40 ratio, brain amyloid by PET and treatment
Low values of plasma Aβ42/40 ratio is recognized as an indicator of elevated amyloid in the brain, and was assessed in a subset of participants in Study 201.1 The plasma Aβ42/40 ratio increased during the core phase and OLE in those treated with lecanemab and decreased during the gap period, potentially demonstrating the relationship between the plasma Aβ42/40 ratio and treatment with lecanemab. The lecanemab treatment related increases in plasma Aβ42/40 ratio were inversely correlated with treatment related reduction of brain amyloid in the core and OLE (Poster No. 57760).

Assessing the long-term effect of continued treatment with lecanemab
Study participants with early AD at the OLE baseline who received placebo during the core phase and were treated for the first time with lecanemab during OLE, as well as those treated with lecanemab both during the core phase and during OLE, showed reduced clinical decline relative to natural disease progression (reference similar population from ADNI). The adjusted mean change from OLE baseline at the end of the 18-month OLE study period for core 10 mg/kg bi-weekly dosing, 10 mg/kg monthly dosing, and placebo groups respectively were 0.102, 0.165 and 0.07 for ADCOMS, all of which showed a slower rate of progression as compared to ADNI (0.214). Similar results were observed for CDR-SB and ADAS-Cog. The results support the concept of increased long-term benefit of continued treatment with lecanemab when initiated in the early AD stage.

These preliminary findings are based on limited data and are being further evaluated in the ongoing Phase 3 Clarity AD study for early AD.

"The findings from the lecanemab Phase 2b OLE study are encouraging as they supply further insights into outcomes with anti-amyloid therapies and we look forward to learning more in the Phase 3 studies, Clarity AD and AHEAD 3-45, currently underway," said Lynn Kramer, M.D., Chief Clinical Officer, Neurology Business Group, Eisai. "The unprecedented confluence of medical knowledge, data analytics, and technological advances make it an incredibly exciting time for Alzheimer's research. This combined with Eisai's precision research approach, which is a treatment paradigm based on a person's pathophysiological biomarker profile along the Alzheimer' disease continuum, makes our company uniquely positioned to research and develop new solutions for patients and their families."

Alfred Sandrock, Jr., M.D., Ph.D., Head of Research and Development at Biogen, said, "The findings from the Open-Label Extension further strengthen our belief in the potential of addressing amyloid beta pathology in Alzheimer's disease. We look forward to our ongoing collaboration with Eisai to study lecanemab and continuing to pioneer to address the high unmet need for Alzheimer's disease patients."

The enrollment of 1,795 patients with early AD in the Phase 3 Clarity AD clinical study was completed in March 2021. The study's primary endpoint is expected to be completed by the end of September 2022. The Phase 3 clinical study, AHEAD 3-45, is currently evaluating lecanemab in individuals with preclinical AD.

The presentation video and slides are available on the investors' section of the Eisai Co., Ltd. website .

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 any investigational uses of such product will successfully complete clinical development or gain health authority approval.

Biogen Safe Harbor Statement
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, relating to the potential clinical effects of lecanemab; the potential benefits, safety and efficacy of lecanemab; the results of the OLE of the Phase 2b study of lecanemab; the clinical development program, clinical trial(s) and data readouts and presentations for lecanemab; potential regulatory discussions, submissions and approvals and the timing thereof; the identification and treatment of Alzheimer's disease; the potential of Biogen's commercial business and pipeline programs, including lecanemab; the anticipated benefits and potential of Biogen's collaboration arrangements with Eisai; and risks and uncertainties associated with drug development and commercialization. These forward-looking statements may be accompanied by such words as "aim," "anticipate," "believe," "could," "estimate," "expect," "forecast," "goal," "intend," "may," "plan," "potential," "possible," "prospect," "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 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; uncertainty of success in the development and potential commercialization of lecanemab; 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; 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; the direct and indirect impacts of the ongoing COVID-19 pandemic on Biogen's business, results of operations and financial condition; and any other risks and uncertainties that are described 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.

[Notes to editors]

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 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. 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, funded by the National Institute on Aging, part of the National Institutes of Health, and Eisai.

About the Joint Development 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 and Biogen serves as the lead in the co-development of aducanumab, an anti-Aβ antibody.

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 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.

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.

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 any investigational uses of such product will successfully complete clinical development or gain health authority approval.

About Biogen
At Biogen, our mission is clear: we are pioneers in neuroscience. Biogen discovers, develops and delivers worldwide innovative therapies for people living with serious neurological and neurodegenerative 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, 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, commercializes biosimilars of advanced biologics and is focused on advancing research programs in multiple sclerosis and neuroimmunology, Alzheimer's disease and dementia, neuromuscular disorders, movement disorders, ophthalmology, neuropsychiatry, immunology, acute neurology and neuropathic pain.

We routinely post information that may be important to investors on our website at www.biogen.com. Follow us on social media – Twitter, LinkedIn, Facebook, YouTube.

References
1 Pérez-Grijalba, V., Romero, J., Pesini, P. et al. Plasma Aβ42/40 Ratio Detects Early Stages of Alzheimer's Disease and Correlates with CSF and Neuroimaging Biomarkers in the AB255 Study. J Prev Alzheimers Dis 6, 34–41 (2019). https://doi.org/10.14283/jpad.2018.41.

Contacts

Eisai Co., Ltd.
Public Relations Department
TEL: +81-(0)3-3817-5120

Investor Relations Department
TEL : +81-(0)3-3817-5121

Eisai Inc.
201-753-1945
Libby_Holman@eisai.com

Biogen Inc.
Media Contact:
Allison Parks
+1 617 679 4945
public.affairs@biogen.com

Investor Contact:
Biogen Inc.
Mike Hencke
+781 464 2442
IR@biogen.com