Biogen and Eisai Announce Design of ADUHELM ICARE AD-US Study, the First Real-World Observational Phase 4 Study in Alzheimer's Disease at AAIC 2021

July 29, 2021

- ICARE AD-US is an observational real-world phase 4 study designed to evaluate the safety and effectiveness of ADUHELM in clinical practice
- ICARE AD-US is one of three programs to generate post-approval data on ADUHELM, including the re-dosing Phase 3b EMBARK study and the planned confirmatory Phase 4 post-marketing requirement study
- Biogen aims to enroll at least 16 percent Latinx and Black/African American patients with Alzheimer's disease in the ICARE AD-US study as part of its commitment to increase participation from traditionally underrepresented communities

CAMBRIDGE, Mass., July 29, 2021 (GLOBE NEWSWIRE) -- Biogen (Nasdaq: BIIB) and Eisai Co., Ltd. (Tokyo) today announced that Biogen led a late-breaking presentation on the design of the first real-world observational Phase 4 study in Alzheimer's disease called ICARE AD-US, at the Alzheimer's Association International Conference (AAIC), being held both virtually and in Denver, Colo. from July 26 – 30, 2021. ICARE AD-US, a prospective study of ADUHELM™ (aducanumab-avwa) 100 mg/mL solution for injection, is designed to collect real-world, long-term effectiveness and safety data on ADUHELM. The virtual oral session (#57522) was titled, "ICARE AD-US: design of a prospective, single-arm, multicenter, noninterventional real-world study of aducanumab in United States."

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).

ICARE AD-US is a real-world study that will provide information on the long-term effectiveness and safety of ADUHELM as prescribed in routine clinical practice in the U.S. based on the label approved by the U.S. Food and Drug Administration (FDA). The primary objective of the study is to characterize and evaluate real-world, long-term changes in cognition, function and neuropsychiatric status in ADUHELM-treated patients. Secondary objectives are related to gaining a better understanding of ADUHELM safety in real-world clinical practice.

The study design includes an important goal to help address the common underrepresentation of Black/African American and Latinx patients in Alzheimer's disease studies, aiming to enroll at least 16 percent of the trial's expected 6,000 participants from these communities. Alzheimer's disease clinical trials commonly have one to two percent enrollment from these groups, even though Black/African Americans and Latinx people are respectively two and one-and-a-half times more likely than older White Americans to have Alzheimer's disease.

The study intends to enroll patients with Alzheimer's disease over four years from approximately 200 sites in the U.S. Patients will be monitored for a period of up to five years.

"Biogen is committed to both generating new data about ADUHELM and supporting steps to bring adequate representation to this trial and other clinical trials from traditionally underrepresented groups," said Ivana Rubino, Ph.D., U.S. and Global Head of Medical, Alzheimer's Disease at Biogen. "We believe this can help us better understand the safety and effectiveness of treatment in patients with Alzheimer's disease across ethnicities, something that has challenged researchers in this field for decades. The ICARE AD-US study, designed in collaboration with Alzheimer's disease experts, underscores both of these commitments."

The ICARE AD-US study is one of three clinical programs designed to generate new data about ADUHELM. The others include EMBARK, the ongoing, Phase 3b re-dosing study for eligible patients previously enrolled in ADUHELM clinical trials, including the PRIME long-term extension, EMERGE and ENGAGE, and the confirmatory Phase 4 trial that is in the process of being designed and will be conducted to verify the clinical benefit of ADUHELM as part of the post-marketing requirements associated with the accelerated approval pathway of ADUHELM in the U.S.

"The ICARE AD-US study will provide important information on the safety, effectiveness and management of Alzheimer's disease with ADUHELM, the first approved treatment for Alzheimer's disease that targets the amyloid pathway, in the real-world setting across diverse populations," said Harald Hampel, M.D., Ph.D., Vice President, Chief Medical Officer, Neurology Business Group, Eisai Inc. "It is important for Eisai and the larger scientific community to recruit patients of diverse ethnicities for clinical trials to help address health disparities."

The presentation on the ICARE AD-US study will be available for 30 days on the AAIC conference website. Biogen will also post the presentation on the investors section of its website at investors.biogen.com.

About ADUHELM™(aducanumab-avwa) injection 100 mg/mL solution

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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.

Please see full Prescribing Information including Medication Guide.

About Biogen

At Biogen, our mission is clear: we are pioneers in neuroscience. Biogen discovers, develops and delivers worldwide innovative therapies for people living with serious neurological and neurodegenerative 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, 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, commercializes biosimilars of advanced biologics and is focused on advancing research programs in multiple sclerosis and neuroimmunology, Alzheimer's disease and dementia, neuromuscular disorders, movement disorders, ophthalmology, neuropsychiatry, immunology, acute neurology and neuropathic pain.

We routinely post information that may be important to investors on our website at www.biogen.com. Follow us 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, relating to: Biogen's strategy and plans; potential of, and expectations for, Biogen's commercial business, including ADUHELM; the potential clinical effects of ADUHELM; the potential benefits, safety and efficacy of ADUHELM; the identification and treatment of Alzheimer's disease; the design and enrollment of the ICARE AD-US study; the anticipated benefits and potential of our collaboration arrangements with Eisai; the clinical development program, clinical trial(s) and data readouts and presentations for ADUHELM; and risks and uncertainties associated with drug development and commercialization. These forward-looking statements may be accompanied by such words as "aim," "anticipate," "believe," "could," "estimate," "expect," "forecast," "goal," "intend," "may," "plan," "potential," "possible," "prospect," "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: risks that we may not fully enroll the ICARE AD-US study or it will take longer than expected; regulatory authorities may require additional information or further studies, or may fail or refuse to approve or may delay approval of our drug candidates, including ADUHELM; unexpected concerns that may arise from additional data or analysis obtained during clinical trials; actual timing and content of submissions to and decisions made by the regulatory authorities regarding ADUHELM; the occurrence of adverse safety events, restrictions on use or product liability claims; risks of unexpected costs or delays; the risk of other unexpected hurdles; failure to protect and enforce our data, intellectual property and other proprietary rights and uncertainties relating to intellectual property claims and challenges; third party collaboration risks; the direct and indirect impacts of the ongoing COVID-19 pandemic on our business, results of operations and financial condition; and any other risks and uncertainties that are described 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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