Press release

BioArctic's partner Eisai submits supplemental Biologics License Application to FDA for traditional approval of LEQEMBI™ (lecanemab-irmb) for the treatment of Alzheimer's disease

Stockholm, January 7, 2023 – BioArctic AB's (publ) (Nasdaq Stockholm: BIOA B) partner Eisai announced today they have submitted a supplemental Biologics License Application (sBLA) to the U.S. Food and Drug Administration (FDA) supporting the conversion of the Accelerated Approval of LEQEMBI™ (lecanemab-irmb[1]) 100 mg/mL injection for intravenous use to a traditional approval. This sBLA is subject to validation of whether the FDA accepts the application for review. LEQEMBI is a humanized immunoglobulin gamma 1 (IgG1) monoclonal antibody directed against aggregated soluble ("protofibrils")[2] and insoluble forms of amyloid beta (Aβ), approved under Accelerated Approval Pathway by the U.S. Food and Drug Administration (FDA) on January 6 for the treatment of AD. Treatment with LEQEMBI should only be initiated in patients with mild cognitive impairment or mild dementia stage of disease and confirmed presence of Aβ pathology. Eisai's submission for traditional approval follows FDA accelerated approval of LEQEMBI on the same day, and is based on data from the confirmatory Phase 3 Clarity AD clinical trial.

Accelerated Approval of LEQEMBI was based on Phase 2b data that demonstrated LEQEMBI reduced the accumulation of Aβ plaque in the brain, a defining feature of AD. Continued approval for this indication is contingent upon verification of LEQEMBI's clinical benefit in a confirmatory trial. The sBLA for LEQEMBI is based on the data from the Phase 3 confirmatory Clarity AD clinical trial. In Clarity AD, LEQEMBI met the primary endpoint and all key secondary endpoints with highly statistically significant results, and the profile of Amyloid-Related Imaging Abnormalities (ARIA) incidence was within expectations. 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, peer-reviewed medical journals.

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 EU by the end the first quarter 2023 at the latest.

"We are very impressed with our partner Eisai's diligent work to progress LEQEMBI with sBLA submission on the same day as the FDA's accelerated approval. Alzheimer's disease is devastating

[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 are large Aβ aggregated soluble species of 75-500 Kd.

and the sBLA submission for LEQEMBI brings us one step closer to a full FDA approval and to potentially being able to offer a new treatment option to millions of patients and their families," said Gunilla Osswald, CEO at BioArctic.

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.

To learn more visit www.LEQEMBI.com.

INDICATION, DOSAGE AND ADMINISTRATION, AND IMPORTANT SAFETY INFORMATION IN THE U.S

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) baseline based on 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 LEQEMBI US 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 7, 2023, at 05.30 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. 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 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. The sBLA for LEQEMBI is based on the data from the Phase 3 confirmatory Clarity AD clinical trial. In Clarity AD, LEQEMBI met the primary endpoint and all key secondary endpoints with highly statistically significant results, and the profile of Amyloid-Related Imaging Abnormalities (ARIA) incidence was within expectations.

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 EU by the end of the first quarter 2023 at the latest.

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.