Update on Regulatory Submission for Aducanumab in the European Union

December 17, 2021

Biogen to seek re-examination following CHMP negative opinion for aducanumab

CAMBRIDGE, Mass., Dec. 17, 2021 (GLOBE NEWSWIRE) -- Biogen Inc. (Nasdaq: BIIB) and Eisai Co., Ltd. (Tokyo, Japan) today announced that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has adopted a negative opinion on the Marketing Authorization Application (MAA) for aducanumab for the treatment of the early stages of Alzheimer's disease known as mild cognitive impairment (MCI) due to Alzheimer's disease and mild Alzheimer's disease dementia. This decision is aligned to the negative trend vote of the committee in November 2021. Biogen will seek a re-examination of the opinion by the CHMP.

"For Europeans impacted by Alzheimer's disease, the lack of options to treat its early stages is felt every day. The longer we wait, the more people will progress toward more advanced dementia and we may miss the opportunity to potentially treat them," said Priya Singhal, M.D., M.P.H., Head of Global Safety & Regulatory Sciences and interim Head of Research & Development at Biogen. "As part of the re-examination process, we will seek to address the CHMP's grounds for refusal, with the goal of making this medicine available in the EU. European patients deserve access to innovative treatments for Alzheimer's disease."

The European Commission's regulations [1] allow an applicant to request a re-examination of a CHMP opinion, followed by submission of documentation with detailed grounds for the request. The Committee has 60 days after receipt of this documentation to re-examine their opinion[2].

The MAA included efficacy, safety and biomarker data from a global, multi-study clinical development program which included approximately 3,600 patients in more than 20 countries.

In June 2021, the U.S. Food and Drug Administration (FDA) granted accelerated approval for ADUHELM® (aducanumab-avwa) 100 mg/mL injection for intravenous use as the first Alzheimer's disease treatment to address a defining pathology of the disease by reducing amyloid beta plaques in the brain. ADUHELM is also approved in the United Arab Emirates (UAE).

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

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 U.S. full Prescribing Information, including Medication Guide, for ADUHELM.

About Alzheimer's Disease
Alzheimer's disease is a progressive neurological condition that impairs thinking, memory and independence, leading to premature death. The disease is a growing global health crisis, affecting those living with the disease and their families. According to the World Health Organization (WHO), more than 30 million people worldwide live with Alzheimer's disease, and the number will grow in the years ahead, outpacing the healthcare resources needed to manage it and costing billions of dollars.

Alzheimer's disease is characterized by changes in the brain, including the abnormal accumulation of toxic amyloid beta plaques, which begins approximately 20 years before patients exhibit symptoms of the disease. Mild cognitive impairment due to Alzheimer's disease is one of the earliest symptomatic stages of the disease when symptoms start to be more visible and can be detected and diagnosed.
For more information about Alzheimer's disease, visit www.ItsTimeWeKnow.com.

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, the potential clinical effects of ADUHELM; the potential benefits, safety and efficacy of ADUHELM; Biogen's strategy and plans; potential of, and expectations for, Biogen's commercial business and pipeline programs, including ADUHELM; planning and timing for the commercial launch of, and access to, ADUHELM; anticipated manufacturing, distribution, and supply of ADUHELM; the treatment of Alzheimer's disease; the anticipated benefits and potential of Biogen's collaboration arrangements with Eisai; the potential of Biogen's commercial business and pipeline programs, including ADUHELM; 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, uncertainty of success in the development and commercialization of ADUHELM; risks relating to the launch of ADUHELM, including preparedness of healthcare providers to treat patients, the ability to obtain and maintain adequate reimbursement for ADUHELM, and other unexpected difficulties or hurdles; unexpected concerns that may arise from additional data or analysis obtained during clinical trials; the occurrence of adverse safety events, restrictions on use, or product liability claims; regulatory authorities may require additional information or further studies, or may fail or refuse to approve or may delay approval of Biogen's drug candidates, including ADUHELM; risks of unexpected costs or delays; the risk of other unexpected hurdles; risks relating to investment in our manufacturing capacity; problems with our manufacturing processes; 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; risks associated with current and potential future healthcare reforms; risks relating to the distribution and sale by third parties of counterfeit or unfit versions of our products; and the direct and indirect impacts of the ongoing COVID-19 pandemic on our 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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[1] EC guideline: REGULATION (EC) No 726/2004 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 31 March 2004 (https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2004:136:0001:0033:en:PDF)

[2] European Medicines Agency, *Procedural Advice on the Re-Examination of CHMP Opinions*, 2009. https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/procedural-advice-re-examination-chmp-opinions_en.pdf