Biogen Presents New Data from Long-Term Extension of Phase 1b Study of Investigational Alzheimer's Disease Treatment Aducanumab

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- *Two-year data from Phase 1b study suggest a continued benefit on amyloid plaque reduction and the rate of clinical decline in the titration regimen group, which received a gradually increased aducanumab dose*
- *The results at two years in the titration regimen group were consistent with the dose- and time-dependent results observed in the treatment groups that received a fixed-dose of 3, 6 or 10 mg/kg aducanumab during the same time period*
- *Results from treatment groups that received a fixed-dose of 3, 6 or 10 mg/kg aducanumab for up to three years were consistent with previously reported analyses from the Phase 1b study and support the design of the ongoing Phase 3 studies of aducanumab for early Alzheimer's disease*

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Biogen (NASDAQ: BIIB) will present new data from the long-term extension (LTE) of its ongoing Phase 1b study of aducanumab, the company's investigational treatment for Alzheimer's disease, at the Clinical Trials on Alzheimer's Disease (CTAD) meeting, Boston, November 1 – 4.

The data include results from patients in the Phase 1b study who were treated with a gradually increased dose of aducanumab for up to 24 months and those who were treated with a fixed dose of 3, 6 or 10 mg/kg aducanumab for up to 36 months. The results are consistent with previously reported analyses from the Phase 1b study and support the design of the ongoing Phase 3 studies of aducanumab for early Alzheimer's disease.

"We now have up to three years of results from the Phase 1b study of aducanumab and during this time period we continued to observe reduction of the biomarker, amyloid plaque," said Alfred Sandrock, M.D., Ph.D., executive vice president and chief medical officer at Biogen. "The results also suggest there is a benefit on clinical decline for patients in the Phase 1b study, especially at the highest doses of aducanumab. Our Phase 3 studies of aducanumab are ongoing to determine whether it may be a potential treatment for early Alzheimer's disease."

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 or mild Alzheimer's disease. The study includes fixed dosing at 1, 3, 6 and 10 mg/kg as well as an arm with a titration regimen in which patients received a gradually increased dose of aducanumab until they reach a maximum dose of 10 mg/kg.

The new analyses presented at CTAD include 143 patients in these groups:

- Patients (n=18) initially randomized to titration dosing that gradually increased aducanumab from 1 to 3 to 6 then 10 mg/kg in the 54-week placebo-controlled period and treated up to 24 months
- Patients (n=69) randomized to aducanumab 3, 6 or 10 mg/kg in the 54-week placebo-controlled period and treated up to 36 months
- Patients (n=48) who were randomized to placebo or aducanumab 1 mg/kg in the 54-week placebo-controlled period who were switched to aducanumab 3 mg/kg or to a 3 to 6 mg/kg titration regimen in the LTE and treated up to 24 months
- Patients (n=8) who were randomized to placebo in the 54-week placebo-controlled period who were switched to titration dosing that gradually increased their dose from 1 to 3 to 6 then 10 mg/kg in the LTE and treated up to 12 months

In the Phase 1b LTE, the most commonly reported adverse events were headache, fall and amyloid-related imaging abnormalities (ARIA). Of the 185 patients dosed with aducanumab in the Phase 1b study, 46 patients experienced ARIA-E (edema). There were no new cases of ARIA-E in patients who continued on the same dose of aducanumab.

The incidence of ARIA-E in patients switching from placebo to aducanumab in the LTE was consistent with the incidence reported in the placebo-controlled portion of the Phase 1b study. Six patients experienced more than one episode of ARIA-E. These recurrent events were consistent with other ARIA events reported to date; they were typically asymptomatic, and most patients continued in the study.

24-Month Data
Patients who completed the 54-week, placebo-controlled period of the Phase 1b study had the option to continue in the LTE. Of the 196 patients who received placebo or aducanumab treatment in the placebo-controlled period of the Phase 1b study, 143 continued into the LTE. All patients who continued in the LTE were switched to or continued on aducanumab treatment.

Amyloid plaque levels were measured by positron emission tomography (PET) using the standardized uptake value ratio[1] (SUVR) and continued to decline in those who remained on treatment for 24 months.

The Clinical Dementia Rating sum of boxes (CDR-SB) and the Mini-Mental State Examination (MMSE), which measure aspects of cognitive and physical function that can be affected by Alzheimer's disease, were exploratory endpoints of the Phase 1b study. The results of these assessments suggest a continued benefit on the rate of clinical decline during the second year of treatment with aducanumab.

By 24 months, patients treated in the titration treatment group had an expected average dose of 7.6 mg/kg.

At 24 months, the mean change from amyloid plaque levels at the start of the Phase 1b study was:

- -0.170 in those who switched from placebo to aducanumab treatment at 12 months
- -0.149 in those who switched from 1 to 3 mg/kg at 12 months
- -0.197 in the 3 mg/kg treatment group
- -0.280 in the 6 mg/kg treatment group
- -0.322 in the 10 mg/kg treatment group
- -0.271 in the titration treatment group

At 24 months, the average decline from the start of the Phase 1b study on the CDR-SB was:

- 3.25 points in those who switched from placebo to aducanumab treatment at 12 months
- 3.52 points in those who switched from 1 to 3 mg/kg at 12 months
- 2.32 points in the 3 mg/kg treatment group
- 2.98 points in the 6 mg/kg treatment group
- 1.69 points in the 10 mg/kg treatment group
- 2.65 in the titration treatment group

At 24 months, the average decline from the start of the Phase 1b study on the MMSE was:

- 4.28 points in those who switched from placebo to aducanumab treatment at 12 months
- 3.65 points in those who switched from 1 to 3 mg/kg at 12 months
- 2.81 points in the 3 mg/kg treatment group
- 5.20 points in the 6 mg/kg treatment group
- 1.97 points in the 10 mg/kg treatment group
- 1.95 in the titration treatment group

36-Month Data
In patients treated up to 36 months, amyloid plaque as measured by PET using SUVR, continued to decrease in a dose- and time-dependent manner, with amyloid plaque levels in the 10 mg/kg fixed-dose treatment group reaching and remaining at a level considered below the quantitative cut-point that discriminates between a positive and negative scan.[2]

At 36 months, the mean change from amyloid plaque levels at the start of the Phase 1b study was:

- -0.226 in those who switched from placebo to 3 mg/kg or 3-6 mg/kg aducanumab treatment at 12 months
- -0.208 in those who switched from 1 to 3 mg/kg at 12 months
- -0.243 in the 3 mg/kg treatment group
- -0.286 in the 6 mg/kg treatment group
- -0.306 in the 10 mg/kg treatment group

At 36 months, the average decline from the start of the Phase 1b study on the CDR-SB was:

- 5.28 points in those who switched from placebo to 3 mg/kg or 3-6 mg/kg treatment at 12 months
- 6.11 points in those who switched from 1 mg/kg to 3 mg/kg at 12 months
- 3.86 points in the 3 mg/kg treatment group
- 4.49 points in the 6 mg/kg treatment group
- 2.84 points in the 10 mg/kg treatment group

At 36 months, the average decline from the start of the Phase 1b study on the MMSE was:

- 7.98 points in those who switched from placebo to 3 mg/kg or 3-6 mg/kg treatment at 12 months
- 6.35 points in those who switched from 1 mg/kg to 3 mg/kg at 12 months

- 4.83 points in the 3 mg/kg treatment group
- 8.97 points in the 6 mg/kg treatment group
- 4.10 points in the 10 mg/kg treatment group

Data presentations for aducanumab at CTAD are scheduled for:

- November 2, approximately 3:30 p.m. ET: *Aducanumab 36-month data from PRIME: A randomized, double-blind, placebo-controlled Phase 1b study in patients with prodromal or mild Alzheimer's disease*
- November 4, approximately 11:15 a.m. ET: *Aducanumab titration dosing regimen: 24-month analysis from PRIME: A randomized, double-blind, placebo-controlled Phase 1b study in patients with prodromal or mild Alzheimer's disease*

These data presentations will be webcast live. To access the live webcasts, please visit the Investors section of Biogen's website at www.biogen.com/investors. An archived version of the webcasts will be available following the presentation.

Phase 3 Clinical Studies
Aducanumab is currently being evaluated in two global Phase 3 studies, ENGAGE and EMERGE, which are designed to evaluate its safety and efficacy in slowing cognitive impairment and the progression of disability in people with early Alzheimer's disease.

For more information about the Phase 3 studies, including information about participating centers, visit www.ClinicalTrials.gov (NCT02477800 or NCT02484547).

About Aducanumab
Aducanumab (BIIB037) is an investigational compound being developed for the treatment of Alzheimer's disease. Aducanumab is a human recombinant 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). Biogen licensed aducanumab from Neurimmune under a collaborative development and license agreement.

Aducanumab is thought to target aggregated forms of beta amyloid including soluble oligomers and insoluble fibrils which can form into amyloid plaque in the brain of AD patients. Based on pre-clinical and Phase 1b data to date, treatment with aducanumab has been shown to reduce amyloid plaque levels**.**

In August 2016 aducanumab was accepted into the European Medicines Agency's PRIME program. In September 2016 the U.S. Food and Drug Administration accepted aducanumab into its Fast Track program and in April 2017 aducanumab was accepted into the Japanese Ministry of Health, Labour and Welfare's (MHLW) Sakigake Designation System.

As of October 2017, Biogen and Eisai entered into a global collaboration agreement to jointly develop and commercialize aducanumab.

About Alzheimer's Disease
Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by cognitive decline and behavioral disturbances that eventually result in a person's inability to perform daily activities. In 2010, it was estimated that 25 million individuals were living with AD worldwide. [3] Evidence suggests that pathophysiological changes typically begin years prior to the symptoms that lead to a clinical diagnosis. As the disease progresses, cognitive impairments, behavioral changes and functional disability commonly associated with AD begin to manifest.

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

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, and the potential clinical effects of aducanumab. These statements may be identified by words such as "anticipate," "believe," "could," "estimate," "expect," "forecast," "intend," "may," "plan," "potential," "possible," "will," and other words and terms of similar meaning, and are based on our current beliefs and expectations. You should not place undue reliance on these statements or the scientific data presented. 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. 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 our drug candidates, the occurrence of adverse safety events, or we may encounter other unexpected hurdles. 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 Securities and Exchange Commission. These statements are based on our current beliefs and expectations and speak only as of the date of this press release. We do not undertake any obligation to publicly update any forward-looking statements, whether as a result of new information, future developments or otherwise.

[1] A composite standardized uptake value ratio (SUVR) of six regions of the brain – frontal, parietal, lateral temporal, sensorimotor, anterior and posterior cingulate – was calculated at baseline, at 26, 54, 110 and 166 weeks using whole cerebellum as a reference.

[2] Landau, S. M., Mintun, M. A., Joshi, A. D., Koeppe, R. A., Petersen, R. C., Aisen, P. S., Weiner, M. W., Jagust, W. J. and for the Alzheimer's Disease Neuroimaging Initiative (2012), Amyloid deposition, hypometabolism, and longitudinal cognitive decline. Ann Neurol., 72: 578–586. doi:10.1002/ana.23650.

[3] World Health Organization Dementia a Public Health Priority. http://www.who.int/mental_health/publications/dementia_report_2012/en/. Accessed 23 May 2016.

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