Eisai and Biogen Present Detailed Results From Phase II Clinical Study of Elenbecestat in MCI and Mild to Moderate Alzheimer's Disease at Alzheimer's Association International Conference (AAIC) 2018

July 25, 2018

TOKYO and CAMBRIDGE, Mass., July 25, 2018 (GLOBE NEWSWIRE) -- Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") and Biogen Inc. (Nasdaq:BIIB) (Headquarters: Cambridge, Massachusetts, United States, CEO: Michel Vounatsos, "Biogen") announced detailed results from a Phase II clinical study (Study 202) of the investigational oral BACE (beta amyloid cleaving enzyme) inhibitor elenbecestat (development code: E2609) at the Alzheimer's Association International Conference (AAIC) 2018 being held in Chicago, Illinois, United States, from July 22 to 26, 2018. This poster presentation was accepted as a Late Breaking Abstract for AAIC (Poster No.: P4-389).

Study 202 (ClinicalTrials.gov identifier NCT02322021) is a multicenter, randomized, double-blind, placebo-controlled parallel-group 18-month Phase II clinical study, conducted in the United States in patients with mild cognitive impairment (MCI) due to Alzheimer's disease, or mild to moderate dementia due to Alzheimer's disease (AD) with confirmed amyloid pathology by positron emission tomography (PET). 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. These patients received elenbecestat 50 mg for three months or longer. Analysis was carried out on the combination of patients in the initial 50 mg treatment arm plus the patients switched to the 50 mg arm, referred to collectively as the "50 mg total group arm" (38 patients). In addition to the primary safety objective, the study assessed amyloid pathology 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 primary objective of the study was to assess the safety and tolerability of elenbecestat after 18 months of treatment. The incidence of treatment-emergent adverse events was similar between elenbecestat and placebo, and no dose-dependent response was observed for adverse events. The six most common adverse events reported were upper respiratory tract infection, abnormal dreams and nightmares, contact dermatitis, headache, diarrhea, and falls. No adverse reactions suggestive of hepatic toxicity were observed in this study.

Regarding the accumulation of amyloid in the brain at 18 months as measured by PET via quantitative evaluation of Standard Uptake Value Ratio (SUVr) using the florbetaben PET tracer (n=28), a statistically significant reduction of brain amyloid load as compared to placebo was observed in the 50 mg total group arm with a reduction in SUVr of 0.104 (p=0.011). Although a small sample size, using the florbetapir PET tracer (n=7) demonstrated a statistically significant decrease in brain amyloid load compared to placebo for the 50 mg total group arm (reduction in SUVr of 0.227) at 18 months (p=0.024).

Clinical efficacy was evaluated using the Clinical Dementia Rating Sum of Boxes (CDR-SB) rating scale. After 18 months of treatment, clinical assessment using CDR-SB demonstrated a mean treatment difference of -0.5 based off of an increase of 1.1 for the elenbecestat 50 mg total group arm (29 patients) versus an increase of 1.6 for the placebo group (12 patients). This represented a 31% slowing in rate of decline for the elenbecestat arm which is potentially considered to be clinically important.

Furthermore, based on information obtained from analyses of changes in CDR-SB and amyloid PET SUVr values from ADNI data, in a sub-population analysis of patients with baseline SUVr range between 1.4 and 1.9 who were identified in this study as being expected to have a higher rate of disease progression, there was 72% less decline in CDR-SB for patients in the 50 mg total group arm (n=10) versus placebo (n=5). While the study was not powered to show statistical significance compared to placebo on clinical symptoms, the results suggest that elenbecestat could slow decline in cognitive function of patients with MCI due to Alzheimer's disease, or mild to moderate dementia due to Alzheimer's disease.

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.

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 agent will successfully complete clinical development or gain health authority approval.

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 clinical effects of elenbecestat; the potential benefits, safety, and efficacy of elenbecestat; the clinical development program for elenbecestat; risks and uncertainties associated with drug development and commercialization; the treatment of Alzheimer's disease; Biogen's strategy and plans; the anticipated benefits and potential of Biogen's collaboration arrangements with Eisai; and the potential of Biogen's commercial business and pipeline programs, including elenbecestat, BAN2401, and aducanumab. 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 clinical trials may not fully enroll or enrollment will take longer than expected; unexpected concerns 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 elenbecestat, BAN2401, and/or aducanumab; the occurrence of adverse safety events; Biogen may encounter other unexpected hurdles; uncertainty of success in the development and potential commercialization of elenbecestat, BAN2401, and/or aducanumab, which may be impacted by, among other things, unexpected concerns that may arise from additional data or analysis, the occurrence of adverse safety events, failure to obtain regulatory approvals in certain jurisdictions, 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; product liability claims; 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 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.

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<Notes to editors>

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

Elenbecestat is an oral BACE (beta amyloid cleaving enzyme) inhibitor discovered by Eisai currently being investigated in Phase III clinical studies for Alzheimer's disease. By inhibiting BACE, a key enzyme in the production of Aβ peptides, elenbecestat reduces Aβ 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 designed to facilitate the development, and expedite the review of drugs to treat serious conditions and fill an unmet medical need.

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 Aβ 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 group arm on 50 mg/day was 11 months. The primary objectives are safety and tolerability after 18 months. Major exploratory endpoints are the change in accumulation of Aβ 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) SUVr (Standard Uptake Value Ratio): SUVr calculates the ratio of strength of accumulation of PET tracer in a region of interest in the brain to an area of the brain (reference region) which shows low and stable accumulation of PET tracer. These SUVr values can be used to quantitatively compare and evaluate the accumulation of amyloid.

2) 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. 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 (Aβ) protofibril antibody, while Biogen serves as the lead for co-development of aducanumab, Biogen's investigational anti-amyloid beta (Aβ) 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®, 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.

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.

Biogen 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.