Biogen Presents Data from Phase 1b Study of Investigational Alzheimer's Disease Treatment Aducanumab at 2016 Clinical Trials on Alzheimer's Disease Meeting

December 8, 2016

Data Includes Analyses of Phase 1b Titration Cohort and Long-Term Extension Cohort

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Biogen (NASDAQ: BIIB) announced it will present new data from the Phase 1b (PRIME) study of aducanumab, its investigational treatment for early Alzheimer's disease (AD), today at the 9 th Clinical Trials on Alzheimer's Disease (CTAD) meeting in San Diego.

Data presentations include interim results from the titration cohort of the placebo-controlled period of the Phase 1b study as well as data from the first year of the long-term extension (LTE). The results support the ongoing Phase 3 studies of aducanumab for early AD.

"The data at CTAD support the positive results we have seen in our Phase 1b study of aducanumab, and they provide insight into the observed effects in patients treated for up to two years," said Samantha Budd Haeberlein, vice president, clinical development at Biogen. "We are committed to advancing our global Phase 3 program for aducanumab as well as the scientific understanding of Alzheimer's disease so we can help identify a treatment for the many people affected by this terrible disease."

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 (n=197) with prodromal or mild AD.

The Phase 1b study includes fixed dosing at 1 (n=31), 3 (n=33), 6 (n=30) and 10 mg/kg (n=32) as well as an arm with a titration regimen (n=23) and pooled placebo (n=48).

Phase 1b also includes an LTE for patients who completed the one-year placebo-controlled portion of the study.

The aducanumab data presented at CTAD are consistent with previously reported analyses from this study.

12-Month Titration Arm
ARIA (amyloid-related imaging abnormalities) was the most commonly reported adverse event in the fixed-dose arms of the Phase 1b study. Rates of ARIA were higher in apolipoprotein E4 (ApoE4) carriers than in non-carriers.

In order to explore the potential effect of titrating aducanumab, ApoE4-carrier patients were enrolled in the titration arm and titrated aducanumab up to 10 mg/kg (n=23).

The incidence of ARIA-E in ApoE4 carriers in the fixed-dose arms 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. The incidence of ARIA-E in ApoE4 carriers in the titration arm was 35 percent.

At 54 weeks, a statistically significant reduction of amyloid plaque (versus placebo) was observed in all fixed-dose arms: 1 mg/kg [-0.050 ($p<0.05$)], 3 mg/kg [-0.130 ($p<0.001$)], 6 mg/kg [-0.206 ($p<0.001$)], 10 mg/kg [-0.263 ($p<0.001$)] and in the titration arm [-0.171 ($p<0.001$)]. The standardized uptake value ratio[1] was virtually unchanged in the placebo group at 54 weeks.

Results from exploratory endpoints, Clinical Dementia Rating sum of boxes (CDR-SB) and the Mini-Mental State Examination (MMSE), were also presented.

The results of the CDR-SB showed that patients in the placebo group worsened by an average of 1.89 points at 54 weeks compared with the following treatment arms:

- 1.69 in the 1 mg/kg
- 1.33 in the 3 mg/kg
- 1.09 in the 6 mg/kg
- 0.63 in the10 mg/kg, p-value <0.05 versus placebo
- 0.70 in the titration arm, p-value<0.05 versus placebo

The results of the MMSE showed that patients in the placebo group worsened by an average of 2.45 points at 52 weeks. Average clinical decline on the MMSE in the treatment arms was:

- 2.21 points in the 1 mg/kg
- 0.75 points in the 3 mg/kg
- 1.99 points in the 6 mg/kg
- 0.55 points in the 10 mg/kg, p-value<0.05 versus placebo

- 1.00 points in the titration arm

Phase 1b Long-Term Extension
Patients who completed the 54-week, placebo-controlled period of Phase 1b had the option to continue in the LTE.

Patients who were randomized to placebo or aducanumab 1 mg/kg in the placebo-controlled period were switched to aducanumab 3 mg/kg or to a 3 - 6mg/kg titration regimen in the LTE. Patients randomized to aducanumab 3, 6 or 10 mg/kg or titration in the placebo-controlled period continued in the same dose group in the LTE.

In the LTE, there were no new cases of ARIA-E in patients initially randomized to aducanumab 3, 6 or 10 mg/kg who were treated up to 24 months. The incidence of ARIA-E in patients switching from placebo to aducanumab was consistent with the incidence reported in placebo-controlled portion of Phase 1b.

Analyses of exploratory endpoints from the first 12 months of the LTE study suggest patients treated with aducanumab for up to 24 months (n=69) continued to have beneficial effects on the reduction of amyloid plaque and the rate of clinical decline as measured by CDR-SB and MMSE.

Aducanumab Data Presentations at CTAD
On Friday, Dec. 9, data presentations for aducanumab are scheduled at:

- 8:00 AM PST / 11:00 AM EST Vissia Viglietta, M.D.: *Aducanumab titration dosing regimen: 12-month interim analysis from prime, a randomized, double-blind, placebo-controlled phase 1B study in patients with prodromal or mild alzheimer's disease*

- 9:15 AM PST / 12:15 PM EST Samantha Budd Haeberlein, Ph.D.: *Aducanumab 24-month data from prime: a randomized, double-blind, placebo-controlled phase 1B study in patients with prodromal or mild alzheimer's disease*

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 early 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 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 EMA's PRIME program. In September 2016 the U.S. FDA accepted aducanumab into its Fast Track program.

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 [2]. 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 worldwide innovative therapies for people living with serious neurological, autoimmune and rare diseases. 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 more information, please visit www.biogen.com. Follow us on Twitter.

Biogen Safe Harbor
This press release contains forward-looking statements, including statements about additional results from the phase 1b study, and the potential 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. 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. Factors which could cause actual results to differ materially from our current expectations include 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, 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] 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.

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

Contact:

MEDIA CONTACT:

Biogen
Catherine Falcetti, +1 781 464 3260
public.affairs@biogen.com
or
INVESTOR CONTACT:
Matt Calistri, +1 781 464 2442
IR@biogen.com