



**FOR IMMEDIATE RELEASE**

June 5, 2018

Eisai Co., Ltd.

Biogen Inc.

**PHASE II CLINICAL STUDY OF ELENBECESTAT DEMONSTRATES SAFETY AND TOLERABILITY IN MCI AND MILD TO MODERATE ALZHEIMER'S DISEASE AT 18-MONTHS**

*RESULTS OF THE PHASE II STUDY DEMONSTRATED A STATISTICALLY SIGNIFICANT DIFFERENCE IN AMYLOID BETA IN BRAIN*

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 elenbecestat was generally safe and well tolerated in a Phase II clinical study (Study 202) of the oral BACE (beta amyloid cleaving enzyme) inhibitor elenbecestat (development code: E2609) conducted in the United States, and the results demonstrated a statistically significant difference in amyloid beta (A $\beta$ ) levels in the brain measured by amyloid-PET (positron emission tomography). A numerical slowing of decline in functional clinical scales of a potentially clinically important difference was also observed, although this effect was not statistically significant. This study, a Phase II study of 70 patients, is the first study of a BACE inhibitor to show a statistically significant difference in amyloid beta in the brain while also suggesting a delay of clinical symptom decline in exploratory endpoints.

Study 202 (ClinicalTrials.gov identifier NCT02322021) is a multicenter, randomized, double-blind, placebo-controlled parallel-group 18-month Phase II clinical study in patients with mild cognitive impairment (MCI) due to Alzheimer's disease, or mild to moderate dementia due to Alzheimer's disease with confirmed amyloid pathology by PET screening. Seventy patients were randomized to four treatment arms receiving elenbecestat (5, 15, or 50 mg) or placebo daily. During the study period, more than half the patients in the elenbecestat 5 mg and 15 mg arms were switched to the 50 mg arm for three months or more. The 50 mg treatment arm plus the group switched to the 50 mg arm are hereafter referred to as "50 mg total arm" (38 subjects) with a mean duration of approximately 11 months on 50 mg per day.

Elenbecestat demonstrated acceptable safety and tolerability profile through 18 months of study drug administration. In the elenbecestat 50 mg total arm, the six most common adverse events observed were contact dermatitis, upper respiratory infection, headache, diarrhea, fall, and dermatitis. No serious adverse reactions suggestive of hepatic toxicity were observed in this study.

In addition to the safety objectives, the study assessed A $\beta$  in the brain at 18 months as measured by amyloid PET as well as efficacy in terms of clinical symptoms, which were exploratory objectives in this study.

The elenbecestat 50 mg total arm demonstrated a statistically significant difference in A $\beta$  levels in the brain as measured by amyloid PET compared with placebo (35 subjects participated in this longitudinal amyloid

PET assessment). This is the first time in which a significant effect in A $\beta$  in the brain using a BACE inhibitor was confirmed in a clinical study of patients with mild cognitive impairment (MCI) through moderate Alzheimer's dementia.

CDR-SB (Clinical Dementia Rating Sum of Boxes) was an exploratory endpoint to assess efficacy in terms of clinical symptoms. The study showed numerically less decline in CDR-SB for the elenbecestat 50 mg total arm as compared to placebo of a potentially clinically important difference (41 subjects participated in this assessment), which was not statistically significant. Further, a similar magnitude and direction of differential in decline was observed in a *post-hoc* analysis of ADCOMS, Eisai's newly developed assessment scale (Alzheimer's Disease Composite Score) in the elenbecestat 50 mg total arm as compared to placebo. The study was not powered to show statistical significance compared to placebo on clinical symptoms.

Eisai plans to present detailed results of the study at a future medical meeting.

Elenbecestat, discovered by Eisai, has been jointly developed by Eisai and Biogen since March 2014. The two companies are currently conducting two global Phase III clinical studies (MISSION AD1/2) in early Alzheimer's disease.

"It is highly encouraging that Study 202 confirmed elenbecestat's treatment effect in reducing amyloid in the brain and suggested a slowing of clinical decline. Eisai and Biogen will continue to work together to advance the ongoing Phase III program (MISSION AD) in order to contribute a new potential treatment option to Alzheimer's disease patients as soon as possible," said Lynn Kramer, MD, Chief Clinical Officer and Chief Medical Officer, Neurology Business Group, Eisai.

"Biogen is heartened by the safety and tolerability results of this study of elenbecestat," said Alfred Sandrock, M.D., Ph.D., executive vice president and chief medical officer at Biogen. "We remain committed to research in Alzheimer's, an area of significant unmet need with a devastating impact on those living with the disease, their families, friends, and society."

### **Biogen Safe Harbor**

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, including statements about results from the Phase II study of elenbecestat, the potential effects of elenbecestat, Biogen's strategy and plans, and the potential of Biogen's commercial business and pipeline programs. These forward-looking statements may be accompanied by words such as "aim," "anticipate," "believe," "could," "estimate," "except," "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 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: the risk that we may not fully enroll our clinical trials or enrollment will take longer than expected, unexpected concerns may arise from additional data, analysis,

or results obtained during our 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, the occurrence of adverse safety events, we may encounter other unexpected hurdles, which may be impacted by, among other things, the occurrence of adverse safety events, failure to obtain regulatory approvals in certain jurisdictions, or failure to protect intellectual property and other proprietary rights, or uncertainty of success in the development and potential commercialization of elenbecestat. The foregoing sets forth many, but not all, of the factors that could cause actual results to differ from our 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 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.

Media Inquiries	
Eisai Co., Ltd. Public Relations Department TEL: +81-(0)3-3817-5120	Biogen Inc. Public Affairs TEL: +1-617-679-4945

## <Notes to editors>

### 1. About Elenbecestat (generic name, development code: E2609)

Elenbecestat is an oral BACE (beta amyloid cleaving enzyme) inhibitor currently being investigated in Phase III clinical studies for Alzheimer's disease discovered by Eisai. By inhibiting BACE, a key enzyme in the production of A $\beta$  peptides, elenbecestat reduces A $\beta$  production, which is thought to lead to a reduction in amyloid plaque formations caused by the aggregation of toxic oligomers and protofibrils in the brain. Currently, two global Phase III clinical studies (MISSION AD1/2) of elenbecestat in early Alzheimer's disease including mild cognitive impairment (MCI) due to AD/Prodromal AD and the early stages of mild AD are underway. In addition, the U.S. Food and Drug Administration (FDA) has granted Fast Track designation for the development of elenbecestat, a process allowing priority reviews by the FDA for drugs deemed as having potential to treat serious conditions and tackle key unmet medical needs.

### 2. About Study 202 (ClinicalTrials.gov identifier NCT02322021)

Study 202 is a placebo-controlled, double-blind, parallel-group, randomized, dose-finding study to evaluate the safety and tolerability of elenbecestat in 70 patients with mild cognitive impairment due to Alzheimer's disease (prodromal Alzheimer's disease) and mild to moderate dementia due to Alzheimer's disease. The study enrolled patients which met the core clinical research criteria of the U.S. National Institute on Aging – Alzheimer's Association for MCI due to AD or AD dementia, with an MMSE score of 16 or higher and confirmed accumulation of A $\beta$  by PET screening. Patients were allocated to a total of four treatment arms, three for elenbecestat (5 mg/day: 17 patients, 15 mg/day: 19 patients, 50 mg/day: 17 patients) and one for placebo (17 patients). More than half the patients in the elenbecestat 5 mg and 15 mg treatment arms had their dose increased to 50 mg/day during the 18 month treatment period. Mean duration of 50 mg total arm on 50 mg/day was 11 months. The primary objectives are safety and tolerability at 18 months. Major exploratory endpoints are the change in accumulation of A $\beta$  as measured by amyloid PET (35 patients) and the change in dementia assessment scales including CDR-SB and ADCOMS (41 patients), at 18 months compared to baseline.

### 3. Glossary of Terms

- 1) NIA-AA: A guideline (NIA-AA) for modernization of the diagnosis of Alzheimer's disease published by The National Institute on Aging (NIA) at National Institutes of Health (NIH) and the Alzheimer's Association.
- 2) MMSE (Mini-Mental State Examination): A method for assessing cognitive function. Comprised of the categories orientation, memorization, attention, calculation, recent and distant memory, comprehension, reading and writing, as well as design. Test scores range from 30 (normal) to 0 (severely impaired).
- 3) CDR-SB (Clinical Dementia Rating scale Sum of Boxes): The Clinical Dementia Rating (CDR) is a numeric scale used to quantify the severity of symptoms of dementia. A qualified health professional assesses a patient's cognitive and functional performance in six areas: memory, orientation, judgment & problem solving, community affairs, home & hobbies, and personal care. The total score of the six areas is the score of CDR-SB, and it is an appropriate item for evaluating the effectiveness of therapeutic drugs targeting early stage AD.
- 4) ADCOMS (AD Composite Score): ADCOMS, developed by Eisai, combines items from the ADAS-Cog scale for assessing cognitive functions, MMSE and the CDR scale for evaluating the severity of dementia to enable highly-sensitive detection of changes in clinical functions of early AD symptoms and changes in memory.

### 4. 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.

## **5. 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).

## **6. 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. 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, and today 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](#).