

EISAI TO PRESENT NEW LECANEMAB DATA EXPLORING DISTINCT MECHANISM OF ACTION AND CLINICAL OUTCOMES, DISEASE STATE (DSE) SYMPOSIUM, AND OTHER PIPELINE ASSETS AT THE AD/PD™ 2022 ANNUAL MEETING

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, “Eisai”) announced today the company will present research from its robust Alzheimer’s disease (AD) pipeline, including the latest findings on lecanemab, Eisai’s investigational anti-amyloid beta (A β) protofibril antibody for the treatment of early AD at the AD/PD™ 2022 International Conference on Alzheimer’s and Parkinson’s Diseases (AD/PD) from March 15-20 in Barcelona, Spain and virtually. The lecanemab data and additional research findings from Eisai’s clinical development programs will be featured in 13 presentations. Lecanemab was granted Breakthrough Therapy and Fast Track designations by the U.S. Food and Drug Administration (FDA) in June and December 2021, respectively. Eisai anticipates completing lecanemab’s rolling submission of a Biologics License Application for the treatment of early AD to the FDA under the accelerated approval pathway in the first quarter of Eisai’s fiscal year 2022, which begins April 1, 2022. Additionally, the readout of the Phase 3 confirmatory Clarity AD clinical trial will occur in the Fall of 2022. Eisai initiated a submission to the Pharmaceuticals and Medical Devices Agency (PMDA) of application data of lecanemab under the prior assessment consultation system in Japan in March 2022.

“Four key presentations at AD/PD 2022 advance our understanding of the mechanism of action of Eisai’s investigational anti- A β protofibril antibody lecanemab and the therapy’s clinical and safety profile, including amyloid related imaging abnormalities, or ARIA, from the Phase 2b study and open-label extension, in the potential treatment of early Alzheimer’s disease,” said Michael Irizarry, M.D., Senior Vice President, Deputy Chief Clinical Officer, Neurology Business Group, Eisai Inc. “In addition to lecanemab, Eisai’s robust pipeline includes compounds targeting the tau pathway, other pathways leading to neurodegeneration, and the testing of combination therapies that may be the optimal approach to treat or even prevent Alzheimer’s disease.”

The focus on AD has historically been on alleviating cognitive, functional, and behavioral symptoms, but there has been significant progress in understanding the biological mechanisms of the disease. Eisai’s investigational pipeline aims to treat the range of underlying pathophysiology, including amyloid, tau and neurodegeneration.

“Because of the robust design of the lecanemab Phase 2b study, Eisai was able to design the Phase 3 confirmatory Clarity AD clinical trial to optimally verify lecanemab’s clinical efficacy and safety in early Alzheimer’s disease,” said Ivan Cheung, Chairman, Eisai Inc., Senior Vice President, President Neurology Business Group and Global Alzheimer’s Disease Officer, Eisai Co., Ltd. “Part of the recruitment strategy for the Clarity AD confirmatory trial was to ensure greater inclusion of ethnic and racial populations. While there is still important work to be done in ensuring minority populations’ participation in clinical trials, Eisai is proud that approximately 25% of the total U.S. enrollment in Clarity AD consists of African American and Hispanic

persons living with early Alzheimer's disease, which mirrors the U.S. Medicare population."

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 such investigational agent will successfully complete clinical development or gain health authority approval.

Major Presentations Provide Deeper Scientific Insights into Lecanemab's Mechanism of Action and Potential as a Treatment for Early AD

Onsite Symposium - A β Targeting Therapies in AD 2

- **Science of the Amyloid Cascade and Distinct Mechanism of Action of Lecanemab** – Data will be presented to show the different anti-A β antibodies and their affinities to different A β species. AD is characterized by the presence of A β plaques and neurofibrillary tangles composed of tau protein. Genetic and biomarker studies point to A β aggregation as occurring early in the disease. There is a spectrum of aggregated A β species, ranging from soluble dimers, oligomers, protofibrils and insoluble fibrillar A β , which exist in a complex equilibrium in the AD brain. Soluble aggregated species such as protofibrils are considered to be toxic to neurons and are implicated in the neurodegenerative process in AD. Immunotherapy against A β has emerged as a promising treatment for AD. mAb158, the mouse precursor antibody to lecanemab, was generated based on protofibrils formed by the Arctic mutation which causes AD due to an enhanced propensity to form protofibrils.
- **Key Trial Design Aspects and Clinical Outcomes of the Lecanemab Phase 2b (Study 201) Trial and Open-Label Extension (OLE) in Early Alzheimer's Disease** – This presentation shares the latest results from the lecanemab Study 201 Core and OLE exploring the reduction of brain amyloid and the incidence and severity of amyloid-related imaging abnormalities (ARIA). Study 201 was a dose ranging study that employed a Bayesian adaptive design with response adaptive randomization. The study demonstrated that lecanemab cleared amyloid plaques in a dose- and time-dependent manner and identified the 10 mg/kg IV biweekly dose as the dose most likely to slow cognitive decline in early AD, a hypothesis that will be verified in the Clarity AD Phase 3 study. In Study 201, lecanemab showed an overall rate of less than <10% incidence of ARIA-E at 10 mg/kg biweekly in the Core and OLE (<15% in ApoE4 carriers). The incidence of symptomatic ARIA-E was <2% in Core and OLE. This safety profile enables lecanemab to be initiated at the therapeutic dose without titration.
- **Phase 2b (Study 201) Lecanemab Early Alzheimer's Disease Study Biomarker Results and Correlations with Clinical Outcomes** – Discussion around the key biomarker findings and their correlation with clinical outcomes from the lecanemab Phase 2b Core and OLE studies. As part of this presentation, Dr. E. McDade from Washington University in St. Louis will provide an update on the Dominantly Inherited Alzheimer Network Trials Unit (DIAN-TU) Tau NexGen trial, which is evaluating lecanemab combined with Eisai's investigational anti-microtubule binding region (MTBR) tau antibody E2814. Researchers will share:
 - Evaluation of the association of amyloid plaque reduction by lecanemab with peripheral measures of AD biomarkers in the randomized Core-phase 201 and the association of changes in peripheral measures of AD biomarkers with change in clinical outcomes during the randomized Core-phase 201.

- Results and modeling of changes in amyloid plaque and peripheral measures of AD biomarkers after lecanemab cessation in the Gap phase, and implications for lecanemab maintenance therapy.
- **Update on Lecanemab Clinical Development, Including New Subcutaneous Formulation (SC)** – Eisai will provide the latest information from the Phase 2b OLE study of lecanemab in early AD dosing substudy, Phase 3 study of lecanemab in early AD (Clarity AD), and Phase 3 study of lecanemab in preclinical AD (AHEAD 3-45). The rationale and clinical development strategy for SC lecanemab will be presented.

Other Key Presentations

- An invited presentation exploring the A β pathway Across Time and Space in AD will be led by Harald Hampel, MD, PhD, MSc, Chief Medical Officer, Senior Vice President, Head of Global Medical Affairs, Neurology Business Group at Eisai Inc.
- Baseline Tau PET in Clarity AD: A Phase 3 Placebo-Controlled, Double-Blind, Parallel-Group, 18-Month Study Evaluating Lecanemab in Early Alzheimer's Disease
- Quantitative Systems Pharmacology (QSP) Amyloid Platform: Multiscale Computational Modeling of A β Biology and Its Interaction with Lecanemab Pharmacology
- Fully Automated Plasma β -Amyloid Immunoassays Predict Amyloid Pathology Defined by Amyloid PET

Eisai Disease State Virtual Symposium

Eisai will hold a virtual symposium titled, “Amyloid β Pathway: Evolving Scientific Knowledge and Clinical Implications for - Alzheimer’s disease,” where esteemed faculty will review the effects of A β across cellular and systemic context, as well as across AD stages and therapeutic approaches. Featured speakers include Dennis J. Selkoe, MD, Bart De Strooper, MD, PhD, Susan Landau, PhD, Randall Bateman, MD.

The symposium will be held virtually Saturday, March 19, 2022, 11:40 - 13:25 Central European Time (GMT+1) and will be available online for three months following AD/PD 2022.

Below please find a list of important presentations and symposia at this year’s meeting. All presentations will be available online to registered participants via the AD/PD virtual platform.

(continued on the following page)

■ Eisai Presentation about Asset in Development and Research

Asset in Development, Session, Topic, Time (Central European Time)	Title, Presenter
Lecanemab Onsite Symposium A β Targeting Therapies in AD 2 Friday, March 18; 17:15 - 17:40	Science of the Amyloid Cascade and Distinct Mechanism of Action of Lecanemab Presenter: L. Lannfelt
Lecanemab Onsite Symposium A β Targeting Therapies in AD 2 Friday, March 18; 17:40 - 17:55	Key Trial Design Aspects and Clinical Outcomes of the Lecanemab Phase 2 Trial and Open-Label Extension in Early Alzheimer's Disease Presenter: M. Sabbagh
Lecanemab Onsite Symposium A β Targeting Therapies in AD 2 Friday, March 18; 17:55 - 18:10	Phase 2 Lecanemab Early Alzheimer's Disease Study Biomarker Results and Correlations With Clinical Outcomes Presenter: E. McDade
Lecanemab Onsite Symposium A β Targeting Therapies in AD 2 Friday, March 18; 18:10 - 18:25	Update on Lecanemab Clinical Development, Including New Subcutaneous Formulation Presenter: M. Irizarry
Lecanemab Oral Session, A β and Other Targeting Therapies in AD Sunday, March 20; 9:05 – 9:20	Quantitative Systems Pharmacology (QSP) Amyloid Platform: Multiscale Computational Modeling of A β Biology and Its Interaction with Lecanemab Pharmacology Presenter: A. Cabal
Lecanemab On demand presentation	Baseline Tau in Clarity AD: A Phase 3 Placebo-Controlled, Double-Blind, Parallel-Group, 18-Month Study Evaluating Lecanemab in Early Alzheimer's Disease Presenter: A. Charil
Lecanemab and E2814 Oral Session, Advances in AD, PD and LBD Drug Development Thursday, March 17; 10:25 - 10:40	Dominantly Inherited Alzheimer's Network Trials Unit (DIAN-TU) Nexgen Platform Trial of The Anti-Tau Antibody, E2814, with Background Lecanemab Therapy Presenter: L. Schneider
E2814 Oral Session, A β and Other Targeting Therapies in AD Sunday, March 20; 10:35 - 10:50	Safety, Pharmacokinetics and Pharmacodynamics of Single and Multiple Ascending Doses of the Novel Anti-Tau Therapeutic Antibody E2814: A Phase 1, First-in-Human Study in Healthy Volunteers Authors: P. Aceves, et al
Imaging On demand presentation	Evaluation of Tau Deposition in Amyloid-Positive MCI and Mild-AD Dementia Subjects from the MissionAD Program Using 18F-PI-2620 Authors: S. Bullich, et al

E2511 Poster (onsite and virtual)	E2511, A Novel Small Compound TrkA Biased Positive Allosteric Modulator, Reinnervates Cholinergic Neuron Via Enhancement of Specific Trophic Signaling of TrkA In Non-clinical Studies Authors: T Tomioka, et al
General AD Invited Lecture Wednesday, March 16; 17:45 – 18:00	Amyloid- β Pathway Across Time and Space in Alzheimer's Disease Presenter: H. Hample
General AD On demand poster	EHR Cohort Development Using Natural Language Processing for Identifying Symptoms of Alzheimer's Disease Authors: H Yu, et al
General AD On demand presentation	Understanding Risk Factors for Alzheimer's Disease Onset in Individuals with Mild Cognitive Impairment Authors: Y. Wang, et al

■ Eisai Disease State Symposium

Session, Time (Central European Time)	Title, Presenter
Virtual Symposium / On-Demand Viewing Saturday, March 19, 11:40 – 13:25	Amyloid β Pathway: Evolving Scientific Knowledge and Clinical Implications for Alzheimer's disease Presenters: Dennis J. Selkoe, Bart De Strooper, Susan Landau, and Randall Bateman

■ Biogen Presentation about Aducanumab

Asset in Development, Session, Topic, Time (Central European Time)	Title, Presenter
Aducanumab A β Targeting Therapies in AD 1 Friday, March 18; 14:45-15:00	Heterogeneity in Symptom Progression and Treatment Response: An Analysis of Participants with Early Alzheimer's Disease From the EMERGE Aducanumab Trial Presenter: J. Murphy
Aducanumab A β Targeting Therapies in AD 1 Friday, March 18; 15:00-15:15	Evaluating the Evidence of Aducanumab Treatment Benefit Using Standardized Test Statistics and Global Statistical Tests Presenter: S. Dickson
Aducanumab A β Targeting Therapies in AD 1 Friday, March 18; 15:15-15:30	Subgroup Analyses of the Plasma P-Tau181 Population From EMERGE/ENGAGE, Phase 3 Clinical Trials Evaluating Aducanumab in Early Alzheimer's Disease Presenter: O. Hansson
Aducanumab On demand poster	Aducanumab Phase 3 Studies: Exposure-Response Analysis Evaluating the Relationship Between Amyloid Removal and Slowing of Clinical Decline on CDR-SB Scores Autohers: KK. Muralidharan, et al

■ Sysmex Presentation

Topic, Session	Title, Presenter
Diagnosis	Fully Automated Plasma β -Amyloid Immunoassays Predict Amyloid Pathology Defined by Amyloid PET
On demand presentation	Presenter: K. Yamashita

Eisai leads all actions on lecanemab, including clinical development, FDA interaction, and commercialization as part of the collaboration agreement with Biogen.

[Notes to editors]

1. About Lecanemab (BAN2401)

Lecanemab is an investigational humanized monoclonal antibody for Alzheimer's disease (AD) that is the result of a strategic research alliance between Eisai and BioArctic. Lecanemab selectively binds to neutralize and eliminate soluble, toxic amyloid-beta ($A\beta$) aggregates (protofibrils) that are thought to contribute to the neurodegenerative process in AD. As such, lecanemab may have the potential to have an effect on disease pathology and to slow down the progression of the disease. Currently, lecanemab is being developed as the only anti- $A\beta$ antibody that can be used for the treatment of early AD without the need for titration. With regard to the results from pre-specified analysis at 18 months of treatment, Study 201 demonstrated reduction of brain $A\beta$ accumulation ($P < 0.0001$) and slowing of disease progression measured by ADCOMS* ($P < 0.05$) in early AD subjects. The study did not achieve its primary outcome measure** at 12 months of treatment. The Study 201 open-label extension was initiated after completion of the Core period and a Gap period off treatment of 9-59 months (average of 24 months, n=180 from core study enrolled) to evaluate safety and efficacy, and is underway.

Currently, lecanemab is being studied in a confirmatory Phase 3 clinical study in symptomatic early AD (Clarity-AD), following the outcome of the Phase 2 clinical study (Study 201). Since July 2020 the 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 Alzheimer's Disease and related dementias in the U.S, funded by the National Institute on Aging, part of the National Institutes of Health, Eisai and Biogen. Furthermore, Eisai has initiated a lecanemab subcutaneous dosing Phase 1 study. Eisai obtained the global rights to study, develop, manufacture and market lecanemab for the treatment of AD pursuant to an agreement concluded with BioArctic in December 2007. In March 2014 Eisai and Biogen entered into a joint development and commercialization agreement for lecanemab and the parties amended that agreement in October 2017.

* Developed by Eisai, ADCOMS (AD Composite Score) combines items from the ADAS-Cog (Alzheimer's Disease Assessment Scale-cognitive subscale), CDR (Clinical Dementia Rating) 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 ADCOMS scale ranges from a score of 0.00 to 1.97, with higher score indicating greater impairment.

** An 80% or higher estimated probability of demonstrating 25% or greater slowing in clinical decline at 12 months treatment measured by ADCOMS from baseline compared to placebo.

2. About ADUHELM® (aducanumab-avwa) 100 mg/mL injection for intravenous use

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).

ADUHELM is a monoclonal antibody directed against amyloid beta. The accumulation of amyloid beta plaques in the brain is a defining pathophysiological feature of Alzheimer's disease. 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 clinical decline.

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. Although most people 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. ADUHELM can also cause serious allergic reactions. The most common side effects of ADUHELM include: swelling in areas of the brain, with or without small spots of bleeding in the brain or on the surface of the brain (ARIA); headache; and fall. Patients should call their healthcare provider for medical advice about side effects.

As of October 2017, Biogen and Eisai Co., Ltd. are collaborating on the global co-development and co-promotion of aducanumab.

Please click here for [full Prescribing Information](#), including [Medication Guide](#), for ADUHELM.

3. About the Joint Development between Eisai and Biogen for Alzheimer's Disease

Eisai and Biogen are collaborating on the joint development and commercialization of AD treatments. Eisai serves as the lead in the co-development of lecanemab.

4. About the Collaboration between Eisai and BioArctic for Alzheimer's Disease

Since 2005, BioArctic has had a long-term collaboration with Eisai regarding the development and commercialization of drugs for the treatment of AD. The commercialization agreement on the lecanemab antibody was signed in December 2007, and the development and commercialization agreement on the antibody lecanemab back-up for AD, which was signed in May 2015. Eisai is responsible for the clinical development, application for market approval and commercialization of the products for AD. BioArctic has no development costs for lecanemab in AD.

5. About collaboration between Eisai and Sysmex

Eisai and Sysmex have entered into a comprehensive non-exclusive collaboration agreement aimed at the creation of new diagnostics in the field of dementia in February, 2016. Leveraging each other's

technologies and knowledge, the two companies aim to discover next-generation diagnostics that will enable early diagnosis, selection of treatment options and the regular monitoring of the effects of treatment for dementia.

6. About E2814

An investigational anti-microtubule binding region (MTBR) tau antibody, E2814 is being developed as a disease modifying agent for tauopathies including sporadic AD. Phase I clinical studies are underway. E2814 was discovered as part of the research collaboration between Eisai and University College London. E2814 is designed to prevent the spreading of tau seeds within the brains of affected individuals. In addition, a Phase II/III Tau NexGen study for the treatment of dominantly inherited Alzheimer's disease (DIAD), conducted by the Dominantly Inherited Alzheimer Network Trials Unit (DIAN-TU) led by Washington University School of Medicine in St. Louis (St. Louis, MO, USA), is underway.

7. About E2511

E2511 is Eisai's in-house discovered and developed investigational novel molecule that directly binds to tropomyosin receptor kinase A (TrkA); a nerve growth factor (NGF) located on the neural cell membrane. E2511 could potentially promote recovery and synaptic remodeling of damaged cholinergic neurons. A Phase 1 study for E2511 is underway.

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