



Biogen Reports New Data from Phase 1b Study of Investigational Alzheimer's Disease Treatment Aducanumab

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Results Support Design of Ongoing Phase 3 Studies of Aducanumab for Early Alzheimer's Disease

CAMBRIDGE, Mass.--([BUSINESS WIRE](#))--Biogen (NASDAQ: BIIB) today announced results from a recently conducted analysis of the long-term extension (LTE) of its ongoing Phase 1b study of aducanumab, the company's investigational treatment for early Alzheimer's disease.

The updated analyses include data from the placebo-controlled period and LTE for patients treated with aducanumab up to 24 months in the titration cohort and up to 36 months in the fixed-dose cohorts. The results are consistent with previously reported analyses from this ongoing Phase 1b study and support the design of the ongoing Phase 3 studies of aducanumab for early Alzheimer's disease.

The Phase 1b 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.

Phase 1b Long-Term Extension

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

The new analyses include 143 patients who remained in the LTE. The LTE cohorts are small populations:

- Patients (n=18) initially randomized to the aducanumab titration regimen in the 12-month placebo-controlled period and treated up to 24 months
- Patients (n=69) initially randomized to aducanumab 3, 6 or 10 mg/kg and treated up to 36 months
- Patients (n=48) who were randomized to placebo or aducanumab 1 mg/kg in the placebo-controlled period who were switched to aducanumab 3 mg/kg or to a 3-6 mg/kg titration regimen in the LTE and treated up to 24 months
- Patients (n=8) who were randomized to placebo in the placebo-controlled period who were switched to aducanumab 1-3-6-10 mg/kg titration regimen 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 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.

In patients treated up to 24 months in the titration cohort, amyloid plaque reduction as measured by positron emission tomography (PET) was consistent with the dose- and time-dependent results observed in the fixed-dose cohorts. Analyses of exploratory clinical endpoints, Clinical Dementia Rating sum of boxes (CDR-SB) and the Mini-Mental State Examination (MMSE), were consistent with the results from the fixed-dose cohorts and suggest a continued benefit on the rate of clinical decline during the second year of treatment.

In patients treated up to 36 months, amyloid plaque as measured by PET continued to decrease in a dose- and time-dependent manner, with amyloid plaque levels in the 10 mg/kg fixed-dose cohort reaching and remaining at a level considered below the quantitative cut-point that discriminates between a positive and negative scan¹. At 36 months, analyses of exploratory clinical endpoints CDR-SB and the MMSE suggest a continued benefit on the rate of clinical decline during the third year of treatment.

Biogen plans to share more data from these analyses at an upcoming medical congress.

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 drug 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 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.

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 worldwide². 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 and neurodegenerative diseases. Founded in 1978, Biogen is a pioneer in biotechnology, and today the company has the leading portfolio of medicines to treat multiple sclerosis; has introduced the first and only approved treatment for spinal muscular atrophy; and is at the forefront of neurology research for conditions including Alzheimer's disease, Parkinson's disease and amyotrophic lateral sclerosis. Biogen also manufactures and commercializes biosimilars of advanced biologics. For more information, please visit www.biogen.com. Follow us on social media – Twitter, LinkedIn, Facebook, YouTube.

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, the occurrence of adverse safety events, 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 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.

² 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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