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EISAI INITIATES ROLLING SUBMISSION TO THE U.S. FDA FOR BIOLOGICS LICENSE APPLICATION OF LECANEMAB (BAN2401) FOR EARLY ALZHEIMER'S DISEASE UNDER THE ACCELERATED APPROVAL PATHWAY

LECANEMAB IS AN ANTI-AMYLOID BETA (Aβ) PROTOFIBRIL ANTIBODY

TOKYO and CAMBRIDGE, Mass, Sep. 28, 2021 (GLOBE NEWSWIRE) - Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") and Biogen Inc. (Nasdaq: BIIB, Corporate headquarters: Cambridge, Massachusetts, CEO: Michel Vounatsos, "Biogen") today announced that Eisai has initiated a rolling submission to the U.S. Food and Drug Administration (FDA) of a Biologics License Application (BLA) for lecanemab (BAN2401), the company's investigational anti-amyloid beta (Aβ) protofibril antibody, for the treatment of early Alzheimer's disease (early AD). The BLA is being submitted under the accelerated approval pathway and is primarily based on clinical, biomarker and safety data from the Phase 2b clinical trial (Study 201) in people with early AD and confirmed amyloid pathology. The lecanemab Phase 2b trial results demonstrated a high degree of Aβ plaque lowering and consistent reduction of clinical decline across several clinical endpoints. The correlation between the extent of Aβ plaque reduction and effect on clinical endpoints in Study 201 further supports Aβ as a surrogate endpoint that is reasonably likely to predict clinical benefit. AD is a serious, progressive and devastating disease with few treatment options. Eisai is utilizing the accelerated approval pathway after discussion with the FDA and aims to bring a new treatment option to people living with early AD, their families and healthcare professionals.

In June, 2021, lecanemab was granted Breakthrough Therapy designation, which is an FDA program intended to expedite the development and review of medicines for serious or life threatening conditions. Eisai has an agreement with the FDA to submit the BLA for lecanemab as a rolling submission. This agreement allows completed portions of the application to be submitted to the FDA for review on an ongoing basis. After all portions are submitted to the FDA and the agency accepts the BLA, the Prescription Drug User Fee Act (PDUFA) action date (target date for completion of examination) will be set.

The BLA submission for lecanemab is primarily based on the results of the proof-of-concept Study 201 in 856 patients with mild cognitive impairment (MCI) due to AD and mild AD (collectively known as early AD) with confirmed presence of amyloid pathology. The results were published in a peer-reviewed journal in April 2021.[1] Study 201 explored the impact of treatment with lecanemab on reducing brain Aβ and clinical decline. At 18 months of treatment, 10 mg/kg biweekly lecanemab reduced brain amyloid by 0.306 SUVr units (from a baseline mean of 1.37), and over 80% of subjects became amyloid negative by visual read. Furthermore, the extent of reduction in amyloid was correlated with slower clinical decline on ADCOMS (Alzheimer's Disease Composite Score), CDR-SB (Clinical Dementia Rating-Sum-of-Boxes), and ADAS-cog (Alzheimer Disease Assessment Scale-Cognitive Subscale) at the treatment group and patient level. The rate of amyloid-related imaging abnormalities-edema/effusion (ARIA-E), an adverse event associated with amyloid targeted therapies, for the 10 mg/kg biweekly dosing was 9.9%.

After completion of the Core period and a Gap period off treatment (average of 24 months), all 180 patients in the Study 201 open-label extension study received 10 mg/kg biweekly lecanemab dosing. The data confirmed lecanemab produces reductions of amyloid PET SUVr, with significant reduction occurring as early as 3 months, and >80% of subjects achieved amyloid negative status by visual read in as early as 12 months [link]. Significant amyloid reduction relative to placebo in those exposed to lecanemab in the Core period was maintained while off-treatment over the Gap period. The rate of ARIA-E was consistent with the Core study at around 10%.

The lecanemab Clarity AD Phase 3 clinical trial in early AD is ongoing and completed enrollment in March 2021 with 1,795 patients. The U.S. FDA has agreed that the results of Clarity AD, when completed, can serve as the confirmatory study to verify the clinical benefit of lecanemab. Blinded safety data from Clarity AD will be included to support the BLA.

“With the worldwide population growing and aging, the number of people living with AD is on the rise. AD imposes an enormous burden on not only people living with AD and their families but also for society. We recognize the strong and urgent expectations from stakeholders to further advance a treatment system for this disease. For many years, Eisai has endeavored to understand the anxieties of people living with AD and has been conducting research and development of novel therapies,” said Haruo Naito, Chief Executive Officer at Eisai Co., Ltd. “The lecanemab rolling BLA submission marks a new milestone toward the advancement of a treatment system for AD. As part of our *human health care* mission, we are committed to bringing new medicines to people living with AD and their families as early as possible.”

“The Alzheimer’s community welcomes scientific innovation that creates more treatment options for people living with this terrible neurodegenerative disease,” said Jeffrey Cummings, M.D., ScD, lecanemab manuscript author and director at the Chambers-Grundy Center for Transformative Neuroscience, University of Nevada Las Vegas. “Based on the efficacy and safety results of the Phase 2b study and preliminary results from the open-label extension study, I am optimistic about the potential lecanemab may have as a treatment choice for patients with early Alzheimer’s to ameliorate the otherwise inevitable decline they face.”

“It is our vision that patients and their families have choice and access to multiple treatment options for Alzheimer’s disease. The rolling submission of lecanemab for FDA review under the accelerated pathway is a positive step toward that goal,” said Michel Vounatsos, Chief Executive Officer at Biogen. “We believe that treatments directed at amyloid beta reduction in the brain have the potential to transform diagnosis and treatment of Alzheimer’s disease. We look forward to continuing to work with Eisai to pioneer science, advance knowledge, and serve the needs of Alzheimer’s patients.”

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[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 (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, and Eisai.

* 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

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.

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.

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.

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.

Reference

1: *Alzheimer's Research & Therap*y volume 13, Article number: 80 (2021)
https://alzres.biomedcentral.com/articles/10.1186/s13195-021-00813-8

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.