# Biogen and Eisai Announce ADUHELM™ (aducanumab-avwa) Data Presentations at Alzheimer's Association International Conference 2021

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- *Item-level analysis from EMERGE trial shows consistency in slowing decline across cognitive, functional and behavioral measures in early Alzheimer's disease*
- *Presentations include an assessment of the correlation between reductions in amyloid beta and other biomarkers of Alzheimer's disease and clinical decline after treatment with ADUHELM*
- *Presentation on ARIA data from Phase 3 trials provides insights for monitoring and management in real-world clinical practice*

CAMBRIDGE, Mass., July 26, 2021 (GLOBE NEWSWIRE) -- Biogen (Nasdaq: BIIB) and Eisai Co., Ltd. (Tokyo, Japan) today announced that Biogen, as part of its Alzheimer's disease (AD) research portfolio, will contribute four virtual posters that showcase data from its clinical trials with ADUHELM™ (aducanumab-avwa) injection 100 mg/mL solution at the Alzheimer's Association International Conference (AAIC), being held in Denver, Colo. and virtually from July 26-30, 2021,

ADUHELM was recently granted accelerated approval by the U.S. Food and Drug Administration (FDA) as a treatment for 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).

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.

"Our presentations to the dementia research community at AAIC of this robust set of clinical trial data will allow us to engage directly with scientists and neurologists on in-depth analyses of our findings," said Alfred Sandrock, Jr., M.D., Ph.D., Head of Research and Development at Biogen. "We are looking forward to sharing our analyses on biomarkers, ARIA and safety management, the pre-specified clinical endpoints in the Phase 3 ADUHELM trials and more."

"The clinical trial results Biogen shared about our joint asset, ADUHELM, at AAIC are important as we believe the data will help inform the scientific community as we continue to explore the strong scientific rationale behind the amyloid beta pathway as one of the earliest changes that occur in Alzheimer's disease," said Lynn Kramer, M.D., Chief Clinical Officer, Neurology Business Group, Eisai.

**ADUHELM Poster Presentations**

**Item-level Analysis of Clinical Measures in Patients with Early Symptomatic Alzheimer's Disease Following Treatment with High-dose Aducanumab in the Phase 3 Study EMERGE**

A poster presentation about item-level data from the EMERGE trial examines results on the individual items, or domains, that comprised the study's pre-specified endpoints measuring cognition, function and behavior. This analysis shows consistency of high-dose aducanumab treatment effect across these individual items and domains of the primary, secondary and tertiary clinical endpoints in the Phase 3 trial.

In this data set from EMERGE, treatment effects were observed across all six domains (three cognitive and three functional) measured by Clinical Dementia Rating-Sum of Boxes (CDR-SB), the primary endpoint of the trial. Secondary endpoints of the trial included change from baseline in the Alzheimer's Disease Assessment Scale – Cognitive Subscale (13 items) (ADAS-Cog13) and the Alzheimer's Disease Cooperative Study-Activities of Daily Living Inventory (Mild Cognitive Impairment version) (ADCS-ADL-MCI). Treatment effects were observed across ADAS-Cog13 items sensitive to cognitive change in early symptomatic Alzheimer's disease and across a broad range of items measuring ability to conduct activities of daily living, as measured by ADCS-ADL-MCI.

Treatment was also associated with a reduction in the behavioral and psychiatric symptoms of Alzheimer's disease, as measured by the Neuropsychiatric Inventory-10 (NPI-10), the tertiary efficacy endpoint of EMERGE.

These results are consistent with the results from the primary analysis of these pre-specified endpoints in EMERGE, endpoints that were selected to measure the broad array of cognitive, functional and behavioral symptoms experienced by individuals with Alzheimer's disease. The analysis concludes that, in EMERGE, treatment with high-dose aducanumab demonstrated reduced clinical decline evidenced by a statistically significant treatment effect on pre-specified primary and secondary clinical efficacy endpoints compared to placebo.

**Reductions in Biomarkers of Alzheimer's Disease Pathophysiology Following Treatment with Aducanumab Were Associated with Slowing in Clinical Decline**

A separate poster presentation examines whether an aducanumab-induced reduction in brain amyloid beta (Aβ) plaques and downstream biomarkers of Alzheimer's disease pathophysiology are associated with a slowing of clinical decline.

The authors assessed this through three analyses. The first, a group-level analysis, examined the association between treatment effect of aducanumab relative to placebo on brain Aβ plaque levels and clinical decline, as measured by amyloid positron emission tomography (PET) imaging and CDR-SB, respectively, across all aducanumab dose groups in the PRIME, EMERGE and ENGAGE clinical trials. Group-level analyses based on

data from these trials demonstrated a positive association between aducanumab treatment effect on brain amyloid beta plaques and clinical measures across dose groups and studies, with the exception of the high-dose group from ENGAGE.

The second set of analyses assessed the relationship between treatment effects of aducanumab on brain Aβ plaque levels, downstream biomarkers of Alzheimer's disease pathophysiology and clinical measures in participant-level analyses. In EMERGE and PRIME, a greater reduction in brain Aβ plaque levels was associated with less decline across clinical endpoints in each study. In EMERGE, greater reduction in brain Aβ plaque levels was also associated with greater reduction in cerebrospinal fluid (CSF) markers of tau and neurodegeneration as well as less decline on clinical endpoints. Several of these relationships were not apparent in ENGAGE, in which a clinical treatment effect of aducanumab was not observed.

The third analysis showed that a smaller magnitude of clinical decline was observed in patients in PRIME, EMERGE and ENGAGE whose brain Aβ plaque levels were lowered to a threshold considered to be amyloid negative relative to patients who did not reach this threshold. Together, these results are consistent with the hypothesized mechanism of action of aducanumab and support a relationship between aducanumab-induced changes in biomarkers of Alzheimer's disease pathophysiology and slowing of clinical decline.

**Additional ADUHELM Poster Presentations**

Biogen will present two additional virtual posters about ADUHELM.

- "Subgroup Analyses of the Amyloid PET Substudies from EMERGE and ENGAGE, Phase 3 Clinical Trials Evaluating Aducanumab in Patients with Early Alzheimer's Disease" is a poster that examines how aducanumab affected brain Aβ plaque levels in Alzheimer's disease patients stratified into 13 pre-specified subgroups based on 6 baseline factors: ApoE ε4 status, baseline clinical stage (MCI due to Alzheimer's disease or mild Alzheimer's disease dementia), baseline severity (MMSE), baseline use of other approved Alzheimer's disease therapies, age and sex. In all 13 pre-specified subgroups, there was a dose-dependent reduction in Aβ plaque levels relative to placebo for patients in the low-dose and high-dose groups across both EMERGE and ENGAGE, consistent with the results of the overall amyloid PET substudy population.
- "Considerations for the real-world management of ARIA from the aducanumab Phase 3 studies EMERGE and ENGAGE" is a poster that describes the characteristics of Amyloid Related Imaging Abnormalities (ARIA) that occurred in participants treated with high-dose (10 mg/kg) aducanumab in EMERGE and ENGAGE, in order to inform ARIA monitoring and management in real-world clinical practice. Included in the poster are data on ARIA incidence, radiographic severity and symptoms in ApoE ε4 carriers and noncarriers; timing of ARIA-E radiographic detection and resolution; the relationship between radiographic severity and symptoms; and outcomes of dosing through mild, asymptomatic ARIA. In the U.S., ARIA monitoring and management should be carried out in accordance with the recommendations in the U.S. Prescribing Information. The poster's conclusions include:
    - ARIA were mostly asymptomatic: 76% of aducanumab-treated participants with ARIA showed no symptoms.
    - ARIA were generally mild or moderate in radiographic severity and were transient.
    - Radiographic severity and symptomatic status were similar for ApoE ε4 carriers and noncarriers.
    - Radiographic severity of ARIA alone is not predictive of symptomatic status.
    - Radiographically severe ARIA-H was generally concurrent with ARIA-E.
    - New-onset symptoms were noted in approximately 6 percent of ARIA events where dosing was continued.

Posters and presentations will be available for 30 days on the AAIC conference website. They will also be available on Biogen.com.

**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.

**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: the potential clinical effects of ADUHELM and BIIB080; the potential benefits, safety and efficacy of ADUHELM and BIIB080; the results of the Phase 3 studies and Phase 1b study of ADUHELM and the Phase 1b study of BIIB080; the identification and treatment of Alzheimer's disease; potential regulatory approvals and the timing thereof; the potential of our commercial business and pipeline programs, including ADUHELM and BIIB080; 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 BIIB080; 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: 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 and BIIB080; 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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