Update on the Phase 4 ENVISION Confirmatory Study of ADUHELM®

January 27, 2022

CAMBRIDGE, Mass., Jan. 27, 2022 (GLOBE NEWSWIRE) -- Biogen Inc. (Nasdaq: BIIB) and Eisai Co., Ltd. (Tokyo, Japan) today announced additional details about the Phase 4 post-marketing confirmatory study, ENVISION, of ADUHELM® (aducanumab-avwa) 100 mg/mL injection for intravenous use in early Alzheimer's disease, including details of the study's goal for diverse enrollment and primary endpoint.

Biogen aims to enroll 18 percent of U.S. participants in ENVISION from Black/African American and Latinx populations. This goal is reflective of Biogen's ongoing commitment to increase diversity in clinical trials.

"Historically, patients from diverse backgrounds have been poorly represented in Alzheimer's disease clinical trials, and we are committed to changing this," said Priya Singhal M.D., M.P.H., Head of Global Safety & Regulatory Sciences and interim Head of Research & Development at Biogen. "This goal matches the diversity among Americans diagnosed with early Alzheimer's disease, while at the same time, the trial will generate substantial data to verify the effectiveness of ADUHELM."

Biogen will implement multiple strategies to help overcome barriers to diverse patient enrollment in Alzheimer's disease trials, such as, lack of access to medical centers, familiarity with benefit/risk profile of treatment, and financial or logistical burdens.

"It's important to see this ambitious focus on diversity being prioritized in enrollment and integrated as a key part of the ENVISION clinical trial, so that we can have data from patients who more closely represent what we see in the clinic," said Dylan Wint, M.D., Cleveland Clinic Lou Ruvo Center for Brain Health, Nevada.

The companies also announced today that the primary endpoint for the global, placebo-controlled ENVISION trial will be measured by the Clinical Dementia Rating–Sum of Boxes (CDR-SB) at 18 months after treatment initiation with ADUHELM. The CDR-SB endpoint is a validated measure of both cognition and function that is widely used in clinical trials of patients with early symptomatic Alzheimer's disease, is consistent with ADUHELM's Phase 3 EMERGE and ENGAGE studies, and capable of generating robust outcomes. The update also includes an increase in the previously announced enrollment, from 1,300 to 1,500 people with early Alzheimer's disease (Mild Cognitive Impairment due to Alzheimer's disease and mild Alzheimer's disease), with confirmation of amyloid beta pathology, to further strengthen the data provided by the study.

Although ENVISION and other ADUHELM clinical trials are already planned or underway, the Centers for Medicare and Medicaid Services (CMS) recently released a draft National Coverage Determination (NCD), which would restrict Medicare coverage of ADUHELM and other amyloid-targeting therapies to patients enrolled in an additional clinical trial. Biogen is committed to engaging with CMS to avoid unnecessary duplication of clinical trials and work towards finding a path to offer immediate access to patients to the first FDA approved treatment for Alzheimer's disease since 2003.

In addition to the primary endpoint, CDR-SB, secondary endpoints include Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog 13), Alzheimer's Disease Cooperative Study - Activities of Daily Living Inventory - Mild Cognitive Impairment Version (ADCS-ADL-MCI), Integrated Alzheimer's Disease Rating Scale (iADRS), Mini-Mental State Examination (MMSE) and Neuropsychiatric Inventory (NPI-10).

The initiation of patient screening for ENVISION is planned for May 2022. Based on enrollment rates from the previous Phase 3 trials with ADUHELM, the primary completion date is expected to be approximately four years after the study begins. The companies are grateful to the healthcare professionals, medical centers, patients and families who will participate in this trial.

Previously, in July 2021, the companies set another substantial diversity goal in the observational Phase 4 ICARE AD trial, which aims to enroll a total of approximately 6,000 patients.

About ADUHELM® (aducanumab-avwa) 100 mg/mL injection for intravenous use
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).

ADUHELM 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 a 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; results from ENVISION; the treatment of Alzheimer's disease; 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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