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Eisai Co., Ltd.

EISAI TO PRESENT FULL FINDINGS FROM LECANEMAB CONFIRMATORY PHASE 3 CLINICAL TRIAL (CLARITY AD) AND OTHER ALZHEIMER'S DISEASE RESEARCH AT THE 15TH CLINICAL TRIALS ON ALZHEIMER'S DISEASE (CTAD) CONFERENCE

Eisai Co., Ltd. (Headquarters: Toyoko, CEO: Haruo Naito, "Eisai") will present the efficacy, safety and biomarker findings from the company's Phase 3 confirmatory Clarity AD clinical trial for lecanemab (development code: BAN2401), an investigational anti-amyloid beta (Aβ) protofibril antibody for the potential treatment of mild cognitive impairment (MCI) due to Alzheimer's disease (AD) and mild AD (collectively known as early AD) with confirmed presence of amyloid pathology in the brain, at the 15th Clinical Trials on Alzheimer's Disease (CTAD) conference. At the meeting, which will be held in San Francisco, CA and virtually from November 29 to December 2, Eisai and esteemed faculty will present the full data in a scientific session on the first day of the meeting (November 29 at 4:50 p.m. PT). Additionally, other important research from the lecanemab clinical development program and Eisai's AD pipeline, including the company's investigational anti-microtubule binding region (MTBR) tau antibody (E2814), will be presented in four oral and ten poster presentations.

Topline results from Clarity AD were announced in late September and showed that lecanemab 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.

Key Eisai Lecanemab CTAD Presentations

- Clarity AD: Full results from the Phase 3 confirmatory Clarity AD clinical trial of lecanemab in patients with early AD will be presented in a scientific session on November 29 at 4:50 p.m. PT. Eisai will host a live webcast of presentations in the session and can be viewed live on the investors section of the Eisai Co., Ltd. website.
- Aβ Protofibrils Binding Properties: Research studying the characterization of Aβ protofibrils and the unique binding properties and mechanisms of Aβ clearance of lecanemab (Poster #P029)
- AHEAD 3-45 Study:
    - An evaluation of tau PET screening data from the Phase 3 AHEAD 3-45 study of lecanemab for associations with plasma p-tau217 and cognitive testing (Late Breaker Oral #LB1)
    - A study exploring increased accuracy of amyloid PET prediction in preclinical AD using plasma levels for Abeta42/40 and p-tau217 ratios from the Phase 3 screening data from the AHEAD 3-45 study (Late Breaker Oral #LB2)

"Based on the Clarity AD results, the investigational anti-amyloid beta protofibril antibody lecanemab has the potential to make a clinically meaningful difference for people living with the early stages of Alzheimer's disease and their families by slowing cognitive and functional decline," said Lynn Kramer, M.D., Chief Clinical Officer, Alzheimer's Disease and Brain Health at Eisai Co., Ltd. "Eisai is excited to share the results of the company's confirmatory Phase 3 Clarity AD clinical study at CTAD and present important data exploring lecanemab's potential efficacy, safety and use in a variety of early AD patient sub-populations."

Eisai aims to file for traditional approval in the U.S. and for marketing authorization applications in Japan and Europe by the end of Eisai's FY2022, which ends March 31, 2023. In July 2022, the U.S. Food and Drug Administration (FDA) accepted Eisai's Biologics License Application (BLA) for lecanemab under the accelerated approval pathway and granted it Priority Review. The Prescription Drug User Fee Act (PDUFA) action date is January 6, 2023. The FDA has agreed that the results of Clarity AD can serve as the confirmatory study to verify the clinical benefit of lecanemab. In an effort to secure traditional FDA approval for lecanemab as soon as possible, Eisai submitted the BLA through the FDA's Accelerated Approval Pathway so that the agency could complete its review of all lecanemab data with the exception of the data from the confirmatory Clarity AD study. In March 2022, Eisai began submitting application data, with the exception of Clarity AD data, to Japan's Pharmaceuticals and Medical Devices Agency (PMDA) under the prior assessment consultation system, with the aim of obtaining early approval for lecanemab so that people living with early AD may have access to the therapy as soon as possible.

CTAD 2022 Presentations Relating to Eisai's Key Compounds, Research and Collaborations

Scientific Session: **Clarity AD: A Phase 3 Placebo-Controlled, Double-Blind, Parallel-Group, 18-Month Study Evaluating Lecanemab in Early Alzheimer's Disease** Tues, Nov 29, 4:50 – 6:05 p.m. PT	
Chairman: Takeshi Iwatsubo, University of Tokyo	
Clarity AD: Clinical Trial Background and Study Design Overview	Michael Irizarry Eisai Inc.
Lecanemab for the Treatment of Early Alzheimer's Disease: Topline Efficacy Results from Clarity AD	Christopher van Dyck Yale School of Medicine
Safety Profile of Lecanemab in Early Alzheimer's Disease	Marwan Sabbagh Barrow Neurological Institute
Imaging, Plasma and CSF Biomarkers Assessments from Clarity AD	Randall Bateman Washington University
Context of Clarity AD Results	Sharon Cohen Toronto Memory Program
Panel Discussion / Q&A	

Oral Presentations

Asset in Development, Session, Time (Pacific Time)	**Presentation Title, Presenter/Authors**
Lecanemab Session: Late Breaking Oral Communications: #LB1 Wed, Nov 30 Session Time: 10:30 – 11:00 a.m. Presentation Time: 10:30 – 10:45 a.m.	Tau PET Associated with Plasma P-Tau217 and Cognitive Testing in Preclinical AD: Screening Data from the AHEAD Study A3 and A45 Trials Presenter: K Johnson Authors: K Johnson, et al

Lecanemab Session: Late Breaking Oral Communications: #LB2 Wed, Nov 30 Session Time: 10:30 – 11:00 a.m. Presentation Time: 10:45 – 11:00 a.m.	Plasma Levels of Abeta42/40 and P-Tau217 Ratios Increase Accuracy of Amyloid PET Prediction in Preclinical AD Presenter: R Rissman Authors: R Rissman, et al
E2814 Session: Late Breaking Oral Communications: #LB4 Wed, Nov 30 Session Time: 3:00 – 3:45 p.m. Presentation Time: 3:15 p.m. – 3:30 p.m.	CSF MTBR-tau243 is a Non-amyloid Specific Biomarker of Neurofibrillary Tangles of Alzheimer's Disease Presenter: K Horie Authors: K Horie, et al
E2027 Session: Oral Communications: #OC2 Wed, Nov 30 Session Time: 11:00 a.m. – 12:15 p.m. Presentation Time: 11:15 – 11:30 a.m.	Results of a Phase 2/3 Placebo-Controlled, Double-Blind, Parallel-Group, Randomized Study to Evaluate the Efficacy and Safety of 12 Week Treatment with the Phosphodiesterase 9 (PDE9) Inhibitor Irsenontrine (E2027) in Subjects with Dementia with Lewy Bodies Presenter: M Irizarry Authors: M Irizarry, et al

Poster Presentations

Asset in Development, Session, Time (Pacific Time)	**Presentation Title, Authors**
Lecanemab Session: Clinical Trials Methodology: #P012 Tues, Nov 29, 4:00 p.m. – Wed, Nov 30, 6:00 p.m.	Development and Feasibility of a Data-Driven Approach to Preclinical Alzheimer's Disease Clinical Trial Recruitment through Centralized Pre-Screening Data Collection Authors: D Kirn, et al
Lecanemab Session: New Therapies and Clinical Trials: #P029 Tues, Nov 29, 4:00 p.m. – Wed, Nov 30, 6:00 p.m.	Characterization of Amyloid-Beta Protofibrils in Alzheimer's Disease Brain and the Unique Binding Properties of Lecanemab Authors: L Lannfelt, et al
E2027 Session: Clinical Trials Results: #P048 Tues, Nov 29, 4:00 p.m. – Wed, Nov 30, 6:00 p.m.	The Effects of the Novel Phosphodiesterase 9 (PDE9) Inhibitor E2027 (irsenontrine) on CSF cGMP, Additional CSF and Plasma Biomarkers, and Clinical Outcomes in Amyloid Positive and Amyloid Negative Patients with Dementia with Lewy Bodies and Parkinson's Disease Dementia Authors: P Sachdev, et al
General AD Session: Clinical Trials Results: #P037 Tues, Nov 29, 4:00 p.m. – Wed, Nov 30, 6:00 p.m.	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 Authors: S Sivakumaran, et al
General AD Session: Clinical Trials Results: #P038 Tues, Nov 29, 4:00 p.m. – Wed, Nov 30, 6:00 p.m.	Critical Path for Alzheimer's Disease (CPAD) Consortium: Accelerating and De-Risking Therapeutic Development in AD by Building Regulatory Decision-Making Tools Authors: S Sivakumaran, et al

General AD Session: Clinical Trials Biomarkers Including Plasma: #LP66 Thu, Dec 1, 8:00 a.m. – 6:00 p.m.	Baseline Plasma pTau181 Improves Prediction of Cognitive Decline in Amyloid Positive Subjects with Mild Cognitive Impairment Authors: V Devanarayan, et al
General AD Session: Epidemiology and Clinical Trials: #P176 Fri, Dec 2, 8:00 a.m. – 5:00 p.m.	Identification of Medical Conditions as Risk Factors for Mild Cognitive Impairment: A US Claims Database Study Authors: G Li, et al
General AD Session: Epidemiology and Clinical Trials: #P184 Fri, Dec 2, 8:00 a.m. – 5:00 p.m.	Prevalence Estimations for the Alzheimer's Disease Continuum in the US Health and Retirement Study Authors: A Abbas Tahami Monfared, et al
General AD Session: Cognitive and Functional Endpoints: #P139 (Virtual Only) Thu, Dec 1, 8:00 a.m. – 6:00 p.m.	Dementia Conversion Rate Differences Between Patients with High- and Low-Risk Amnestic Mild Cognitive Impairment in the Real-World: A Prospective, Multicenter, Observational Study Authors: H Jang, et al

Sysmex Poster Presentation

Asset in Development, Session, Time (Pacific Time)	**Presentation Title, Authors**
General AD Session: Clinical Trials Biomarkers Including Plasma: #LP84A Thu, Dec 1, 8:00 a.m. – 6:00 p.m.	Three Group Classification of Participants Based on Fully Automated Plasma β-amyloid Measurements to Achieve High Positive and Negative Predictive Values Authors: K Yamashita, et al

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.

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.

Media Inquiries:
Public Relations Department,
Eisai Co., Ltd.
+81-(0)3-3817-5120

Eisai Inc. (U.S.)
Libby Holman
+1-201-753-1945
Libby_Holman@eisai.com

Eisai Europe, Ltd.
(Europe, Australia, New Zealand and Russia)
EMEA Communications Department
EMEA-comms@eisai.net

[Notes to editors]

1. About Clarity AD

Study title	A Study to Confirm Safety and Efficacy of Lecanemab in Participants with Early AD (Clarity AD)
Study population	1,795 participants of mild cognitive impairment (MCI) due to AD and mild AD (collectively known as early AD) with confirmed presence of amyloid pathology in the brain in the global study, and an additional 111 subjects ongoing in China
Treatment administered	10 mg/kg bi-weekly of lecanemab
Duration of treatment	18 months
Study locations	Japan, the U.S., Europe and China
Primary endpoint	Change from baseline in the Clinical Dementia Rating-Sum of Boxes (CDR-SB*) at 18 months
Key secondary endpoints	Change From Baseline in Amyloid Positron Emission Tomography (PET) using Centiloids, AD Assessment Scale - Cognitive Subscale 14 (ADAS-cog14**), AD Composite Score (ADCOMS***) and AD Cooperative Study-Activities of Daily Living Scale for Mild Cognitive Impairment (ADCS MCI-ADL****) at 18 months

* CDR-SB is a numeric scale used to quantify the various severity of symptoms of dementia. Based on interviews of people living with AD and family/caregivers, qualified healthcare professionals assess cognitive and functional performance in six areas: memory, orientation, judgment and problem solving, community affairs, home and hobbies, and personal care. The total score of the six areas is the score of CDR-SB, and CDR-SB is also used as an appropriate item for evaluating the effectiveness of therapeutic drugs targeting the early stages of AD.

** ADAS-cog is the most common cognitive assessment instrument used in AD clinical trials all over the world. ADAS-cog14 consists of 14 competencies: word recall, commands, constructional praxis, object and finger naming, ideational praxis, orientation, word recognition, remembering word recognition instructions, comprehension of spoken language, word finding difficulty, spoken language ability, delayed word recall, number cancellation and maze task. ADAS-cog has been used in clinical trials for earlier stages of AD including MCI.

*** Developed by Eisai, ADCOMS combines items from the ADAS-cog scale for assessing cognitive functions, MMSE and the CDR scale for evaluating the severity of dementia to enable highly sensitive detection of changes in clinical functions of early AD symptoms and changes in memory.

**** ADCS MCI-ADL assesses the competence of patients with MCI in activities of daily living (ADLs), based on 24 questions to the patient's partner about actual recent activities of daily living.

2. About Lecanemab (Development code: BAN2401)

Lecanemab is an investigational humanized monoclonal antibody for 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 (Aβ) 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-Aβ antibody that can be used for the treatment of early AD without the need for titration.

In the global Phase 3 confirmatory Clarity AD study, lecanemab treatment met the primary endpoint and reduced clinical decline on the global cognitive and functional scale, CDR-SB, compared with placebo at 18 months by 27%, which represents a treatment difference in the score change of -0.45 (p=0.00005) in the analysis of Intent-to-treat (ITT) population. Starting as early as six months, across all time points, the treatment showed highly statistically significant changes in CDR-SB from baseline compared to placebo

(all p-values are less than 0.01). All key secondary endpoints were also met with highly statistically significant results compared with placebo ($p<0.01$). Key secondary endpoints were the change from baseline at 18 months compared with placebo of treatment in amyloid levels in the brain measured by amyloid positron emission tomography (PET), the AD Assessment Scale-cognitive subscale14 (ADAS-cog14), AD Composite Score (ADCOMS) and the AD Cooperative Study-Activities of Daily Living Scale for Mild Cognitive Impairment (ADCS MCI-ADL). The incidence of amyloid-related imaging abnormalities-edema/effusion (ARIA-E), an adverse event associated with anti-amyloid antibodies, was 12.5% in the lecanemab group and 1.7% in the placebo group. The incidence of symptomatic ARIA-E was 2.8% in the lecanemab group and 0.0% in the placebo group. The ARIA-H (ARIA cerebral microhemorrhages, cerebral macrohemorrhages, and superficial siderosis) rate was 17.0% in the lecanemab group and 8.7% in the placebo group. The incidence of symptomatic ARIA-H was 0.7% in the lecanemab group and 0.2% in the placebo group. There was no imbalance in isolated ARIA-H (i.e., ARIA-H in patients who did not also experience ARIA-E) between lecanemab (8.8%) and placebo (7.6%). The total incidence of ARIA (ARIA-E and/or ARIA-H) was 21.3% in the lecanemab group and 9.3% in the placebo group. Overall, lecanemab's ARIA incidence profile was within expectations.

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 in combination with E2814 MTBR-tau antibody or placebo.

Furthermore, Eisai has initiated a lecanemab subcutaneous dosing Phase 1 study.

3. 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.

4. About the Collaboration between Eisai and Biogen for AD

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.

5. About the Collaboration between Eisai and BioArctic for AD

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 with BioArctic in December 2007. The development and commercialization agreement on the antibody lecanemab back-up was signed in May 2015.

6. About the Collaboration between Eisai and Sysmex

Eisai and Sysmex 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 regular monitoring of the effects of treatment for dementia.