



## Adaptive Phase II Study of BAN2401 in Early Alzheimer's Disease Continues toward 18-Month Endpoint

December 21, 2017

*Criteria for Success at 12-Month Analysis of ADCOMS Not Met*

*Study to Remain Blinded Per Protocol until Final Readout of Comprehensive 18-Month Data*

CAMBRIDGE, Mass. & TOKYO--([BUSINESS WIRE](#))--Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") and Biogen Inc. (NASDAQ: BIIB) (Headquarters: Cambridge, Massachusetts, United States, CEO: Michel Vounatsos, "Biogen") announced today that an Independent Data Monitoring Committee has determined that BAN2401, an anti-amyloid beta protofibril antibody, did not meet the criteria for success based on a Bayesian analysis at 12 months as the primary endpoint in an 856-patient Phase II clinical study (Study 201). Following the predefined study protocol, the blinded study will continue and a comprehensive final analysis will be conducted at 18 months seeking to demonstrate clinically significant results. The results of the final analysis are expected to be obtained during the second half of 2018.

Study 201 (ClinicalTrials.gov identifier NCT01767311) is a placebo-controlled, double-blind, parallel-group, randomized study in patients with prodromal or mild Alzheimer's disease (collectively known as early Alzheimer's disease) and with positive biomarkers for brain amyloid pathology. The study design included 16 interim analyses that assessed potential for futility or stopping for safety. Neither of these conditions was met and the study continues to a full analysis at 18 months. The efficacy of five dose groups of BAN2401 was evaluated at 12 months based on Eisai's in-house developed novel endpoint Alzheimer's disease Composite Score (ADCOMS). According to the Bayesian analysis at 12 months, success was judged as an 80% or higher probability of achieving a Clinically Significant Difference (CSD: a 25% or greater reduction in the rate of decline in ADCOMS compared to placebo).

In the final analysis at 18 months, a comprehensive evaluation which includes assessing changes from baseline in the clinical evaluation indicators ADCOMS and Clinical Dementia Rating Sum of Boxes (CDR-SB), as well as changes in biomarkers such as brain amyloid levels as measured by amyloid PET and total hippocampal volume using vMRI, will be assessed.

"By using Bayesian statistics in this uniquely-designed trial we had hoped that it would enable us to demonstrate clinical success faster than more traditional study designs. We now await the final study analysis which will be conducted after 18 months of treatment, which represents an amount of treatment time that is considered as appropriate for assessing efficacy in disease modifying agents for Alzheimer's disease," said Lynn Kramer, MD, Chief Clinical Officer and Chief Medical Officer, Neurology Business Group, Eisai.

BAN2401 is a humanized monoclonal antibody for Alzheimer's disease that is the result of a strategic research alliance between Eisai and BioArctic AB (Headquarters: Stockholm, Sweden, CEO: Gunilla Osswald, "BioArctic"). Since March 2014, Eisai and Biogen have been jointly developing BAN2401.

Eisai and Biogen have a wide reaching collaboration to develop and commercialize Alzheimer's disease treatments.

### Biogen Safe Harbor Statement

This press release contains forward-looking statements, including statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 about results from the Phase 2 study of BAN2401, the potential clinical effects of BAN2401, risks and uncertainties associated with drug development and commercialization, the potential benefits, safety and efficacy of BAN2401, the timing and status of current and future regulatory filings, the anticipated benefits and potential of Biogen's collaboration arrangements with Eisai and the potential of Biogen's commercial business and pipeline programs, including BAN2401, elenbecestat and aducanumab. These forward-looking statements may be accompanied by words such as "aim," "anticipate," "believe," "could," "estimate," "expect," "forecast," "intend," "may," "plan," "potential," "possible," "will" 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 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; 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 BAN2401, elenbecestat and/or aducanumab; the occurrence of adverse safety events; risks of unexpected costs or delays; uncertainty of success in the development and potential commercialization of BAN2401, elenbecestat and/or aducanumab, which may be impacted by, among other things, failure to protect and enforce Biogen's data, intellectual property and other proprietary rights and uncertainties relating to intellectual property claims and challenges; uncertainty as to whether the anticipated benefits and potential of Biogen's collaboration arrangement with Eisai can be achieved; and third party collaboration risks. 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 Securities and Exchange Commission. These statements are based on Biogen's current beliefs and expectations and speak only as of the date of this press 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>

#### 1. About BAN2401

BAN2401 is a humanized monoclonal antibody for Alzheimer's disease that is the result of a strategic research alliance between Eisai and BioArctic. BAN2401 selectively binds to neutralize and eliminate soluble, toxic A $\beta$  aggregates that are thought to contribute to the neurodegenerative process in Alzheimer's disease. As such, BAN2401 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 BAN2401 for the treatment of Alzheimer's disease 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 BAN2401 and the parties amended that agreement in October 2017.

## 2. About Study 201 (ClinicalTrials.gov identifier NCT01767311)

Study 201 is a placebo-controlled, double-blind, parallel-group study to evaluate safety, tolerability and efficacy of BAN2401 in patients with prodromal or mild Alzheimer's disease (collectively known as early Alzheimer's disease) and with positive biomarkers for brain amyloid pathology, using Bayesian Adaptive Randomization Design which allows for automatic changes to the design during the study, including adaptively changing the subject allocation ratio to treatment arms with higher probabilities based on the results of interim analyses in order to more efficiently identify the effectiveness and optimal dose regimen of BAN2401. The study will explore efficacy and the dose response of BAN2401 with 16 interim analyses for early success, a 12-month evaluation based on ADCOMS and an 18-month comprehensive assessment of treatment with placebo or 5 active arms. The 5 treatment arms consist of 3 dose levels (2.5 mg/kg, 5 mg/kg, 10mg/kg) given biweekly and 2 dose levels (5 mg/kg, 10 mg/kg) given monthly.

After 12 months of treatment, change from baseline in the ADCOMS is evaluated. In the final analysis at 18 months, comprehensive evaluation including changes from baseline in ADCOMS and Clinical Dementia Rating Sum of Boxes (CDR-SB), as well as changes in brain amyloid levels as measured by amyloid PET and in total hippocampal volume using vMRI, will be conducted.

## 3. About the Joint Development Agreement between Eisai and Biogen for Alzheimer's Disease

Eisai and Biogen are widely collaborating on the joint development and commercialization of Alzheimer's disease treatments. Eisai serves as the lead in the co-development of elenbecestat\*, a BACE inhibitor, and BAN2401, an anti-amyloid beta (A $\beta$ ) protofibril antibody, while Biogen serves as the lead for co-development of aducanumab, Biogen's investigational anti-amyloid beta (A $\beta$ ) antibody for patients with Alzheimer's disease, and the companies plan to pursue marketing authorizations for the three compounds worldwide. If approved, the companies will also co-promote the products in major markets, such as the United States, the European Union and Japan.

As to BAN2401 and elenbecestat, both companies will equally split overall costs, including research and development expenses. Eisai will book all sales for elenbecestat and BAN2401 following marketing approval and launch, and profits will be equally shared between the companies.

Under a new agreement between the parties that was effective October 22, 2017, Biogen will remain solely responsible for all development costs for aducanumab until April 2018, and Eisai will reimburse Biogen for 15 percent of expenses from April 2018 through December 2018, and 45 percent from January 2019 onwards. Regarding the respective share of profits from potential sales of aducanumab following commercialization, Biogen will receive 55 percent of the potential profits in the United States and 68.5 percent of the potential profits in Europe while Eisai will receive 80 percent of the potential profits in Japan and Asia (excluding China and South Korea). The companies will have a 50:50 co-promotion split of potential profits in the rest of the world. Furthermore, Biogen will book sales in the United States, Europe, and rest of world markets while Eisai will book sales in Japan and Asia (excluding China and South Korea).

\* The generic name is not yet fixed at this time.

## 4. About Eisai Co., Ltd.

Eisai Co., Ltd. is a leading global research and development-based pharmaceutical company headquartered in Japan. We define our corporate mission as "giving first thought to patients and their families and to increasing the benefits health care provides," which we call our *human health care (hhc)* philosophy. With approximately 10,000 employees working across our global network of R&D facilities, manufacturing sites and marketing subsidiaries, we strive to realize our *hhc* philosophy by delivering innovative products to address 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 Aricept<sup>®</sup>, a treatment for Alzheimer's disease and dementia with Lewy bodies, Eisai has been working to establish a social environment that involves patients in each community in cooperation with various stakeholders including the government, healthcare professionals and care workers, and is estimated to have held over ten thousand dementia awareness events worldwide. As a pioneer in the field of dementia treatment, Eisai is striving to not only develop next generation treatments but also to develop diagnosis methods and provide solutions.

For more information about Eisai Co., Ltd., please visit [www.eisai.com](http://www.eisai.com).

## 5. 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. Founded in 1978 as one of the world's first global biotechnology companies by Charles Weissman, 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 and only approved treatment for spinal muscular atrophy; and is focused on advancing neuroscience research programs in Alzheimer's disease and dementia, neuroimmunology, movement disorders, neuromuscular disorders, pain, ophthalmology, neuropsychiatry, and acute neurology. Biogen also manufactures and commercializes biosimilars of advanced biologics.

We routinely post information that may be important to investors on our website at [www.biogen.com](http://www.biogen.com). To learn more, please visit [www.biogen.com](http://www.biogen.com) and follow us on social media – Twitter, LinkedIn, Facebook, Youtube.

## 6. About BioArctic AB

BioArctic AB is a Swedish research based biopharma company focusing on disease modifying treatments and reliable biomarkers and diagnostics for neurodegenerative diseases, such as Alzheimer's disease and Parkinson's disease. The company also develops a potential treatment for Complete Spinal Cord Injury. BioArctic focuses on innovative treatments in areas with high unmet medical needs. Collaborations with universities are of great importance to the company together with our strategically important global partners in the Alzheimer (Eisai) and Parkinson (AbbVie) projects. The project portfolio is a combination of fully funded projects run in partnership with global pharmaceutical companies and innovative in-house projects with significant market- and out-licensing potential. [www.bioarctic.com](http://www.bioarctic.com)

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