New Phase 3 Data Show Positive Correlation Between ADUHELM™ Treatment Effect on Biomarkers and Reduction in Clinical Decline in Alzheimer's Disease

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- In a pre-specified analysis, ADUHELM significantly lowered plasma p-tau181, a biomarker of the hallmark tau tangles in Alzheimer's disease, in both Phase 3 trials in a dose- and time-dependent manner vs. placebo
- Change in plasma p-tau181 was significantly correlated with change in amyloid beta plaque and reduced cognitive and functional decline on all primary and secondary outcome measures
- These data provide further evidence of ADUHELM's effect on clinical decline by lowering amyloid beta plaque and tangles of tau proteins, two defining pathologies of Alzheimer's disease

CAMBRIDGE, Mass., Nov. 11, 2021 (GLOBE NEWSWIRE) -- Biogen Inc. (Nasdaq: BIIB) and Eisai Co., Ltd. (Tokyo, Japan) announced that data from approximately 7,000 plasma samples from more than 1,800 patients in the ADUHELM™ (aducanumab-avwa) Phase 3 clinical trials showed a statistically significant correlation between plasma p-tau reduction and less cognitive and functional decline in Alzheimer's disease. Reductions in plasma p-tau181 were also correlated with a lowering of amyloid beta plaque. The pre-specified analysis of plasma samples was conducted by an independent lab, drawing from the two pivotal ADUHELM Phase 3 EMERGE and ENGAGE trials. The findings were presented today at the Clinical Trials on Alzheimer's Disease conference (CTAD), held November 9-12 virtually and in Boston, Massachusetts.

The analysis highlighted that ADUHELM significantly reduced tau pathology, a defining feature of Alzheimer's disease, as measured by plasma p-tau181, when compared to placebo. The effect was greater with higher doses and longer duration of ADUHELM treatment. Greater reduction in plasma p-tau181 also had a statistically significant correlation with less decline in cognition and function in ADUHELM-treated patients. Furthermore, the analysis demonstrated a statistically significant correlation between change in plasma p-tau181 and lowering of amyloid beta plaque, showing the effect of ADUHELM on the two core pathological features of Alzheimer's disease.

"We now have robust and concordant data that ADUHELM has effect on two core defining pathologies of Alzheimer's disease, and substantial evidence of treatment correlation between changes in plasma p-tau181 and the slowing of disease progression," said Alfred Sandrock, Jr., M.D., Ph.D., Head of Research and Development at Biogen. "We are committed to continuing to generate data, and we believe these new findings can help inform treatment choice and advance Alzheimer's research including in diagnosis and disease monitoring."

The findings showed that ADUHELM significantly lowered plasma p-tau181 in a dose- and time-dependent manner vs. placebo in both Phase 3 trials. In the EMERGE high-dose group, p-tau decreased 13% from baseline ($p<0.001$), while placebo rose 8%; in the ENGAGE high-dose group, p-tau decreased 16% from baseline ($p<0.001$), while placebo rose 9%.

Greater reduction in plasma p-tau181 was correlated with less clinical decline in all four clinical outcome measures in the Phase 3 trials. Correlation values across these endpoints were as follows for EMERGE and ENGAGE, respectively: Clinical Dementia Rating Sum of Boxes Score (CDR-SB) $R = 0.11$ ($p = 0.0166$) and $R = 0.14$ ($p = 0.0005$); Mini-Mental State Examination (MMSE) $R = -0.21$ ($p < 0.0001$) and $R = -0.15$ ($p = 0.0002$); Alzheimer's Disease Assessment Scale–Cognitive Subscale (ADAS-Cog 13) $R = 0.17$ ($p = 0.0001$) and $R = 0.15$ ($p = 0.0002$); and Alzheimer's Disease Cooperative Study/Activities of Daily Living scale adapted for MCI (ADCS-ADL-MCI) $R = -0.12$ ($p = 0.0086$) and $R = -0.14$ ($p = 0.0010$).

Changes in plasma p-tau181 was also significantly correlated with change in amyloid beta positron emission tomography (PET) standardized uptake value ratio (SUVR): EMERGE $R = 0.38$, $p < 0.0001$; ENGAGE $R = 0.42$, $p < 0.0001$.

"These data not only show an important link between the ability of ADUHELM to clear amyloid beta plaque and reduce plasma p-tau levels, but also significantly correlate those reductions with slowing cognitive decline," said Oskar Hansson, M.D., Ph.D., Professor of Neurology at Lund University and Skåne University Hospital, Sweden, who led the oral late-breaker presentation at the CTAD conference. "Having research from nearly two thousand patients provides invaluable insights into the dynamics of the interconnected pathologies within this complex disease."

The two pathological hallmarks of Alzheimer's disease—amyloid beta plaque and neurofibrillary tangles (composed of abnormal p-tau)—disrupt communication between neurons, which leads to the loss of brain function, as well as neurodegeneration and clinical decline, which can begin in the early stages of Alzheimer's disease.

Biogen also presented data from the Phase 3b redosing study, EMBARK, which examined the impact of patients with Alzheimer's disease stopping ADUHELM treatment for an extended period of time (average length of 1.7 years) before re-initiating treatment. The study showed that reductions in amyloid beta plaque were maintained in the high-dose group during the treatment gap period compared to the placebo group. Although the disease continued to progress after treatment discontinuation, numerical differences in favor of ADUHELM were maintained across clinical endpoints.

The EMBARK baseline data underscore that further scientific evidence is needed to better understand the impact of discontinuation from anti-amyloid treatment and the role that other underlying pathological processes may play in disease progression.

EMBARK is not a randomized study and there may be selection bias for the enrolling patients; Interpretation of these data must weigh the potential influence of the heterogeneity of dose, duration of exposure, and treatment gap periods across individuals in the study. The analysis is from the largest clinical trial dataset available in early Alzheimer's disease, which included 1,856 screened patients from EMERGE, ENGAGE, PRIME and EVOLVE.

About ADUHELM ™ (aducanumab-avwa) injection 100 mg/mL solution
ADUHELM is indicated for the treatment of Alzheimer's disease. Treatment with ADUHELM should be initiated in patients with mild cognitive impairment or mild dementia stage of disease, the population in which treatment was initiated in clinical trials. There are no safety or effectiveness data on initiating treatment at earlier or later stages of the disease than were studied. This indication is approved under accelerated approval based on reduction in amyloid beta plaques observed in patients treated with ADUHELM. Continued approval for this indication may be contingent upon verification of clinical benefit in confirmatory trial(s).

Aducanumab-avwa is a monoclonal antibody directed against amyloid beta. The accumulation of amyloid beta plaques in the brain is a defining pathophysiological feature of Alzheimer's disease. The accelerated approval of ADUHELM has been granted based on data from clinical trials showing the effect of ADUHELM on reducing amyloid beta plaques, a surrogate biomarker that is reasonably likely to predict clinical benefit, in this case a reduction in clinical decline.

ADUHELM can cause serious side effects including: Amyloid Related Imaging Abnormalities or "ARIA". ARIA is a common side effect that does not usually cause any symptoms but can be serious. Although most people do not have symptoms, some people may have symptoms such as: headache, confusion, dizziness, vision changes and nausea. The patient's healthcare provider will do magnetic resonance imaging (MRI) scans before and during treatment with ADUHELM to check for ARIA. ADUHELM can also cause serious allergic reactions. The most common side effects of ADUHELM include: swelling in areas of the brain, with or without small spots of bleeding in the brain or on the surface of the brain (ARIA); headache; and fall. Patients should call their healthcare provider for medical advice about side effects.

As of October 2017, Biogen and Eisai Co., Ltd. are collaborating on the global co-development and co-promotion of aducanumab.

Please click here for full Prescribing Information, including Medication Guide, for ADUHELM.

About Biogen
As pioneers in neuroscience, Biogen discovers, develops, and delivers worldwide innovative therapies for people living with serious neurological diseases as well as related therapeutic adjacencies. One of the world's first global biotechnology companies, Biogen was founded in 1978 by Charles Weissmann, Heinz Schaller, Sir Kenneth Murray, 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 approved treatment for spinal muscular atrophy, and is providing the first and only approved treatment to address a defining pathology of Alzheimer's disease. Biogen is also commercializing biosimilars and focusing on advancing the industry's most diversified pipeline in neuroscience that will transform the standard of care for patients in several areas of high unmet need.

In 2020, Biogen launched a bold 20-year, $250 million initiative to address the deeply interrelated issues of climate, health, and equity. Healthy Climate, Healthy Lives™ aims to eliminate fossil fuels across the company's operations, build collaborations with renowned institutions to advance the science to improve human health outcomes, and support underserved communities.

The company routinely posts information that may be important to investors on its website at www.biogen.com. To learn more, please visit www.biogen.com and follow Biogen on social media – Twitter, LinkedIn, Facebook, YouTube.

About Eisai Co., Ltd.
Eisai Co., Ltd. is a leading global pharmaceutical company headquartered in Japan. Eisai's corporate philosophy is based on the human health care (hhc) concept, which is to give first thought to patients and their families, and to increase the benefits that health care provides to them. With a global network of R&D facilities, manufacturing sites and marketing subsidiaries, we strive to realize our hhc philosophy by delivering innovative products to target diseases with high 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 a treatment for Alzheimer's disease, Eisai aims to establish the "Eisai Dementia Platform." Through this platform, Eisai plans to deliver novel benefits to those living with dementia and their families through constructing a "Dementia Ecosystem," by collaborating with partners such as medical organizations, diagnostic development companies, research organizations, and bio-ventures in addition to private insurance agencies, finance industries, fitness clubs, automobile makers, retailers, and care facilities. For more information about Eisai Co., Ltd., please visit https://www.eisai.com.

Biogen Safe Harbor

This news release contains forward-looking statements, including statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995, about the potential clinical effects of ADUHELM; the potential benefits, safety and efficacy of ADUHELM; the treatment of Alzheimer's disease; results from the EMBARK study; the anticipated benefits and potential of Biogen's collaboration arrangements with Eisai; clinical development programs, clinical trials and data readouts and presentations; and risks and uncertainties associated with drug development and commercialization. These statements may be identified by words such as "aim," "anticipate," "believe," "could," "estimate," "expect," "forecast," "intend," "may," "plan," "possible," "potential," "will," "would" 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; the occurrence of adverse safety events; risks of unexpected costs or delays; the risk of other unexpected hurdles; failure to protect and enforce Biogen's data, intellectual property and other proprietary rights and uncertainties relating to intellectual property claims and challenges; risks associated with current and potential future healthcare reforms; product liability claims; third party collaboration risks; and the direct and indirect impacts of the ongoing COVID-19 pandemic on Biogen's business, results of operations and financial condition. 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 U.S. Securities and Exchange Commission. These statements are based on Biogen's current beliefs and expectations and speak only as of the date of this news 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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