Press release

Eisai initiates rolling Biologics License Application to US FDA for Leqembi® (lecanemab-irmb) for subcutaneous maintenance dosing

Stockholm, Sweden, May 15, 2024 – BioArctic AB's (publ) (Nasdaq Stockholm: BIOA B) partner Eisai announced today that they have initiated the rolling submission of a Biologics License Application (BLA) to the U.S. Food and Drug Administration (FDA) for lecanemab-irmb (U.S. brand name: Leqembi) subcutaneous autoinjector for weekly maintenance dosing after it was granted Fast Track designation by the FDA. In the US, Leqembi is indicated for the treatment of Alzheimer's disease (AD) in patients with Mild Cognitive Impairment (MCI) or mild dementia stage of disease (collectively referred to as early AD).

Leqembi is approved for biweekly intravenous (IV) treatment, which is normally done at medical facilities. Subcutaneous administration with an autoinjector simplifies home treatment and the injection process requires less time than the IV formulation. This makes the treatment easier for patients and their care partners and may reduce the need for hospital visits and nursing care compared to IV administration, in addition to being more convenient for patients to continue the treatment.

Alzheimer's disease is an ongoing neurotoxic process that begins before and continues after amyloid-beta (Aβ) plaque deposition, which is a hallmark of the disease. Data suggests that early and continued treatment may prolong the benefit even after Aβ plaque is cleared from the brain. If approved by the FDA, patients who have completed the biweekly IV initiation phase could transfer to the subcutaneous autoinjector 360 mg weekly maintenance regimen, currently under review. This would maintain effective drug concentrations to sustain the clearance of highly toxic protofibrils[i] which can continue to cause neuronal injury even after the Aβ plaque has been cleared from the brain. The BLA is based on data from the Phase 3 Clarity AD open-label extension (OLE) study, and modeling of observed data.

Leqembi is now approved in the U.S., Japan and China, and applications have been submitted for review in the European Union, Australia, Brazil, Canada, Hong Kong, Great Britain, India, Israel, Russia, Saudi Arabia, South Korea, Taiwan, Singapore and Switzerland. In March 2024, Eisai submitted to the FDA a Supplemental Biologics License Application (sBLA) for less frequent monthly IV maintenance dosing of Leqembi.

Eisai serves as the lead of Leqembi development and regulatory submissions globally with both Eisai and Biogen co-commercializing and co-promoting the product and Eisai having final decision-making authority. BioArctic has the right to commercialize lecanemab in the Nordic region, pending European approval, and currently Eisai and BioArctic are preparing for a joint commercialization in the region.

This information is information that BioArctic AB (publ) is obliged to disclose pursuant to the EU Market Abuse Regulation. The information was released for public disclosure, through the agency of the contact persons below, on May 15, 2024, at 01.30 a.m. CET.

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About lecanemab (generic name, U.S., Japan and China brand name: Leqembi®)
Lecanemab (Leqembi) is the result of a strategic research alliance between BioArctic and Eisai. It is a humanized immunoglobulin gamma 1 (IgG1) monoclonal antibody directed against aggregated soluble (protofibril) and insoluble forms of amyloid-beta (Aβ). Lecanemab is approved in the U.S., Japan, and China with the following indications:

- U.S.: For the treatment of Alzheimer's disease (AD). It should be initiated in patients with mild cognitive impairment or mild dementia stage of disease. See full US prescribing information including boxed waring.
- Japan: For slowing progression of mild cognitive impairment (MCI) and mild dementia due to AD.
- China: For the treatment of MCI due to AD and mild AD dementia.

Lecanemab approvals were based on the large global Phase 3 Clarity AD study. In the Clarity AD study, lecanemab met its primary endpoint and all key secondary endpoints with statistically significant results. In November 2022, the results of the Clarity AD study were presented at the 2022 Clinical Trials on Alzheimer's Disease (CTAD) conference, and simultaneously published in the New England Journal of Medicine, a peer-reviewed medical journal.

Eisai has also submitted applications for approval of lecanemab in 14 countries and regions, including the European Union (EU).

Eisai has completed a lecanemab subcutaneous bioavailability study, and subcutaneous dosing is currently being evaluated in the Clarity AD (Study 301) open-label extension (OLE) study. A maintenance dosing regimen has been evaluated as part of the Phase 2b study (Study 201).

Since July 2020 Eisai's Phase 3 clinical study (AHEAD 3-45) for individuals with preclinical AD, meaning they are clinically normal and have intermediate or elevated levels of amyloid in their brains, is ongoing. AHEAD 3-45 is conducted as a public-private partnership between the Alzheimer's Clinical Trial Consortium that provides the infrastructure for academic clinical trials in AD and related dementias in the U.S, funded by the National Institute on Aging, part of the National Institutes of Health and Eisai. Since January 2022, the Tau NexGen clinical study for Dominantly Inherited AD (DIAD), that is conducted by Dominantly Inherited Alzheimer Network Trials Unit (DIAN-TU), led by Washington University School of Medicine in St. Louis, is ongoing and includes lecanemab as the backbone anti-amyloid therapy.

About the collaboration between BioArctic and Eisai
Since 2005, BioArctic has a long-term collaboration with Eisai regarding the development and

commercialization of drugs for the treatment of Alzheimer's disease. The most important agreements are the Development and Commercialization Agreement for the lecanemab antibody, which was signed 2007, and the Development and Commercialization agreement for the antibody Leqembi back-up for Alzheimer's disease, which was signed 2015. In 2014, Eisai and Biogen entered into a joint development and commercialization agreement for lecanemab. Eisai is responsible for the clinical development, application for market approval and commercialization of the products for Alzheimer's disease. BioArctic has the right to commercialize lecanemab in the Nordic region under certain conditions and is currently preparing for commercialization in the Nordics together with Eisai. BioArctic has no development costs for lecanemab in Alzheimer's disease and is entitled to payments in connection with regulatory approvals, and sales milestones as well as royalties on global sales.

About BioArctic AB

BioArctic AB (publ) is a Swedish research-based biopharma company focusing on treatments that can delay or stop the progression of neurodegenerative diseases. The company invented Leqembi® (lecanemab) – the world's first drug proven to slow the progression of the disease and reduce cognitive impairment in early Alzheimer's disease. Leqembi has been developed together with BioArctic's partner Eisai, who are responsible for regulatory interactions and commercialization globally. In addition to Leqembi, BioArctic has a broad research portfolio with antibodies against Parkinson's disease and ALS as well as additional projects against Alzheimer's disease. Several of the projects utilize the company's proprietary BrainTransporter™ technology, which has the potential to actively transport antibodies across the blood-brain barrier to enhance the efficacy of the treatment. BioArctic's B share (BIOA B) is listed on Nasdaq Stockholm Large Cap. For further information, please visit www.bioarctic.se.

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[i] Protofibrils are believed to contribute to the brain injury that occurs with AD and are considered to be the most toxic form of Aβ, having a primary role in the cognitive decline associated with this progressive, debilitating condition.[ii] Protofibrils cause injury to neurons in the brain, which in turn, can negatively impact cognitive function via multiple mechanisms, not only increasing the development of insoluble Aβ plaques but also increasing direct damage to brain cell membranes and the connections that transmit signals between nerve cells or nerve cells and other cells. It is believed the reduction of protofibrils may prevent the progression of AD by reducing damage to neurons in the brain and cognitive dysfunction.[iii]

[ii] Amin L, Harris DA. Aβ receptors specifically recognize molecular features displayed by fibril ends and neurotoxic oligomers. Nat Commun. 2021;12:3451. doi:10.1038/s41467-021-23507-z

[iii] Ono K, Tsuji M. Protofibrils of Amyloid-β are Important Targets of a Disease-Modifying Approach for Alzheimer's Disease. Int J Mol Sci. 2020;21(3):952. doi: 10.3390/ijms21030952. PMID: 32023927; PMCID: PMC7037706.