An open letter to the Alzheimer's disease community from our Head of Research and Development, Alfred Sandrock, M.D., Ph.D.

July 22, 2021

NOTE: *ADUHELM* [TM] *(aducanumab-avwa) injection 100 mg/mL solution 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).*
Please see full Prescribing Information including Medication Guide.

CAMBRIDGE, Mass., July 22, 2021 (GLOBE NEWSWIRE) -- Biogen Inc. (Nasdaq: BIIB) - On June 7, 2021, ADUHELM became the first approved treatment to address a defining pathology of Alzheimer's disease: targeting the reduction of amyloid plaques in the brain. We believe patients, family members and physicians deserve the facts about the therapy and the process by which it was approved so they may make informed decisions.

The approval of ADUHELM by the U.S. Food and Drug Administration (FDA) came after an extensive development, testing and review process. Over more than a decade, we at Biogen engaged in rigorous and science-driven research and development that assessed whether ADUHELM could help patients worldwide who suffer from Alzheimer's disease. We are proud of the work our dedicated team has done to develop ADUHELM, and of the potential it brings to Alzheimer's patients. We are equally proud of the professionalism both our team and the FDA demonstrated during a thorough review process.

Unfortunately, ADUHELM's approval has been the subject of extensive misinformation and misunderstanding. It is normal for scientists and clinicians to discuss data from experiments and clinical trials, to debate, and to disagree, on the interpretation of data. That is how science advances and we welcome these discussions. Recently, however, there has been a turn outside the boundaries of legitimate scientific deliberation.

We welcome a formal review into the interactions between the FDA and Biogen on the path to the approval of aducanumab. A better understanding of the facts is good for everyone involved to assure confidence in both the therapy and the process by which it was approved as we prioritize the issues that affect patients.

A step toward such transparency is to correct some of the misinformation we have seen:

More than 250 drugs have been granted Accelerated Approval by the FDA.

The FDA instituted its Accelerated Approval Program in 1992 to allow for earlier approval of drugs that treat serious conditions, and to fill an unmet medical need based on a surrogate endpoint that is reasonably likely to predict a clinical outcome. Since 1992, 253 accelerated approvals have been granted to drugs to treat HIV/AIDS, sickle cell anemia, Duchenne muscular dystrophy (DMD), multiple sclerosis (MS) and particularly in the oncology therapeutic area. In oncology, for example, the surrogate may be tumor shrinkage, as this is likely to predict increased survival. Many cancer patients have benefitted from novel immunotherapy treatments that have received accelerated approval, and death rates from cancer have declined dramatically.

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 the rate of clinical decline. We believe that this will be further established as we collect more data from the ongoing EMBARK study and the post-marketing confirmatory trial.

Several people have stated that all previously studied anti-amyloid antibodies clear amyloid from the brain but have failed as a class to demonstrate benefit. This is factually incorrect. First generation anti-amyloid antibodies were not specific for aggregated forms of amyloid beta, or targeted soluble monomeric amyloid beta, or were deficient in effector function. As a result, these antibodies do not clear amyloid from the brain. As such, there is no basis for using the failure of these antibodies as a reason to question the approval of ADUHELM.

The review process that led to accelerated approval was extensive and thorough, during which we responded to numerous questions and requests from the FDA. The approval is supported by data of more than 3,000 patients and 2.2 million pages of clinical data and analyses.

Separately, we have seen statements that all of ADUHELM's results are "post hoc" – in other words, that a filter was applied after the fact to interpret the data in a certain way. That is also factually incorrect. The primary and secondary endpoints had been pre-specified in the Phase 3 trial protocols, before the first patient was enrolled into the trials. The ADUHELM label shows the results on these pre-specified endpoints, based on data that had already been collected at the sites by the time the trials were prematurely terminated on March 21, 2019. Safety data were also extensively reviewed and are well documented in the label, so that physicians can make informed benefit-risk decisions and take appropriate actions as they monitor their patients under treatment.

It is important to recognize that collaboration between industry and regulatory agencies is common, appropriate and beneficial. That was exemplified at its best with the COVID-19 vaccine development. As a doctor, a scientist and the Head of Research and Development at Biogen, I believe scientists at regulatory agencies and drug manufacturers must work together in an effort to defeat other devastating public health threats.

The FDA's decision to approve ADUHELM to treat patients with Alzheimer's disease was based on thorough analysis of the data.

As stated by Dr. Patrizia Cavazzoni, Director, the FDA Center for Drug Evaluation and Research, in discussing the agency's decision to approve the treatment: "In all studies in which it was evaluated… ADUHELM consistently and very convincingly reduced the level of amyloid plaques in the brain in a dose- and time-dependent fashion." At the time of approval of ADUHELM, the FDA further stated: "The clinical trials for ADUHELM were the first to show that a reduction in these plaques—a hallmark finding in the brain of patients with Alzheimer's—is expected to lead to a reduction in the clinical decline of this devastating form of dementia."[1]

The FDA also stated: "Although the ADUHELM data are complicated with respect to its clinical benefits, FDA has determined that there is substantial

evidence that ADUHELM reduces amyloid beta plaques in the brain and that the reduction in these plaques is reasonably likely to predict important benefits to patients."[1] The FDA also shared that it "is requiring Biogen to conduct a post-approval clinical trial to verify the drug's clinical benefit."[1]

In the announcement of its decision to approve ADUHELM through its Accelerated Approval pathway, the FDA explained the rigor underlying its analysis: "We examined the clinical trial findings with a fine-tooth comb, we solicited input from the Peripheral and Central Nervous System Drugs Advisory Committee, we listened to the perspectives of the patient community, and we reviewed all relevant data. We ultimately decided to use the Accelerated Approval pathway—a pathway intended to provide earlier access to potentially valuable therapies for patients with serious diseases where there is an unmet need, and where there is an expectation of clinical benefit despite some residual uncertainty regarding that benefit. In determining that the application met the requirements for Accelerated Approval, the Agency concluded that the benefits of ADUHELM for patients with Alzheimer's disease outweighed the risks of the therapy."[1]

ADUHELM is the first Alzheimer's treatment approved since 2003. An important question is being overlooked by many: what would be the impact of deferring access to this treatment, despite the clinical data underlying its approval? Based on our current estimates of the progression rates of the disease, every day over 1,000 Americans will advance from early stages of disease to moderate and severe stages of disease, and thus may progress beyond the stages during which ADUHELM should be initiated.[2] We feel a strong obligation to be able to offer new options to patients with this devastating disease.

ADUHELM's approval is paving the way for more innovation and competition in Alzheimer's disease.

The approval of ADUHELM has already renewed investment activity in Alzheimer's disease research and development, and we are optimistic that other innovative treatments will soon join ADUHELM.

This cycle of innovation is common in the biopharmaceutical industry. It is how HIV/AIDS and many forms of cancer were changed from untreatable diseases into conditions with viable treatment options. MS is another good example. The first MS therapy, introduced in 1993 via the first accelerated approval of a biologic product, set in motion a cycle of innovation that resulted in now more than 20 treatments approved, including six developed by Biogen. These precedents contradict the claims by some who have opined that the approval of ADUHELM would inhibit the development of other drugs for Alzheimer's disease.

We recognize that ADUHELM's dataset was complex and its journey to this point did not follow a conventional path. But the road to innovation is rarely straightforward, and ADUHELM is not an exception. Throughout, our team has worked with steadfast determination to follow the science and be driven by an acute understanding of the pain and suffering Alzheimer's disease inflicts on patients, families and society. We stand behind the clinical evidence provided by the studies and the data-driven scientific approach taken.

We will continue to put science first, be transparent with our data and do all we can to assure that physicians have accurate and complete information on which to base the important decisions regarding their patients' care.

INDICATION and IMPORTANT SAFETY INFORMATION

INDICATION
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).

IMPORTANT SAFETY INFORMATION
What is the most important information a patient should know about ADUHELM?
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.** It is most commonly seen as temporary swelling in areas of the brain that usually resolves over time. Some people may also have small spots of bleeding in or on the surface of the brain with the swelling. Although most people with swelling in areas of the brain 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. **Patients should call their healthcare provider or go to the nearest hospital emergency room right away if they have any of the symptoms listed above.**

Before receiving ADUHELM, patients should tell their healthcare provider about all of their medical conditions, including if: they are pregnant or plan to become pregnant or are breastfeeding or plan to breastfeed. It is not known if ADUHELM will harm their unborn baby or if aducanumab-avwa (the active ingredient in ADUHELM) passes into breast milk.

What are the possible side effects of ADUHELM? ADUHELM can cause serious side effects, including: See above "What is the most important information a patient should know about ADUHELM?"

Serious allergic reactions. Swelling of the face, lips, mouth, or tongue and hives have happened during an ADUHELM infusion. Patients should tell their healthcare provider if they have any of the symptoms of a serious allergic reaction during or after an ADUHELM infusion.

The most common side effects of ADUHELM include: swelling in areas of the brain, with or without small spots of bleeding in or on the surface of the brain (ARIA); headache and fall. Patients should call their healthcare provider for medical advice about side effects. Patients may report side effects to FDA at 1-800-FDA-1088.

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.

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 anticipated benefits and potential of our collaboration arrangements with Eisai; the clinical development program and future clinical trial(s) 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: regulatory submissions may take longer or be more difficult to complete 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.

[1] https://www.fda.gov/drugs/news-events-human-drugs/fdas-decision-approve-new-treatment-alzheimers-disease

[2] Biogen date on file

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