Biogen Presents New Data from Phase 1B Study of Investigational Alzheimer's Disease Treatment Aducanumab (BIIB037) at Alzheimer's Association International Conference® 2015

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Results Demonstrate Statistically Significant Reduction of Beta Amyloid, Dose-Dependent Slowing of Clinical Decline and Acceptable Safety

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Today Biogen (NASDAQ: BIIB) announced new results from a prespecified interim analysis of PRIME, the Phase 1b placebo-controlled study of aducanumab (BIIB037) in patients with prodromal or mild Alzheimer's disease (AD). In this analysis, which includes patients treated up to 54 weeks with the 6 mg/kg dose, aducanumab demonstrated acceptable safety and tolerability, and the findings reinforce the previously reported results from PRIME. These data are being presented today at the Alzheimer's Association International Conference ® 2015 (AAIC®) in Washington, D.C.

Consistent with previously reported results, the 54-week data from the 6 mg/kg arm demonstrated a statistically significant reduction of beta amyloid in the brain. In exploratory analyses, the 6 mg/kg dose showed an improvement in the slowing of clinical decline, as measured by the Mini Mental State Examination (MMSE) and Clinical Dementia Rating sum of boxes (CDR-SB) scales, which was not statistically significant. In a pre-specified analysis across placebo and all doses of aducanumab, the slowing of clinical decline was shown to be dose-dependent, and this dose-dependence achieved statistical significance for both scales.

"We are encouraged by these new results, which continue to show that treatment of prodromal and mild Alzheimer's disease patients with aducanumab resulted in a statistically significant, dose-dependent reduction in amyloid plaque, as well as a dose-dependent slowing of cognitive decline," said Alfred Sandrock, M.D., Ph.D., group senior vice president and chief medical officer at Biogen. "We have begun screening patients for our Phase 3 clinical trials. The results of the PRIME study give us hope that aducanumab may one day make a meaningful difference for people with Alzheimer's disease."

PRIME Study
PRIME is an ongoing Phase 1b 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 AD. The PRIME study includes fixed dosing at 1 (n=31), 3 (n=33), 6 (n=30) and 10 (n=32) mg/kg, as well as placebo (n=40). In addition there is an ongoing titration regimen.

The previously reported results from the 1, 3, and 10 mg/kg arms showed dose- and time-dependent effects on the reduction of beta amyloid and slowing of clinical decline (as measured by MMSE and CDR-SB) compared to placebo at 54 weeks. In the same analysis, the 26-week results were available for the 6 mg/kg arm, which was shown to reduce amyloid plaque compared to placebo.

The new analysis presented at AAIC 2015 includes data from the 6 mg/kg dose arm and its corresponding placebo arm (n=10) up to 54 weeks. The updated results from all other fixed doses (1, 3 and 10 mg/kg) reflect a larger pooled placebo group (n=40), which now includes the placebo patients from 6 mg/kg cohort, per the prespecified statistical model.

Radiologic Results for Amyloid Plaque
PET imaging using the radiotracer florbetapir[1], which binds to amyloid plaque, was used to measure plaque levels in the brain. In the updated analysis, the standardized uptake value ratio[2] was virtually unchanged in the placebo group at 54 weeks. A statistically significant reduction of amyloid plaque was observed in the 3 mg/kg [-0.135 ($p<0.001$)], 6 mg/kg [-0.210 ($p<0.001$)] and 10 mg/kg [-0.268 ($p<0.001$)] arms. The reduction of amyloid plaque in the 1 mg/kg (-0.055) arm was not statistically significant.

Clinical Results
The updated results of the MMSE showed that patients in the placebo group worsened by an average of 2.81 points at 52 weeks. Clinical decline on the MMSE in the treatment arms was 2.18 points in the 1 mg/kg, 0.70 in the 3 mg/kg, 1.96 in the 6 mg/kg and 0.56 in the 10 mg/kg.

Relative to placebo, the 3 and 10 mg/kg doses demonstrated a statistically significant slowing of cognitive decline on the MMSE, both with p-values <0.05. The 1 and 6 mg/kg were not statistically significant. The linear trend for dose response was statistically significant with a p-value less than 0.05.

The updated results of the CDR-SB showed that patients in the placebo group worsened by an average of 1.87 points at 54 weeks compared to 1.72 in the 1 mg/kg, 1.37 in the 3 mg/kg, 1.11 in the 6 mg/kg and 0.63 in the 10 mg/kg treatment arm.

The 10 mg/kg arm demonstrated a statistically significant slowing of clinical decline compared to placebo on the CDR-SB with p-value <0.05. The 1, 3 and 6 mg/kg were not statistically significant. The linear trend for dose response was statistically significant with a p-value less than 0.05.

Pharmacokinetic activity and exposure were linear with dose. Treatment-emergent immunogenicity, which occurred in three percent of aducanumab treated patients, was transient and without an apparent effect on aducanumab PK.

Safety Results
Aducanumab demonstrated an acceptable safety and tolerability profile in this analysis that was consistent with previously reported analyses from this study. The most frequently reported treatment-related serious adverse event (SAE) and adverse event (AE) was ARIA (amyloid-related imaging abnormalities).

Based on MRI scans, the incidence of ARIA-E (edema) was dose- and apolipoprotein E4- (ApoE4) status-dependent. In general, the onset of ARIA-E was observed early in the course of treatment and was asymptomatic or with mild, transient symptoms. The majority of patients with ARIA-E continued treatment at a lower dose.

In ApoE4 carriers, the incidence of ARIA-E was 5 percent in the 1 mg/kg and 3 mg/kg arms, 43 percent in the 6 mg/kg arm and 55 percent in the 10 mg/kg arm. In ApoE4 non-carriers, the incidence of ARIA-E was 9 percent in the 3 mg/kg, 22 percent in the 6 mg/kg and 17 percent in the 10 mg/kg aducanumab arm; no cases were reported in the 1 mg/kg arm.

In ApoE4 carriers, the incidence of patients who developed ARIA-E and discontinued treatment was 5 percent in the 1 mg/kg arm, 10 percent in the 6 mg/kg arm and 35 percent in the 10 mg/kg arm. There were no discontinuations in the 3 mg/kg arm. In ApoE4 non-carriers, the incidence of patients who developed ARIA-E and discontinued treatment was 11 percent in the 6 mg/kg arm and 8 percent in the 10 mg/kg arm. There were no discontinuations in the 1 mg/kg and 3 mg/kg arms. Overall, 56 percent of subjects who developed ARIA-E continued treatment at the same or lower dose and none developed recurrent ARIA-E.

Headache occurred in 20 percent of patients receiving aducanumab compared to 5 percent in the placebo groups and appeared to be dose-dependent. Three deaths were reported in the time period of this analysis, two in the placebo group and one in the 10 mg/kg study arm; none were considered to be treatment related. Other AEs and SAEs were consistent with what is typically observed in the study population.

About Aducanumab (BIIB037)
Aducanumab (BIIB037) is an investigational compound being developed for the treatment of Alzheimer's disease (AD). 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 and 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 targets aggregated forms of beta amyloid including soluble oligomers and insoluble fibrils deposited into the amyloid plaque in the brain of AD patients. Based on pre-clinical and interim Phase 1b data, treatment with aducanumab has been shown to reduce amyloid plaque levels.

The global Phase 3 studies of aducanumab, ENGAGE and EMERGE, are currently enrolling and will assess the efficacy and safety of aducanumab in people with early AD. Each study will be conducted at approximately 150 sites in more than 20 countries in North America, Europe and Asia Pacific. For more information visit www.aducanumabclinicaltrials.com or clinicaltrials.gov.

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
Through cutting-edge science and medicine, Biogen discovers, develops and delivers to patients worldwide innovative therapies for the treatment of neurodegenerative diseases, hematologic conditions and autoimmune disorders. Founded in 1978, Biogen is one of the world's oldest independent biotechnology companies and patients worldwide benefit from its leading multiple sclerosis and innovative hemophilia therapies. For product labeling, press releases and additional information about the company, please visit www.biogen.com.

Biogen Safe Harbor
This press release contains forward-looking statements, including statements about the potential safety and clinical effects of aducanumab. These statements may be identified by words such as "believe," "expect," "may," "plan," "potential," "will" and similar expressions, and are based on our current beliefs and expectations. 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. Interim results in early stage clinical trials may not be indicative of full results or results from later stage or larger scale clinical trials and does not ensure regulatory approval. Factors which could cause actual results to differ materially from our current expectations include the risk that unexpected concerns may arise from additional data, analysis of the full results or results obtained during other clinical trials, regulatory authorities may require additional information or further studies, or may fail to approve or may delay approval of our drug candidates, or we may encounter other unexpected hurdles. For more detailed information on the risks and uncertainties associated with our drug development and commercialization activities, please review the Risk Factors section of our most recent annual or quarterly report filed with the Securities and Exchange Commission. Any forward-looking statements speak only as of the date of this press release and we assume no obligation to update any forward-looking statements.

[1] Amyvid™ (florbetapir) is a trademark of Eli Lilly and Company.

[2] 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 weeks and at 54 weeks using whole cerebellum as a reference.

[3] World Health Organization Dementia a Public Health Priority, http://www.who.int/mental_health/publications/dementia_report_2012/en/. Accessed 10 Dec 2014.

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