Biogen and Eisai Announce Presentation of Detailed Analyses from the Phase 1b Long-Term Extension Study of Aducanumab at Clinical Trials on Alzheimer's Disease (CTAD)

Three- and four-year data continued to show reduction in amyloid plaque and to suggest a slowing of the rate of clinical decline in patients

October 29, 2018 – Biogen (Nasdaq: BIIB) and Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") announced that Biogen presented results at the Clinical Trials on Alzheimer's Disease (CTAD) meeting, in Barcelona, Spain, from the recent 36- and 48-month analyses of the ongoing long-term extension (LTE) of the Phase 1b study of aducanumab, an investigational treatment for mild cognitive impairment (MCI) due to Alzheimer's disease (AD) and mild AD.

A late-breaking oral presentation and a poster included data from patients treated with aducanumab for up to 36 and 48 months. Data from both analyses showed a reduction in amyloid plaque levels in a dose- and time-dependent manner, as measured by positron emission tomography (PET). In addition, analyses of exploratory clinical endpoints, Clinical Dementia Rating Sum of Boxes (CDR-SB) and the Mini-Mental State Examination (MMSE), suggested a continued slowing of clinical decline over 36 months and 48 months. The results in each dosing arm were generally consistent with previously reported analyses of this study, and there were no changes to the risk-benefit profile of aducanumab.

"This Phase 1b study now has four years of aducanumab results, and we are encouraged by these data, which continued to show a reduction in amyloid plaque levels and suggest our investigational therapy may slow clinical progression of the disease," said Alfred Sandrock, Jr., M.D., Ph.D., executive vice president and chief medical officer at Biogen. "The Phase 3 studies are now fully enrolled, and we remain driven by the profound unmet needs of patients, families, caregivers and society."

About the Phase 1b Study

The Phase 1b study is a randomized, double-blind, placebo-controlled, multiple-dose study evaluating the safety, tolerability, pharmacokinetics (PK), pharmacodynamics (PD) and clinical effects of aducanumab in patients with prodromal AD or mild AD dementia. The primary endpoint for the study was safety. Other endpoints (amyloid reduction, CDR-SB and MMSE) were exploratory.

The study included fixed dosing at 1, 3, 6 and 10 mg/kg as well as an arm with a titration regimen up to 10 mg/kg in a cohort of ApoE ε4 carriers only.

In the Phase 1b study, 196 patients received aducanumab or placebo, of which 143 entered the LTE. All patients who continued in the LTE were switched to, or continued on, aducanumab treatment. The LTE cohorts were allocated across six dosing arms including: placebo switchers (n=37), 1 mg/kg switchers to 3 mg/kg (n=19), fixed doses (3 mg/kg [n=26], 6 mg/kg [n=24], 10 mg/kg [n=19]) and titration (n=18). There were discontinuations, as expected in studies of 36 or more months. As a result, there are smaller patient numbers in the LTE over time.

Of the 185 patients dosed with aducanumab in the Phase 1b study, 46 patients experienced amyloid-related imaging abnormalities (ARIA)-E (edema). Eight patients experienced more than one episode of ARIA-E. The majority of ARIA events occurred early in the course of treatment; they were typically mild radiographically, clinically asymptomatic and resolved or stabilized within 4-12 weeks, with most

patients continuing treatment. In the Phase 1b study, the most commonly reported adverse events were headache, fall and ARIA. There were no new incident cases of ARIA-E since the last interim analysis.

36-Month Data

Amyloid plaque levels were measured by PET using the standardized uptake value ratio (SUVR), and continued to decline in those who remained on treatment for 36 months. Amyloid plaque levels in the 10 mg/kg fixed dose at 36 months remained at a level considered below the quantitative cut-point that discriminates between a positive and negative scan.

The exploratory endpoints, CDR-SB and the MMSE, measure cognitive and functional decline associated with AD. The results of these assessments suggest a continued slowing of clinical decline during the third year of treatment with aducanumab in certain groups. Clinical effects with titrated aducanumab in the second year of the LTE were generally consistent with findings in the 10 mg/kg fixed-dose cohorts.

The expected average dose for the titration cohort at 36 months was 8.4 mg/kg.

At 36 months, a reduction of amyloid plaque (versus placebo) was observed in all fixed-dose and titration arms in a dose- and time-dependent manner. The changes in amyloid plaque, CDR-SB and MMSE are detailed below.

At 36 months from the start of the Phase 1b study:	Adjusted Mean Change from Baseline in Amyloid PET SUVR*	Adjusted Mean Change from Baseline in CDR-SB	Adjusted Mean Change from Baseline in MMSE
Placebo switchers to aducanumab	-0.248	4.83	-6.75
Switchers from 1 to 3 mg/kg	-0.198	6.21	-6.24
3 mg/kg treatment group	-0.241	3.86	-4.98
6 mg/kg treatment group	-0.278	4.50	-9.07
10 mg/kg treatment group	-0.301	2.87	-4.23
Titration treatment group	-0.308	3.10	-4.28

* Parameter: Amyloid PET composite ROI SUVR measure (Reference Region = cerebellum)

48-Month Data

In patients treated up to 48 months, amyloid plaque continued to decrease in a dose- and time-dependent manner. Amyloid plaque levels in the 10 mg/kg fixed-dose at 48 months remained at a level considered below the quantitative cut-point that discriminates between a positive and negative scan. The changes in amyloid plaque, CDR-SB and MMSE are detailed below.

At 48 months from the start of the Phase 1b study:	Adjusted Mean Change from Baseline in Amyloid PET SUVR*	Adjusted Mean Change from Baseline in CDR-SB	Adjusted Mean Change from Baseline in MMSE
Placebo switchers to aducanumab	-0.260	6.95	-10.24
Switchers from 1 to 3 mg/kg	-0.232	8.44	-9.49
3 mg/kg treatment group	-0.261	5.57	-8.22
6 mg/kg treatment group	-0.324	7.75	-12.62
10 mg/kg treatment group	-0.340	3.87	-4.82

* Parameter: Amyloid PET composite ROI SUVR measure (Reference Region = cerebellum)

Phase 3 Studies

In July 2018, enrollment was completed for the Phase 3 aducanumab ENGAGE and EMERGE studies, designed to evaluate the efficacy and safety of aducanumab in slowing cognitive and functional impairment in people with early Alzheimer's disease.

About Aducanumab

Aducanumab (BIIB037) is an investigational compound being studied for the treatment of early Alzheimer's disease. Biogen licensed aducanumab from Neurimmune under a collaboration and license agreement. Aducanumab is a human monoclonal antibody (mAb) derived from a de-identified library of B cells collected from healthy elderly subjects with no signs of cognitive impairment or cognitively impaired elderly subjects with unusually slow cognitive decline using Neurimmune's technology platform called Reverse Translational Medicine (RTM). As of October 2017, Biogen and Eisai Co., Ltd. are collaborating on the development and commercialization of aducanumab globally.

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, multiple sclerosis and 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. To learn more, please visit www.biogen.com and follow us on social media – Twitter, LinkedIn, Facebook, YouTube.

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 https://www.eisai.com.

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 about additional results from the Phase 1b study of aducanumab; the potential clinical effects of aducanumab; the potential benefits, safety and efficacy of aducanumab; the treatment of AD; and risks and uncertainties associated with drug development and commercialization. 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 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; 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 aducanumab; the occurrence of adverse safety events; risks of unexpected costs or delays; the risks of other unexpected hurdles; uncertainty of success in the development and potential commercialization of aducanumab; 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; 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.

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