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Eisai Co., Ltd.

EISAI TO PRESENT NEW DATA FROM LEQEMBI® (LECANEMAB-IRMB) PHASE 3 CLARITY AD STUDY AND OTHER ALZHEIMER'S DISEASE PIPELINE RESEARCH AT THE CLINICAL TRIALS ON ALZHEIMER'S DISEASE (CTAD) CONFERENCE

Update on LEQEMBI Investigational Subcutaneous Formulation

Eisai Co. Ltd (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") announced today that the company will present new data from the phase 3 Clarity AD study for its Alzheimer's disease (AD) treatment LEQEMBI® (lecanemab-irmb) 100 mg/mL injection for intravenous use and new data on the subcutaneous formulation in development at the 16th annual Clinical Trials on Alzheimer's Disease (CTAD) conference. The conference will be held in Boston, Massachusetts, United States and virtually from October 24 to 27, 2023. In addition to the data presented on Eisai's anti-amyloid beta (A β) protofibril* antibody LEQEMBI, phase 1 data for E2511, an investigational tropomyosin receptor Kinase A (TrkA) positive allosteric modulator (PAM), will be presented as well as other research from the company's AD pipeline. At the conference, Eisai will present data and research in five oral and ten poster presentations. BioArctic will give an oral presentation on lecanemab.

Late-Breaking Symposium 4 – Lecanemab for early Alzheimer's Disease: Long-Term Outcomes, Predictive Biomarkers, and Novel Subcutaneous Administration

- In a late-breaking symposium on October 25 from 17:25-18:05 EDT, Eisai will present the latest data from the Clarity AD optional tau PET longitudinal substudy. The presentation will include a post-hoc analysis of the low and intermediate + high-tau subgroups, with the low-tau subgroup representing early stages of disease studied specifically in the phase 3 core study, and the open-label extension study. An update on the investigational subcutaneous formulation, including interim safety and effect on amyloid in the brain measured by amyloid PET, will be provided.
- Distinguished faculty members Christopher van Dyck M.D., Keith Johnson M.D. and Reisa Sperling M.D. will discuss the findings in a panel led by Michael Irizarry, M.D., MPH, Eisai.
- A live webcast of this symposium can be viewed on the [Eisai Co., Ltd. website](https://www.eisai.com/en-us/clinical-trials-on-alzheimers-disease-ctad-2023).

"Alzheimer's disease is a progressive and relentless condition that requires early diagnosis^{1,2,3} and continued treatment. LEQEMBI supports neuronal function in Alzheimer's disease^{1,4,5} by clearing highly toxic protofibrils^{3,4} that can continue to cause neuronal injury and death well after plaques are cleared,"^{5,6,7,8} said Michael Irizarry, MD, MPH, Senior Vice President, Clinical Research, Neurology, Deputy Chief Clinical Officer, Clinical Evidence Generation, Eisai. "We look forward to sharing the new LEQEMBI low-tau subgroup data and subcutaneous data at CTAD 2023."

Other major oral presentations include:

- Lecanemab: Binding profiles of lecanemab and donanemab to different amyloid-beta species (OC19, presentation by BioArctic).
- E2511, a novel TrkA modulator, engages its CNS cholinergic target in a phase 1 clinical study (OC34).
- Novel CSF tau biomarkers can be used for disease staging of sporadic Alzheimer's disease (OC2).

The full list of presentations about Eisai assets and research follows.

■ **Late Breaking Symposium 4**

The Symposium title: Lecanemab for Early Alzheimer’s Disease: Long-Term Outcomes, Predictive Biomarkers and Novel Subcutaneous Administration from 17:25 to 18:05 EDT on October 25, 2023.

Presentation Title
Clarity AD: Review of the Mechanism-Based Rationale and Results of the Lecanemab Phase 3 Trial
Biomarker Assessments from Clarity AD: A Focus on Downstream Implications of Targeting Protofibrils* and Tau as a Predictive Biomarker
Lecanemab for the Treatment of Early Alzheimer’s Disease: The Extension of Efficacy Results from Clarity AD
Preliminary Update on Lecanemab Safety in Clarity AD Open-Label Extension, Including Subcutaneous Formulation
Panel discussion, Q&A

■ **Oral Presentations**

Asset/Project, Presentation Time (EDT)	Presentation Number, Title
Lecanemab October 26 (Thu) 14:50-15:05	OC19 Binding Profiles of Lecanemab and Donanemab to Different Amyloid-beta Species (presentation by BioArctic)
Lecanemab October 26 (Thu) 17:05-17:45 (Late breaking symposium 6)	Presentation 3 in Late breaking symposium 6 Aβ42/Aβ40 and Phospho-tau217 Concentration Ratios Increase the Accuracy of Amyloid PET Classification in Preclinical Alzheimer's Disease
E2511 October 27 (Fri) 14:45-14:55	OC34 E2511, a Novel TrkA Modulator, Engages its CNS Cholinergic Target in a Phase 1 Clinical Study
Biomarker October 25 (Wed) 8:45-9:00	LB7 PrecivityAD2™ Blood Test: An Analytically and Clinically Validated Test Combining p-Tau217/np-Tau217 and Aβ42/40 Ratios to Identify Brain Amyloid (presentation by C2N)
Biomarker October 25 (Wed) 11:35-11:50	OC2 Novel CSF Tau Biomarkers Can Be Used for Disease Staging of Sporadic Alzheimer's Disease
AD general October 27 (Fri) 11:45-12:00	OC29 AI-based Enrichment Tools to Increase Efficiency of Alzheimer’s Disease Clinical Trials

■ **Poster Presentations**

Asset/Project	Presentation Number, Title
Lecanemab	P018 Recruitment Source, Eligibility and Reason for Prescreen-Fail Across Sex, Race and Ethnicity: Preliminary Analysis of Prescreening Data from the AHEAD Study
Lecanemab	P045 ARIA by Clinical Subgroup and Baseline Amyloid PET Centiloid Levels from the Lecanemab Clarity AD
Lecanemab	LP011 Impact of a Site Supplemental Funding Program to Alleviate Recruitment Burden: Experiences in the Preclinical Alzheimer's Disease AHEAD Study
E2511	P044 Safety and Pharmacokinetics of Multiple Ascending Doses of E2511, a Novel TrkA Allosteric Modulator, in Healthy Volunteers
Biomarker	P070 Systematic Literature Review of the Clinical and Non-clinical Value of Imaging and Fluid Biomarker Testing to Diagnose, Identify and Monitor Patients with Alzheimer's Disease
AD general	P032 Planning the Next Generation of Alzheimer's Disease Clinical Trials Using Diverse Patient-level Database from the Critical Path for Alzheimer's Disease (CPAD) Consortium
AD general	P033 Critical Path for Alzheimer's Disease (CPAD) Consortium: Data-Driven Solutions for Clinical Trial Design and Informed Decision Making
AD general	LP003 Implications of Missing Data and Dropouts in Randomized Clinical Trials in Early Alzheimer's Disease
AD general	P145 Age-Specific Relative Comorbidity Burden of MCI: a US Database Study
AD general	P179 Development of a Mild Cognitive Impairment Risk Prediction Model Using Electronic Health Record Data

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**

- One of the AD pathological features is the accumulation of clusters (plaques) of amyloid beta (A β) in the brain. The formation of these plaques is the result of a continuous process by which individual A β proteins join together, latching onto each other, one at a time, like adding links to a chain.⁹ In the early part of this process these small chains of A β are soluble and are toxic to the nerves within the brain.^{10,11}

- The most toxic of the soluble chains is called a protofibril.³ Protofibrils are believed to contribute to the brain injury that occurs with AD and are considered to be the most toxic form of A β , having a primary role in the cognitive decline associated with this progressive, debilitating condition.^{1,2}
- Protofibrils cause injury to neurons in the brain, which in turn, can negatively impact cognitive function via multiple mechanisms, not only increasing the development of insoluble A β plaques but also increasing direct damage to brain cell membranes and the connections that transmit signals between nerve cells or nerve cells and other cells. It is believed the reduction of protofibrils may prevent the progression of AD by reducing damage to neurons in the brain and cognitive dysfunction.¹²

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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 (A β). In the U.S., LEQEMBI was granted traditional approval by the U.S. Food and Drug Administration (FDA) on July 6, 2023. LEQEMBI is an amyloid beta-directed antibody indicated as a disease-modifying treatment for Alzheimer's disease (AD) in the U.S. Treatment with LEQEMBI should be initiated in patients with mild cognitive impairment (MCI) 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. In Japan, Eisai received approval from the Ministry of Health, Labour and Welfare (MHLW) on September 25, 2023 to manufacture and market lecanemab as a treatment for slowing progression of MCI and mild dementia due to AD.

Please see full [Prescribing Information](#), including Boxed WARNING in the United States.

Eisai has also submitted applications for approval of lecanemab in EU, China, Canada, Great Britain, Australia, Switzerland, South Korea and Israel. In China and Israel, 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 a lecanemab subcutaneous bioavailability study, and subcutaneous dosing is currently being evaluated in the Clarity AD (Study 301) open-label extension (OLE). A maintenance dosing regimen

has been evaluated as part of 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 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 and includes lecanemab as the backbone anti-amyloid therapy.

2. 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.

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 Eisai and Biogen co-commercializing and co-promoting the product and Eisai having final decision-making authority. In Japan, Eisai and Biogen Japan will co-promote lecanemab, with Eisai distributing the product as the Marketing Authorization Holder.

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 LEQEMBI for the treatment of AD pursuant to an agreement with BioArctic in December 2007. The development and commercialization agreement on the antibody LEQEMBI back-up was signed in May 2015.

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