# Biogen Submits Final Protocol for ADUHELM® (aducanumab-avwa) Phase 4 ENVISION Trial to FDA

March 30, 2022

- *Confirmatory trial's completion is expected in an accelerated timeline of four years with patient screening to start in May*
- *Multiple strategies in place to enroll patients that are representative of diverse American population*

CAMBRIDGE, Mass., March 30, 2022 (GLOBE NEWSWIRE) -- Biogen Inc. (Nasdaq: BIIB) has submitted the final study protocol for the confirmatory Phase 4 ENVISION trial to the U.S. Food and Drug Administration (FDA) for review and approval. This is in line with the company's commitment to accelerate the timelines for the trial, including submitting the final study protocol to the FDA in March 2022, as previously announced. Biogen expects the first patient to enter screening in May 2022 and the trial's primary completion approximately four years after the study begins.

The confirmatory ENVISION trial is a requirement based on FDA's accelerated approval of ADUHELM ® (aducanumab-avwa) 100 mg/mL injection for intravenous use in early Alzheimer's disease (Mild Cognitive Impairment due to Alzheimer's disease and mild Alzheimer's disease).

The study, as previously announced, will be a global, placebo-controlled trial, aiming to enroll around 1,500 patients with early Alzheimer's disease and confirmation of amyloid beta pathology.

The company has also reaffirmed the trial's goal of recruiting at least 18 percent of patients in the U.S. from Black/African American and Latino communities.

"Our unwavering commitment is to ensure that the trial is completed swiftly and that the diversity of patients in it reflects that of Americans diagnosed with early Alzheimer's disease," said Samantha Budd Haeberlein, Ph.D., SVP, Head of Neurodegeneration Development at Biogen. "We plan to work hand-in-hand with underrepresented communities and Alzheimer's disease groups to achieve our diversity and inclusion goal."

To increase participation among historically underrepresented patients, Biogen is leveraging multiple initiatives and working with several community groups, such as the National Minority Quality Forum and others who have expertise and a commitment in helping to overcome traditional enrollment barriers for diverse populations. These efforts are being addressed by three key strategies:

- Selecting sites with diverse staff, located in communities of color, with access to diverse patient populations;
- Supporting trial sites in identification, outreach, and engagement of underrepresented communities; and
- Engaging with community and patient organizations to increase Alzheimer's disease awareness, education, and access to research.

The primary endpoint for the trial will be measured by the Clinical Dementia Rating–Sum of Boxes (CDR-SB) at 18 months, as announced in January 2022. The trial will also include a planned long-term extension to collect treatment data for up to 48 months.

Secondary endpoints include changes in Amyloid Positron Emission Tomography (PET) and Tau PET, as well as the 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).

**About ADUHELM® (aducanumab-avwa) injection 100 mg/mL 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.

From 2017 to March 13, 2022, Biogen and Eisai jointly collaborated on the development, commercialization and manufacturing of ADUHELM. Effective March 14, 2022, Biogen has sole decision-making authority over the development, commercialization and manufacturing of ADUHELM. In 2022 the parties will continue in a global profit/loss sharing arrangement subject to a cap on Eisai's expenses for 2022. Eisai will be entitled to a tiered royalty on net sales of ADUHELM as of January 1, 2023.

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 our website at www.biogen.com. To learn more, please visit www.biogen.com and follow Biogen on social media – Twitter, LinkedIn, Facebook, YouTube.

**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; 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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