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Eisai Co., Ltd.

EISAI TO PRESENT THE LATEST ALZHEIMER'S DISEASE PIPELINE AND RESEARCH, INCLUDING LECANEMAB AND ANTI-MTBR TAU ANTIBODY E2814, AT THE ALZHEIMER'S ASSOCIATION INTERNATIONAL CONFERENCE (AAIC) 2023

Eisai Co. Ltd (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") announced today that the company will present the latest findings on its Alzheimer's disease (AD) pipeline and research, including Eisai's anti-amyloid beta (Aβ) protofibril* antibody for the treatment of Alzheimer's disease (AD), lecanemab (generic name, U.S. brand name: LEQEMBI®), and the company's investigational anti-MTBR** tau antibody, E2814, at the Alzheimer's Association International Conference (AAIC). The conference will be held in Amsterdam, the Netherlands and virtually from July 16 to 20, 2023. Eisai will present data and research in eight oral and 19 poster presentations at the meeting. Two of the AAIC oral presentations will be presented as posters at the Alzheimer's Disease Imaging Consortium (AIC), which will be held at the same venue as AAIC on July 15.

"At AAIC 2023 Eisai will present the latest data on lecanemab, an anti-Aβ protofibril antibody, that recently received traditional approval in the U.S. for patients with mild cognitive impairment (MCI) due to AD and mild AD. Leqembi was studied in a broad population, which included a mix of racial and ethnic groups and patients with common comorbid conditions and concomitant medications." Additionally, Eisai will present important new data on E2814, an anti-MTBR tau antibody, which is currently in Phase II/III clinical trials with the Dominantly Inherited Alzheimer's Network Trials Unit at Washington University St. Louis," said Michael Irizarry, M.D., Deputy Chief Clinical Officer and Senior Vice President of Clinical Research, Alzheimer's Disease and Brain Health, Eisai Inc. "As part of Eisai's commitment to transparency and our *human health care (hhc)* and ecosystem mission, we will continue to present and publish data and information about our AD pipeline and research."

Key Eisai AAIC Presentations

- **Amyloid Reduction and Evidence of Downstream Biomarker Modification** Presentation of results of Aβ, tau, neurodegeneration, gliosis, and imaging biomarkers in the Phase III Clarity AD study of lecanemab (#80907)
- **Drug Development in the Era of Anti-Amyloid Therapies** Discussion of considerations in the development of new drugs for AD and rational drug combinations based on pathophysiology (#70444)
- **Subcutaneous Lecanemab is Predicted to Achieve Comparable Efficacy and Improved Safety Compared to Lecanemab IV in Early Alzheimer's Disease** Presentation and discussion of results from studies to date on a subcutaneous formulation of lecanemab under development to potentially improve convenience and safety profile for patients (#82852)
- **E2814: An Anti-Tau Therapy Engages its CNS Target and Affects the Downstream Tangle-Specific Biomarker MTBR-tau243 in Dominantly Inherited Alzheimer's Disease** Report on the safety, pharmacokinetics, and biomarkers of anti-MTBR tau antibody E2814 in clinical trials in healthy adults and dominant inherited AD patients (#82771)

■ **Eisai Oral Presentations**

Asset/Project, Session, Presentation Time (Central European Summer Time)	**Presentation Number, Title**
Lecanemab Plenary Panel Wednesday, July 19, 2023 Session Time: 11:15 - 12:30 AAIC ASK Session (Q&A): 13:00	#80907 Amyloid Reduction and Evidence of Downstream Biomarker Modification
Lecanemab Perspectives Session Monday, July 17, 2023 Session Time: 14:15 - 15:30	#70444 Drug Development in the Era of Anti-Amyloid Therapies
Lecanemab Monday, July 17, 2023 Session Time: 8:00 - 8:45	#82852 Subcutaneous Lecanemab is Predicted to Achieve Comparable Efficacy and Improved Safety Compared to Lecanemab IV in Early Alzheimer's Disease
Lecanemab Monday, July 17, 2023 Session Time: 8:00 - 8:45	#83020 Racial and Ethnic Differences in Plasma Biomarker Eligibility in a Preclinical Alzheimer's Disease Trial
Lecanemab Thursday, July 20, 2023 Session Time: 8:00 - 9:15	#80393 Exposure-Response Modeling to Describe Change in Brain Amyloid Following Lecanemab Administration in Patients with Early Alzheimer's Disease
E2814 Sunday, July 16, 2023 Session Time: 8:00 - 8:45	#82771 E2814: An Anti-Tau Therapy Engages its CNS Target and Affects the Downstream Tangle-Specific Biomarker MTBR-tau243 in Dominantly Inherited Alzheimer's Disease
Biomarkers Sunday, July 16, 2023 Session Time: 14:15 - 15:30 Alzheimer's Imaging Consortium (AIC), Poster AIC-P-243	#80421 Harmonization of Tau PET in Alzheimer’s Disease: Comparison of Methods to Derive CenTauR Units for [18F]RO948, [18F]Flortaucipir and [18F]MK-6240
Biomarkers Monday, July 17, 2023 Session Time: 16:15 - 17:30 Alzheimer's Imaging Consortium (AIC), Poster AIC-P-061	#75367 Novel CSF Tau Biomarkers Can Be Used For Disease Staging of Sporadic Alzheimer’s Disease

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■ **Eisai Poster Presentations**

Asset/Project, Session, Presentation Time (Central European Summer Time)	Poster Number, Title
Lecanemab Sunday, July 16, 2023 Poster Session Time: 8:45 - 16:15	Poster P1-746 PK/PD Analysis of ARIA-E and Isolated ARIA-H in Lecanemab Clarity AD Study
E2814 Sunday, July 16, 2023 Poster Session Time: 8:45 - 16:15	Poster P1-909 Safety, Pharmacokinetics and Immunogenicity of Single and Multiple Ascending Doses of the Anti-Tau Therapeutic Antibody E2814: A Phase 1, First-in-Human Study in Healthy Subjects
E2814 Wednesday, July 19, 2023 Poster Session Time: 8:45 - 16:15	Poster P4-673 Efficacy of the Murine Version of E2814 in a Validated AD Brain Seed-Injection Model in hTau Mice
Biomarkers Sunday, July 16, 2023 Poster Session Time: 8:45 - 16:15	Poster P1-504 Detection of Brain Tau Deposition Across Braak Stages Using Plasma pTau181, MRI and Cognitive Function Assessments
Biomarkers Monday, July 17, 2023 Poster Session Time: 8:45 - 16:15	Poster P2-288 Deciphering the Components of Amyloid-Beta-Driven Dementia Using a Novel Peptide-Focused Global Proteomics Platform
Biomarkers Monday, July 17, 2023 Poster Session Time: 8:45 - 16:15	Poster P2-911 Discordance in Amyloid Positivity Defined by Visual Reads and Centiloids
Biomarkers Monday, July 17, 2023 Poster Session Time: 8:45 - 16:15	Poster P2-955 Estimating Braak Stage From [18F]MK6240 PET Scans
Biomarkers Tuesday, July 18, 2023 Poster Session Time: 8:45 - 16:15	Poster P3-257 A New De Novo-Assisted Mass Spectrometry Method for Novel Antimicrobial Peptide Expression Profiling in Cerebrospinal Fluid of Demented Subjects
Biomarkers Tuesday, July 18, 2023 Poster Session Time: 8:45 - 16:15	Poster P3-281 Targeted Proteomic Profiling in Cerebrospinal Fluid and Plasma Identifies Biomarkers for Alzheimer's Disease
Machine-Learning Models Wednesday, July 19, 2023 Poster Session Time: 8:45 - 16:15	Poster P4-655 Prognostic Prediction of the Longitudinal Cognitive Trajectory of Amyloid-Positive Patients with Mild Dementia
Drug Development Wednesday, July 19, 2023 Poster Session Time: 8:45 - 16:15	Poster P4-642 Development of Clinical Trial Simulation Tools for Alzheimer's Disease through the Critical Path for Alzheimer's Disease Consortium

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Public Health Monday, July 17, 2023 Poster Session Time: 8:45 - 16:15	Poster P2-790 Development of a Triage Algorithm for Mild Cognitive Impairment Using Electronic Health Record Data
Epidemiology Sunday, July 16, 2023 Poster Session Time: 8:45 - 16:15	Poster P1-771 Age-Related Relative Comorbidity Burden of Mild Cognitive Impairment: A US Database Study
Epidemiology Sunday, July 16, 2023 Poster Session Time: 8:45 - 16:15	Poster P1-775 Prevalence and Severity Distribution of Alzheimer's Disease in the United States from the Health and Retirement Study
Epidemiology July 17, 2023 Poster Session Time: 8:45 - 16:15	Poster P2-760 Incidence of Alzheimer's Disease Dementia and Mild Cognitive Impairment in the United States Medicare Population
Epidemiology July 17, 2023 Poster Session Time: 8:45 - 16:15	Poster P4-721 Prevalence of Alzheimer's Disease Dementia and Mild Cognitive Impairment in the United States Medicare Population
Health Services Research Poster Virtual Only Sunday, July 16 - Thursday, July 20, 2023	Abstract 70962 Retrospective Cohort Study to Quantify the Economic Impact of Mild Cognitive Impairment
Health Services Research Poster Virtual Only Sunday, July 16 - Thursday, July 20, 2023	Abstract 72143 Economic Impact of Progression from Mild Cognitive Impairment to Alzheimer's Disease in Commercially Insured Subjects
Others Poster Virtual Only Sunday, July 16 - Thursday, July 20, 2023	Abstract 73976 Association between Auditory Impairment and the Onset of Alzheimer's Disease: The LIFE Study

Eisai serves as the lead of lecanemab development and regulatory submissions globally with both companies co-commercializing and co-promoting the product and Eisai having final decision-making authority.

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

* Protofibrils are large Aβ aggregated soluble species of 75-5000 Kd.[1,2,3]

** MTBR: microtubule binding region

References

1. https://www.alzforum.org/news/conference-coverage/lecanemab-sweeps-toxic-av-protofibrils-catches-eyes-trialists
2. Sehlin D, Englund H, Simu B, Karlsson M, Ingelsson M, Nikolajeff F, Lannfelt L, Pettersson FE. Large aggregates are the major soluble Aβ species in AD brain fractionated with density gradient ultracentrifugation. *PLoS One.* 2012;7(2):e32014. doi: 10.1371/journal.pone.0032014. Epub 2012 Feb 15. PMID: 22355408; PMCID: PMC3280222.
3. Söderberg, L., Johannesson, M., Nygren, P. et al. Lecanemab, Aducanumab, and Gantenerumab — Binding Profiles to Different Forms of Amyloid-Beta Might Explain Efficacy and Side Effects in Clinical Trials for Alzheimer's Disease. *Neurotherapeutics.* 2023;20:195-206. doi: 10.1007/s13311-022-01308-6.

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[Notes to editors]

1. About Lecanemab (generic name, U.S. brand name: LEQEMBI®),
Lecanemab is the result of a strategic research alliance between Eisai and BioArctic. Lecanemab is a humanized immunoglobulin gamma 1 (IgG1) monoclonal antibody directed against aggregated soluble (protofibril) and insoluble forms of amyloid-beta (Aβ). In the U.S., LEQEMBI was granted traditional approval by the U.S. Food and Drug Administration (FDA) on July 6, 2023. 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.

Please see full Prescribing Information, including Boxed WARNING in the United States.

Eisai has also submitted applications for approval of lecanemab in Japan, EU, China, Canada, Great Britain and South Korea. In Japan and China, the applications have been designated for priority review, and in Great Britain, lecanemab has been designated for the Innovative Licensing and Access Pathway (ILAP), which aims to reduce the time to market for innovative medicines.

Eisai has completed lecanemab subcutaneous bioavailability study, and subcutaneous dosing is currently being evaluated in the Clarity AD (Study 301) OLE. A maintenance dosing regimen has been evaluated as part of Study 201 as well as the Clarity AD (Study 301) OLE. Separate supplemental Biologics License Applications for subcutaneous dosing and a maintenance dosing regimen will be submitted to the FDA at the end of Eisai's fiscal year.

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 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.

2. 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.

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

Eisai and Biogen have been collaborating on the joint development and commercialization of AD treatments since 2014. Eisai serves as the lead of lecanemab development and regulatory submissions globally with both companies co-commercializing and co-promoting the product and Eisai having final decision-making authority.

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

Since 2005, Eisai and BioArctic have had a long-term collaboration regarding the development and commercialization of AD treatments. 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 The development and commercialization agreement on the antibody lecanemab back-up was signed in May 2015.