Press release

BioArctic announces additional BAN2401 Phase 2b study results in early Alzheimer's disease presented by Eisai at the 2018 CTAD conference

Stockholm, Sweden, October 25, 2018 – BioArctic AB (publ) (Nasdaq Stockholm: BIOA B) previously announced on July 6, 2018 the positive topline results from the clinical Phase 2b study with BAN2401 in 856 patients with early Alzheimer's disease (AD). BAN2401 is a selective anti-amyloid beta (Aβ) protofibril antibody. Statistically significant benefits were observed on the key efficacy endpoints at 18 months on slowing progression in Alzheimer's Disease Composite Score (ADCOMS) and on reduction of amyloid accumulated in the brain as measured by using amyloid-PET (Positron Emission Tomography) at the highest treatment dose (10 mg/kg twice a month) compared to placebo in the study. Pre-specified analyses demonstrated a good tolerability profile of BAN2401 with dose-dependent, clinically meaningful and statistically significant effects on several clinical endpoints as well as dose-dependent and significant effects on PET and other biomarkers.

Additional results were presented on October 25 at the 11th Clinical Trials on Alzheimer's Disease (CTAD) conference in Barcelona, Spain. Pre-specified sub-group analyses demonstrated consistent and pronounced effects of BAN2401 with reduced amyloid-burden on PET in both ApoE4 carriers and non-carriers, mild cognitive impairment due to AD (MCI) as well as mild AD, whether with or without concomitant symptomatic AD medication.

Results on clinical endpoints (ADCOMS, ADAS-Cog and CDR-SB) generally showed supportive signs of efficacy in these sub-groups. Treatment with the highest dose also resulted in less decline in disease progression on ADCOMS at 18 months versus placebo across sub-groups of clinical stage (MCI due to AD sub-group; 33% and mild AD sub-group; 35%) and use of concomitant Alzheimer's disease medications (with concomitant AD medications; 23% and without concomitant AD medications; 41%). At the highest treatment dose, ApoE4 carriers treated with BAN2401 saw 63% less decline in disease progression, while non-carriers saw 7% less decline, as measured by ADCOMS versus placebo at 18 months. The per protocol statistical analysis was designed to assess the overall patient population, and was not powered to show statistically significant differences across sub-groups. These results suggest that the treatment effect for the 10 mg/kg twice a month dose was driven by treatment with BAN2401 and not due to an imbalance in subject allocation by ApoE4 status, nor were there any significant difference in the rate of disease progression due to ApoE4 status.

In the PET sub-study clearance of brain amyloid correlated with the slowing of clinical decline on ADCOMS (Pearson's correlation coefficient of 0.838). The patient-groups included in this PET sub-study showed greater numerical signs of efficacy at 18 months.

Exploratory data on CSF biomarkers of neurodegeneration that are elevated in AD were also presented from a small CSF sub-study. To increase the sample size of the CSF sub-group, analyses were conducted on samples from the combined 10 mg/kg twice a month and 10 mg/kg monthly cohorts. Markers of synaptic damage (neurogranin), tau pathology (phosphorylated-tau, p-Tau), and axonal degeneration (neurofilament light chain, NfL) were found to show trends consistent with treatment benefit on underlying disease pathophysiology. Further indications of effects of BAN2401 over time were observed from a linear regression model testing the slope of change from baseline on the rate of disease progression with a significant slope difference on ADCOMS for the highest treatment dose versus placebo over 18 months ($p<0.001$).

BioArctic's partner Eisai is responsible for the Phase 2b study and the development of BAN2401 for Alzheimer's disease. The full CTAD presentation is available on the Investor Relations section of the Eisai website **www.eisai.com/ir/index.html**.

Eisai is currently discussing the next steps for BAN2401 with regulatory authorities. An open-label extension for patients previously enrolled in the Phase 2b clinical study is being planned, with enrollment expected to begin this year.

"The clinical results reinforce the utility of BAN2401 as a potential treatment for a broad population of early Alzheimer's disease patients addressing the unmet medical need of patients and their families. The additional biomarkers findings in the BAN2401 Phase 2b clinical study are also advancing the science in Alzheimer field of research," said Gunilla Osswald, CEO, Ph.D., BioArctic.

This release discusses investigational uses of an agent in development and is not intended to convey conclusions about efficacy or safety. There is no guarantee that any investigational uses of such product will successfully complete clinical development or gain health authority approval.

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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 above, on October 25, 2018, at 02.30 p.m. CET.

Notes to editors

About BAN2401
BAN2401 is a humanized monoclonal antibody that is the result of a strategic research alliance between BioArctic and Eisai. BAN2401 selectively binds to neutralize and eliminate soluble, toxic amyloid-beta aggregates that are thought to contribute to the neurodegenerative process in Alzheimer's disease. As such, BAN2401 has the potential to have an effect on the disease pathology and to slow down the progression of the disease. Eisai obtained the global rights to study, develop, manufacture and market BAN2401 for the treatment of Alzheimer's disease pursuant to an agreement concluded with BioArctic in December 2007. Eisai is responsible for the Phase 2b study and the development of BAN2401 for Alzheimer's disease. In March 2014, Eisai and Biogen entered into a joint development and commercialization agreement for BAN2401.

About the study
The Phase 2b study with BAN2401 (ClinicalTrials.gov identifier NCT01767311) is a placebo-controlled, double-blind, parallel-group, randomized study in 856 patients with mild cognitive impairment (MCI) due to Alzheimer's disease (AD) or mild Alzheimer's dementia (collectively known as early Alzheimer's disease) with confirmed amyloid pathology in the brain at the start of the study. Efficacy was analyzed up to 18 months with ADCOMS as the key endpoint for assessing clinical symptoms in the study. ADAS-Cog and CDR-SB further served as important secondary efficacy parameters. Pre-specified efficacy analyses were performed with conventional statistical methods; Mixed-effects Models for Repeated Measures Analysis (MMRM) as well as Bayesian Analyses on ADCOMS. Biomarker endpoints included for most patients changes in Aβ accumulated in the brain as measured with amyloid PET as well as for some patients biomarker assessments from cerebrospinal fluid (CSF) samples.

Patients were randomized to five dose regimens, 2.5 mg/kg twice a month, 5 mg/kg monthly, 5 mg/kg twice a month, 10 mg/kg monthly and 10 mg/kg twice a month, or placebo. This study used a Bayesian Adaptive Randomization Design to automatically allocate newly enrolled patients to treatment arms showing higher probability of efficacy based on interim analyses. Through the

interim analyses, the higher doses of 10 mg/kg twice a month and 10 mg/kg monthly were early in the trial determined to be the treatment dosages with higher efficacy, and as a result, the proportions of patients allocated to these treatment arms were greater (placebo: 247 patients, 2.5 mg/kg twice a month: 52 patients, 5 mg/kg monthly: 51 patients, 5 mg/kg twice a month: 92 patients, 10 mg/kg monthly: 253 patients, 10 mg/kg twice monthly: 161 patients). A request from a Health Authority in July 2014, the allocation of ApoE4 carriers to the 10 mg/kg twice a month treatment arm was restricted, resulting in fewer ApoE4 carriers in this arm and more patients being allocated to the 10 mg/kg monthly treatment arm.

As reported in December 2017, the study did not achieve its primary outcome measure which was designed to enable a potentially more rapid entry into Phase 3 development based on Bayesian analysis at 12 months of treatment. In a Bayesian analysis of ADCOMS at 12 months, the estimated probability that the highest dose of BAN2401 slows clinical decline more than placebo was 98%. While the criteria for early success at 12 months was pre-specified as an 80% or higher estimated probability of demonstrating a clinically significant difference (a 25% or greater slowing in clinical decline) from baseline compared to placebo, the estimated probability for this criteria was 64% according to Bayesian analysis.

Following the pre-defined study protocol, the blinded study continued with a comprehensive final analysis on treatment conducted at 18 months. Upon the final analysis at 18 months using pre-defined conventional statistical method (MMRM), the study did demonstrate a statistically significant slowing of disease progression on the key clinical endpoint (ADCOMS) after 12 months of treatment in patients receiving the highest treatment dose (10 mg/kg twice a month) as compared to placebo. The study will deliver data from a follow-up assessment at 21 months, 3 months after completed treatment with BAN2401.

The data presented at the Alzheimer's Association International Conference® (AAIC®) 2018 in Chicago, US, on July 25 display with pre-specified analysis applying conventional statistical methods dose-dependent, clinically meaningful and statistically significant effects of BAN2401 on several clinical endpoints as well as dose-dependent and significant effects on PET and other biomarkers with a good tolerability profile. At the 18 month final efficacy time point a dose-dependent slowing in cognitive decline from baseline on ADCOMS was demonstrated. The highest treatment dose of 10 mg/kg twice a month demonstrated a significant slowing of clinical decline of 30% compared to placebo at 18 months ($p=0.034$). A statistically significant slowing of decline on ADCOMS was observed as early as 6 months ($p<0.05$) as well as at 12 months ($p<0.05$). Dose-dependent slowing in cognitive decline from baseline on ADAS-Cog was also observed for BAN2401, with the highest treatment dose of BAN2401 demonstrating a significant slowing of clinical decline compared to placebo at 18 months (47% slower decline, $p=0.017$). Furthermore, on

CDR-SB, slowing of clinical decline for BAN2401 at the highest treatment dose also surpassed 25% over the duration of the study, which was pre-specified as a clinically significant difference. Compared to placebo at 18 months the difference was 26% ($p>0.05$). The rate of clinical decline for the placebo group was consistent with the results of research by the Alzheimer's Disease Neuroimaging Initiative (ADNI) in the United States.

Highly statistically significant and dose-dependent biomarker effects of all BAN2401 treatment groups were observed with amyloid PET. BAN2401 demonstrated a dose dependent reduction in amyloid in the brain at 18 months, and this reduction was significant at all doses. At the highest dose of BAN2401 (10 mg/kg twice a month), using standardized PET as measured at the Centiloid scale, the mean reduction in accumulated amyloid in the brain was 70 units at 18 months based on Mixed-effects Model with Repeated Measures, MMRM, ($p<0.0001$), the observed baseline mean was 74.5 units, and observed 18-month mean was 5.5 units. In amyloid PET image visual read, BAN2401 demonstrated a dose-dependent conversion from amyloid positive to negative, and at the highest dose, 81% of patients converted from amyloid positive to negative at 18 months ($p<0.0001$). Further evidence for biomarker effects of the treatment with BAN2401 were observed in the analysis of Aβ1-42 and tau in cerebrospinal fluid (CSF) samples in the limited number of the subjects that provided such samples in a sub-study. Aβ1-42 demonstrated target engagement at all doses of BAN2401. A combined analysis of patients receiving BAN2401 at 10 mg/kg (either monthly or twice a month) demonstrated a statistically significant reduction in total tau over time compared to placebo ($p<0.05$), an observation supportive of an intervention with disease-modifying properties.

BAN2401 was well tolerated during the 18 months of study drug administration. The incidence rate of treatment-related adverse events was 26.5% for the placebo arm, 53.4% for the 10 mg/kg monthly treatment arm and 47.2% for the 10 mg/kg twice a month treatment arm. The most common treatment emergent adverse events were infusion-related reactions and Amyloid Related Imaging Abnormalities (ARIA). Infusion related reactions were mostly mild to moderate in severity. Incidence of ARIA-E (edema) was not more than 10% in any of the treatment arms and the vast majority of the observed ARIA-E in the study were asymptomatic (43 of 48 subjects, 90%). Symptoms included headache, visual disturbances, and confusion. 60 percent of ARIA-E occurred within the first three months of treatment and approximately 89 percent of cases were mild to moderate in severity. Incidence of ARIA-E (edema) was 9.9% at the highest treatment dose and the incidence of ARIA-E in ApoE4 carriers was 14.6% at this dose. Per protocol, all patients presenting with ARIA-E on Magnetic Resonance Imaging (MRI) were discontinued in the study. The incidence rate of serious adverse events was 17.6% for the placebo arm, 12,3% for the 10 mg/kg monthly treatment arm and 15.5% for the 10 mg/kg twice a month arm.

About ADCOMS
Developed by Eisai, ADCOMS (AD Composite Score) combines items from the ADAS-Cog (Alzheimer's Disease Assessment Scale-cognitive subscale), CDR-SB (Clinical Dementia Rating Sum of Boxes) and the MMSE (Mini-Mental State Examination) scales to enable a sensitive detection of changes in clinical functions of early AD symptoms and changes in memory. The Phase 2b study with BAN2401 utilizes ADCOMS as its key endpoint for assessing clinical symptoms.

About Amyloid PET Imaging
Amyloid PET (Positron Emission Tomography) imaging is a diagnostic method that enables the visualization of amyloid plaque present in the brain as well as the quantitative evaluation of amyloid plaque distribution and accumulation in the brain via administration of a minute amount of PET tracer, which specifically binds to amyloid plaque. Amyloid PET imaging enables the assessment of pathology change and assistance of diagnosis of patients with Alzheimer's disease including MCI, and estimates the clinical effect of disease modifiers based on the amyloid hypothesis. SUVr (Standard Uptake Value Ratio) calculates the ratio of strength of accumulation of PET tracer in a region of interest in the brain to an area of the brain (reference region) which shows low and stable accumulation of PET tracer. These SUVr values can be used to quantitatively compare and evaluate the accumulation of amyloid. When integrating and assessing biomarkers of the change in Aβ accumulation measured by different tracers it is necessary to compensate for the difference in measured values between the PET tracers. This has led to the development of a 100-point scale by the GAIIN Centiloid project, termed "Centiloid," which is an average value of zero in "high certainty" amyloid negative subjects and an average of 100 in "typical" Alzheimer's disease (AD) patients (Klunk et al., 2015). In this study, this Centiloid scale was used to standardize SUVr measurement values to evaluate the decrease in amyloid burden. Visual read is a method that assigns experienced investigators to determine with support of method protocols whether there is amyloid accumulation in relevant areas of the brain. A negative visual read is accordingly not in support of a diagnosis of Alzheimer's disease and a conversion from positive to negative represents an improvement.

About Correlation Coefficient
The correlation coefficient indicates the strength of the relationship between two variables from two quantitative data distributions. The correlation coefficient ranges in value from -1 to 1, and as it approaches the absolute value of 1, it indicates a total positive linear correlation. In general, if a correlation coefficient is 0.6 or greater, it suggests there is a relationship between the variables.

About Apolipoprotein E
About Apolipoprotein E (ApoE) transports fats in the blood. There are three isoforms of ApoE (ApoE2, ApoE3 and ApoE4).
Individuals expressing ApoE4 develop more Alzheimer changes in the form of plaques and amyloid-beta in the brain blood vessel walls. The risk of developing Alzheimer's disease is four times higher

among carriers of ApoE4 compared to persons with ApoE3. Disease progression or the effect of pharmacological treatment in persons with Alzheimer's disease have not been demonstrated to differ dependent on ApoE genotype.

About the collaboration between BioArctic and Eisai
Since 2005, BioArctic has 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 on the BAN2401 antibody, which was signed in December 2007, and the development and commercialization agreement on the antibody BAN2401 back-up for Alzheimer's disease, which was signed in May 2015. Eisai is responsible for the clinical development, application for market approval and commercialization of the products for Alzheimer's disease.

About BioArctic AB
BioArctic AB (publ) is a Swedish research-based biopharma company focusing on disease-modifying treatments and reliable biomarkers and diagnostics for neurodegenerative diseases, such as Alzheimer's disease and Parkinson's disease. The company also develops a potential treatment for Complete Spinal Cord Injury. 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 our strategically important global partners in the Alzheimer (Eisai) and Parkinson (AbbVie) projects. 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 B-share is listed on Nasdaq Stockholm Mid Cap (ticker: BIOA B). For more information about BioArctic, please visit **www.bioarctic.com.**

About Eisai Co., Ltd.
Eisai Co., Ltd. is a leading global research and development-based pharmaceutical company headquartered in Japan. Eisai defines their corporate mission as "giving first thought to patients and their families and to increasing the benefits health care provides," which Eisai calls their *human health care* (*hhc*) philosophy. With approximately 10,000 employees working across the global network of R&D facilities, manufacturing sites and marketing subsidiaries, Eisai strives to realize their *hhc* philosophy by delivering innovative products to address 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 Aricept®, a treatment for Alzheimer's disease and dementia with Lewy bodies, Eisai has been working to establish a social environment that involves patients in each community in cooperation with various stakeholders including the government, healthcare professionals and care workers, and is estimated to have held over ten thousand dementia awareness events worldwide. As a pioneer in the field of

dementia treatment, Eisai is striving to not only develop next generation treatments but also to develop diagnosis methods and provide solutions. For more information about Eisai Co., Ltd., please visit **www.eisai.com**.