BIOARCTIC

Press release

FDA approves LEQEMBI™ (lecanemab-irmb) under the Accelerated Approval pathway for the treatment of Alzheimer's disease

Stockholm, January 6, 2023 – BioArctic AB's (publ) (Nasdaq Stockholm: BIOA B) partner Eisai announced today that under the Accelerated Approval pathway the U.S. Food and Drug Administration (FDA) has approved lecanemab-irmb[1] (Brand Name in the U.S.: LEQEMBI™) 100 mg/mL injection for intravenous use, a humanized immunoglobulin gamma 1 (IgG1) monoclonal antibody directed against aggregated soluble ("protofibrils[2]") and insoluble forms of amyloid beta (Aβ) for the treatment of Alzheimer's disease (AD). The accelerated approval is based on Phase 2b data in early AD patients which demonstrated that LEQEMBI reduced the accumulation of Aβ plaque in the brain, a defining feature of AD. Using the recently published data from the large global confirmatory Phase 3 clinical trial, Clarity AD, Eisai will work quickly to file a Supplemental Biologics License Application (sBLA) to the FDA for approval under the traditional pathway. The approval of lecanemab-irmb by the FDA entitles BioArctic to a milestone payment of MEUR 25 from Eisai.

Indication
LEQEMBI is indicated for the treatment of Alzheimer's disease. Treatment with LEQEMBI 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. This indication is approved under accelerated approval based on reduction in amyloid beta plaques observed in patients treated with LEQEMBI. Continued approval for this indication may be contingent upon verification of clinical benefit in a confirmatory trial.

Dosage and administration (patient selection, dosing instructions, monitoring and dosing interruption for ARIA)
The recommended dosage of LEQEMBI is 10 mg/kg administered intravenously once every two weeks to eligible patients with confirmed presence of Aβ pathology prior to initiating treatment. Enhanced clinical vigilance for amyloid-related imaging abnormalities (ARIA) is recommended during the first 14 weeks of treatment with LEQEMBI. Baseline, recent (within one year) brain MRI prior to initiating treatment with LEQEMBI and periodic monitoring with MRI prior to the 5th, 7th, and 14th infusions are obtained.

[1] Lecanemab has been given the -irmb add-on by the FDA for the approved substance. -irmb is a suffix required by the FDA. Suffixes are used to differentiate originator biological products, related biological products, and biosimilar products containing related drug substances
[2] protofibrils is large Aβ aggregated soluble species of 75-500 Kd.

Adverse reactions
The safety of LEQEMBI has been evaluated in 763 patients who received at least one dose of LEQEMBI. The most common adverse reactions reported in at least 5% of patients treated with LEQEMBI 10 mg/kg biweekly (N=161) and at least 2% higher incidence than patients on placebo (N=245) were infusion-related reactions (LEQEMBI, 20%; placebo, 3%), headache (LEQEMBI, 14%; placebo, 10%), ARIA-E (LEQEMBI, 10%; placebo, 1%), cough (LEQEMBI, 9%; placebo, 5%) and diarrhea (LEQEMBI, 8%; placebo, 5%). The most common adverse reaction leading to discontinuation of LEQEMBI was infusion-related reactions which happened in 2% (4/161) of patients treated with LEQEMBI compared to 1% (2/245) of patients on placebo.

Concomitant antithrombotic medication and other risk factors for intra-cerebral hemorrhage
In Phase 2b, patients who received LEQEMBI and an antithrombotic medication (aspirin, other antiplatelets, or anticoagulants) did not have an increased risk of ARIA-H compared to patients who received placebo and an antithrombotic medication. The majority of exposures to antithrombotic medications were to aspirin; few patients were exposed to other antiplatelet drugs or anticoagulants, limiting any meaningful conclusions about the risk of ARIA or intracerebral hemorrhage in patients taking other antiplatelet drugs or anticoagulants. Because intracerebral hemorrhages greater than 1 cm in diameter have been observed in patients taking LEQEMBI, additional caution should be exercised when considering the administration of antithrombotics or a thrombolytic agent (e.g., tissue plasminogen activator) to a patient already being treated with LEQEMBI. Additionally, patients were excluded from enrollment in Phase 2b for the following risk factors for intracerebral hemorrhage: prior cerebral hemorrhage greater than 1 cm in greatest diameter, more than 4 microhemorrhages, superficial siderosis, evidence of vasogenic edema, evidence of cerebral contusion, aneurysm, vascular malformation, infective lesions, multiple lacunar infarcts or stroke involving a major vascular territory, and severe small vessel or white matter disease. Caution should be exercised when considering the use of LEQEMBI in patients with these risk factors.

“The FDA’s approval of LEQEMBI under the Accelerated Approval pathway is an important milestone not only for BioArctic and our partner Eisai, but for the whole field as well as for patients, families and caregivers who can now benefit from the more than 20 years of research and development that lies behind this achievement. We are impressed by our partner Eisai’s excellent work with LEQEMBI and are proud of our long-standing relationship that has led us to today’s announcement,” said Gunilla Osswald, CEO at BioArctic.

LEQEMBI's access and initiatives to support people living with Alzheimer’s disease
The Eisai Patient Support Program will be available to offer several support programs to help patients and care partners. Dedicated Patient Navigators will work directly with patients and families to navigate treatment and coverage for eligible and appropriate patients and to help with what to expect regarding insurance coverage, co-pay and patient access programs. To learn more visit LEQEMBI.com, call 1-833-4-LEQEMBI (1-833-453-7362), Monday-Friday, 8 a.m. to 8 p.m. Eastern Time or by fax at 1-833-770-7017.
In addition, to support access to LEQEMBI for certain financially disadvantaged patients, Eisai’s Patient Assistance Program (PAP) will provide LEQEMBI at no cost, for eligible uninsured and

underinsured patients, including Medicare beneficiaries, who meet financial need and other program criteria.

Eisai has stated that they will continue to engage constructively with various payors, including the Centers for Medicare and Medicaid (CMS), TRICARE, the U.S. Veteran's Health Administration and private health insurance companies to ensure appropriate beneficiaries have access to this new therapy. Currently Medicare patients do not have access to LEQEMBI. Medicaid sole beneficiaries who are diagnosed by a healthcare professional with early AD and with confirmed presence of amyloid plaque in the brain will have access to LEQEMBI under the Medicaid program post accelerated approval, depending on individual state processes.

Furthermore, Eisai is developing a multi-faceted educational initiative to further advance the understanding in the AD healthcare community of the real-world management and monitoring of ARIA. This initiative, *Understanding ARIA*™, will provide resources and programs that will include peer-to-peer education, individual and group educational sessions and subject-matter-expert evaluation of historical case studies. *Understanding ARIA* will include engagements with leading experts in medical imaging as well as major professional societies. Initial resources will be available by January 2023.

LEQEMBI will be available during or before the week of January 23, 2023. Eisai has announced the U.S. pricing and rationale for LEQEMBI today in a separate news release. Eisai has based on a health economic analysis estimated the yearly societal value of Leqembi to be 37,600 USD per patient in the US. Eisai has decided to set the US launch price for Leqembi to 26,500 USD per year for the average patient, aiming to promote broader patient access, reduce overall financial burden and support health system sustainability.

Eisai has also issued a separate news release today regarding Eisai´s commitment to scientific evidence and patient safety. Both these news releases can be found on Eisai's website.

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 right to commercialize lecanemab in the Nordic under certain conditions and is currently preparing for commercialization in the Nordics together with Eisai.

INDICATION, dosage and administration, and important safety information in the U.S.

INDICATION
LEQEMBI is indicated for the treatment of Alzheimer's disease. Treatment with LEQEMBI 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 LEQEMBI. Continued approval for this indication may be contingent upon verification of clinical benefit in a confirmatory trial.

IMPORTANT SAFETY INFORMATION
WARNINGS AND PRECAUTIONS
Amyloid Related Imaging Abnormalities
LEQEMBI can cause amyloid related imaging abnormalities-edema (ARIA-E) and -hemosiderin deposition (ARIA-H) ARIA-E can be observed on MRI as a brain edema or sulcal effusions, and ARIA-H as microhemorrhage and superficial siderosis. ARIA is usually asymptomatic, although serious and life-threatening events, including seizure and status epilepticus, rarely can occur. Reported symptoms associated with ARIA may include headache, confusion, visual changes, dizziness, nausea, and gait difficulty. Focal neurologic deficits may also occur. Symptoms associated with ARIA usually resolve over time.

ARIA monitoring and dose management guidelines

- Obtain recent (within one year) brain magnetic resonance imaging (MRI) prior to initiating treatment with LEQEMBI. Obtain an MRI prior to the 5th, 7th, and 14th infusions.
- Recommendations for dosing in patients with ARIA-E and ARIA-H depend on clinical symptoms and radiographic severity. Depending on ARIA severity, use clinical judgment in considering whether to continue dosing, continue treatment, or permanently discontinue LEQEMBI.
- Enhanced clinical vigilance for ARIA is recommended during the first 14 weeks of treatment with LEQEMBI. If a patient experiences symptoms suggestive of ARIA, clinical evaluation should be performed, including MRI if indicated. If ARIA is observed on MRI, careful clinical evaluation should be performed prior to continuing treatment.
- There is no experience in patients who continued dosing through symptomatic ARIA-E or through asymptomatic, but radiographically severe, ARIA-E. There is limited experience in patients who continued dosing through asymptomatic but radiographically mild to moderate ARIA-E. There are limited data in dosing patients who experienced recurrent ARIA-E.

Incidence of ARIA

- In Study 1 (Phase 2b), symptomatic ARIA-E occurred in 3% (5/161) of LEQEMBI-treated patients. Clinical symptoms associated with ARIA resolved in 80% of patients during the period of observation.
- Including asymptomatic cases, ARIA was observed in LEQEMBI: 12% (20/161), placebo: 5% (13/245). ARIA-E was observed in LEQEMBI: 10% (16/161), placebo: 1% (2/245). ARIA-H was

observed in LEQEMBI: 6% (10/161), placebo 5% (12/245). There was no increase in isolated ARIA-H for LEQEMBI compared to placebo.
- Intracerebral hemorrhage >1 cm in diameter was reported after one treatment in LEQEMBI: 1 patient, placebo: zero patients. Events of intracerebral hemorrhage, including fatal events, in patients taking LEQEMBI have also been reported in other studies.

Apolipoprotein E ε4 (ApoE ε4) carrier status and risk of ARIA

- In Study 1 (Phase 2b), 6% (10/161) of patients in the LEQEMBI group were ApoE ε4 homozygotes, 24% (39/161) were heterozygotes, and 70% (112/161) were noncarriers.
- The incidence of ARIA was higher in APOE ε4 homozygotes than in heterozygotes and noncarriers among patients treated with LEQEMBI. Of the 5 LEQEMBI-treated patients who had symptomatic ARIA, 4 were ApoE ε4 homozygotes, 2 of whom experienced severe symptoms. An increased incidence of symptomatic and overall ARIA in ApoE ε4 homozygotes compared to heterozygotes and noncarriers in LEQEMBI-treated patients has been reported in other studies.
- The recommendations on management of ARIA do not differ between ApoE ε4 carriers and noncarriers.
- Consider testing for ApoE ε4 status to inform the risk of developing ARIA when deciding to initiate treatment with LEQEMBI.

Radiographic findings

- The majority of ARIA-E radiographic events occurred early in treatment (within the first 7 doses), although ARIA can occur at any time and patients can have more than 1 episode. The maximum radiographic severity of ARIA-E in patients treated with LEQEMBI was mild in 4% (7/161) of patients, moderate in 4% (7/161) of patients, and severe in 1% (2/161) of patients. Resolution on MRI occurred in 62% of ARIA-E patients by 12 weeks, 81% by 21 weeks, and 94% overall after detection. The maximum radiographic severity of ARIA-H microhemorrhage in patients treated with LEQEMBI was mild in 4% (7/161) of patients and severe in 1% (2/161) of patients; 1 of the 10 patients with ARIA-H had mild superficial siderosis.

Concomitant antithrombotic medication and other risk factors for intra-cerebral hemorrhage

- Patients were excluded from enrollment in Study 1 (Phase 2b) based on baseline use of anticoagulant medications. Antiplatelet medications such as aspirin and clopidogrel were allowed. If anticoagulant medication was used because of intercurrent medical events that required treatment for ≤4 weeks, treatment with LEQEMBI was to be temporarily suspended.
- Most exposures to antithrombotic medications were to aspirin; few patients were exposed to other antiplatelet drugs or anticoagulants, limiting any meaningful conclusions about the risk of ARIA or intracerebral hemorrhage in patients taking other antiplatelet drugs or anticoagulants. Because intracerebral hemorrhages >1 cm in diameter have been observed in patients taking LEQEMBI, additional caution should be exercised when considering the administration of antithrombotics or a thrombolytic agent (e.g., tissue plasminogen activator) to a patient already being treated with LEQEMBI.
- Patients were excluded from enrollment in Study 1 (Phase 2b) for the following risk factors for intra-cerebral hemorrhage: prior cerebral hemorrhage greater than> 1 cm in greatest

diameter, more than 4 microhemorrhages, superficial siderosis, evidence of vasogenic edema, evidence of cerebral contusion, aneurysm, vascular malformation, infective lesions, multiple lacunar infarcts or stroke involving a major vascular territory, severe small vessel or white matter disease. Caution should be exercised when considering the use of LEQEMBI in patients with these risk factors.

Infusion-related reactions

- Infusion-related reactions were observed in LEQEMBI: 20% (32/161), placebo: 3% (8/245, and the majority (88%, 28/32) occurred with the first infusion. All infusion-related reactions were mild (56%) or moderate (44%) in severity. Infusion-related reactions resulted in discontinuations in 2% (4/161) of patients treated with LEQEMBI. Symptoms of infusion-related reactions include fever and flu-like symptoms (chills, generalized aches, feeling shaky, and joint pain), nausea, vomiting, hypotension, hypertension, and oxygen desaturation.
- After the first infusion, 38% of LEQEMBI-treated patients had transient decreased lymphocyte counts to less than 0.9 $x10^9$/L compared to 2% in patients on placebo, and 22% of patients treated with LEQEMBI had transient increased neutrophil counts to greater 7.9 $x10^9$/L compared to 1% of patients on placebo.
- In the event of an infusion-related reaction, the infusion rate may be reduced, or the infusion may be discontinued, and appropriate therapy initiated as clinically indicated. Prophylactic treatment with antihistamines, acetaminophen, nonsteroidal anti-inflammatory drugs, or corticosteroids prior to future infusions may be considered.

ADVERSE REACTIONS

- In Study 1 (Phase 2b), 15% of LEQEMBI-treated patients, compared to 6% of placebo-treated patients, stopped study treatment because of an adverse reaction. The most common adverse reaction leading to discontinuation of LEQEMBI was infusion-related reactions that led to discontinuation in 2% (4/161) of patients treated with LEQEMBI compared to 1% (2/245) of patients on placebo.
- The most common adverse reactions reported in ≥5% of patients treated with LEQEMBI (N=161) and ≥2% higher than placebo (N=245) in Study 1 (Phase 2b) were infusion-related reactions (LEQEMBI, 20%; placebo, 3%), headache (LEQEMBI, 14%; placebo, 10%), ARIA-E (LEQEMBI, 10%; placebo, 1%), cough (LEQEMBI, 9%; placebo, 5%) and diarrhea (LEQEMBI, 8%; placebo, 5%).

Please see full Prescribing Information.

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 person below, on January 6, 2023, at 20:30 a.m. CET.

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About LEQEMBI™ (lecanemab-irmb)
LEQEMBI™ (lecanemab-irmb) is a humanized immunoglobulin gamma 1 (IgG1) monoclonal antibody directed against aggregated soluble and insoluble forms of amyloid-beta (Aβ). LEQEMBI is indicated for the treatment of Alzheimer's disease (AD) in the U.S. This indication is approved under accelerated approval based on reduction in Aβ plaques observed in patients treated with LEQEMBI. Continued approval for this indication may be contingent upon verification of clinical benefit in a confirmatory trial. Using the recently published data from the large global confirmatory Phase 3 clinical trial, Clarity AD, Eisai will work quickly to file a Supplemental Biologics License Application (sBLA) to the FDA for approval under the traditional pathway.

Lecanemab is the result of a strategic research alliance between Eisai and BioArctic. Eisai has initiated submission of data for BLA to the National Medical Products Administration (NMPA) of China in December 2022. Eisai plans to file for marketing authorization applications of lecanemab in Japan and Europe by the end of the first quarter 2023.

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, Eisai and Biogen.

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. Eisai has completed a LEQEMBI subcutaneous bioavailability study and subcutaneous dosing is currently being evaluated in the Clarity AD open label extension study.

About Amyloid-Related Imaging Abnormalities (ARIA)
ARIA is an important adverse event of amyloid-lowering therapies that is critical to monitor and manage during treatment. ARIA is most commonly seen as temporary swelling/effusion (ARIA-E) 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 (ARIA-H) with the swelling. Although most people with ARIA-E do not have symptoms, some people may have symptoms such as headache, confusion, dizziness, vision changes and nausea.

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 in December 2007, and the Development and Commercialization agreement for the antibody BAN2401 back-up for Alzheimer's disease, which was signed in May 2015. In March 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 right to commercialize lecanemab in the Nordic 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 filings, 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 disease-modifying treatments for neurodegenerative diseases, such as Alzheimer's disease, Parkinson's disease and ALS. BioArctic focuses on innovative treatments in areas with high unmet medical needs. The company was founded in 2003 based on innovative research from Uppsala University, Sweden. Collaborations with universities are of great importance to the company together with its strategically important global partner Eisai in Alzheimer disease. The project portfolio is a combination of fully funded projects run in partnership with global pharmaceutical companies and innovative in-house projects with significant market and out-licensing potential. BioArctic's Class B share is listed on Nasdaq Stockholm Mid Cap (ticker: BIOA B). For more information about BioArctic, please visit www.bioarctic.com.