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Eisai Co., Ltd.

EISAI TO PRESENT THE LATEST LECANEMAB DATA, INCLUDING ARIA-E AND SUBCUTANEOUS FORMULATION, AND OTHER ALZHEIMER'S DISEASE RESEARCH AT THE ALZHEIMER'S ASSOCIATION INTERNATIONAL CONFERENCE (AAIC) 2022

Eisai Co. Ltd (Headquarters: Toyoko, CEO: Haruo Naito, "Eisai") announced today that the company will present research from its Alzheimer's disease (AD) pipeline, including new data for lecanemab (BAN2401), an investigational anti-amyloid beta (Aβ) protofibril antibody for the 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 Alzheimer's Association International Conference (AAIC) to be held in San Diego, CA and virtually from July 31 to August 4, 2022. Eisai will present data and research in three oral and 18 poster presentations at the meeting.

On July 5, 2022 (U.S), Eisai announced that the U.S. Food and Drug Administration (FDA) accepted the Biologics License Application (BLA) for lecanemab under the accelerated approval pathway and was granted priority review, with a Prescription Drug User Fee Act (PDUFA) action date of January 6, 2023. The readout of the primary endpoint data of Clarity AD will occur in the Fall of 2022. The FDA has agreed that the results of Clarity AD when completed, can serve as the confirmatory study to verify the clinical benefit of lecanemab.

Key Eisai AAIC Presentations

- **Effect of Genotype on ARIA-E Incidence by Lecanemab:** Results from a modeling simulation to evaluate the effect of APOE4 genotype on ARIA-E incidence from study 201 Core and comparison to the observed incidence in the open-label extension among those newly treated with lecanemab. (Virtual Developing Topics #69402)
- **Lecanemab Subcutaneous Dosing**:
  - Results from a study in healthy subjects to evaluate the absolute bioavailability, pharmacokinetics, safety, and immunogenicity of lecanemab following a single fixed 700 mg subcutaneous dose. (Poster/Abstract #69438)
  - Modeling and simulation analysis aimed at showing the equivalence of fixed weekly subcutaneous dose of lecanemab to body weight-based 10mg/kg biweekly intravenous dose. (Poster/Abstract #69429)
- **Ethnic and Racial Diversity in Eisai Clinical Trials:** An evaluation of US enrollment across lecanemab (Study 201 and Clarity AD) and elenbecestat MissionAD studies in early AD to assess racial and ethnic groups and the impact of eligibility criteria in the United States. (Poster/Abstract # 69198)
- **β-Amyloid Assays Predict Brain β-Amyloid Pathology:** Data from the Eisai and Sysmex collaboration reporting on the fully automated plasma Aβ40 and Aβ42 immunoassays and their performance for predicting brain Aβ pathology defined by amyloid PET. (Poster/Abstract # 68727)

- **Comprehensive CSF Tau Profiling from Dominantly Inherited Alzheimer Network (DIAN):** An oral presentation that shares results from a study in patients enrolled in Washington University School of Medicine's DIAN-observational cohort that used Eisai's anti-microtubule binding region (MTBR) antibody, E2814, to profile MTBR-tau and then assessed timing to MTBR-tau changes in CSF and correlation to clinical, cognitive, and biomarker changes. (Oral Presentation # 65313)

"The lecanemab data Eisai will present at AAIC 2022 continues to build the body of knowledge about our investigational anti-amyloid beta protofibril antibody as we work toward the Phase 3 confirmatory Clarity AD readout this fall," said Michael Irizarry, M.D., Senior Vice President, Deputy Chief Clinical Officer, Alzheimer's Disease and Brain Health, Eisai Inc. "Additional research presented will highlight Eisai's efforts to improve ethnic and racial diversity in our early Alzheimer's disease clinical trials in the United States so that study populations mirror the U.S. Medicare population, as well as research from our collaboration with Sysmex on potential biomarkers that may contribute to early diagnosis of Alzheimer's disease."

AAIC 2022 Presentations Relating to Eisai's Key Compounds and Research

■ Eisai Oral Presentations

Asset in Development, Session, Time (Pacific Time)	**Oral Presentation Number, Title, Presenter/Authors**
E2814 Session: Using Novel Data to Refine Future Studies Sun, July 31, 2022 Session Time: 2:15 - 3:30 pm Presentation Time: 2:15 - 2:25 pm	Oral Presentation # 65313 Comprehensive CSF Tau Profiling Identifies Soluble Tau Pathophysiological Stages in Dominantly Inherited Alzheimer Network (DIAN): Implications for the DIAN-TU Tau Next Generation Platform Presenter: K. Horie Authors: K. Horie, et al
Lecanemab Session VDT-4-29: Developing Topics V Wed, Aug 3, 2022 Session Time: 8:00 - 8:45 am Presentation Time: 8:14 - 8:21 am	Virtual Developing Topics #69402 Modeled Impact of APOE4 Genotype on ARIA-E Incidence in Patients Treated with Lecanemab Presenter: L Reyderman Authors: L. Reyderman, et al
General AD Session VO-5-12: Biomarkers (non-neuroimaging): Proteomics in AD and DLB Thu, Aug 4, 2022 Session Time: 9:45 - 11:00 am Presentation Time: 10:25 - 10:35 am	Oral Presentation # 66599 Novel Peptide-Driven Global Proteomics Platform to Identify Unique Peptide Profiles Linked to Alzheimer's Disease Presenter: S. Saxena Authors: S. Saxena, et al

■ Eisai Poster Presentations

Asset in Development, Session, Time (Pacific Time)	**Abstract Number, Title, Authors**
Lecanemab Session P1-01 Sun, Jul 31, 2022, 12:30 - 2:15 pm	Abstract # 66289 Lecanemab (BAN2401) Infusion Reactions and Immunogenicity: Results from Randomized Phase 2 Study and an Open-Label Extension (OLE) Authors: I. Landry, et al

Lecanemab Session P1-13 Sun, Jul 31, 2022, 12:30 - 2:15 pm	Abstract #68222 Strategies for Diverse Participant Recruitment to a Preclinical Alzheimer's Disease Prevention Trial: The AHEAD Study Authors: D. Molina-Henry, et al
Lecanemab Session P1-16 Sun, Jul 31, 2022, 12:30 - 2:15 pm	Abstract #69220 Neuropathological Autopsy Findings in an Individual with Alzheimer's Disease who Received Long-Term Treatment with Lecanemab Authors: L. Honig, et al
Lecanemab Session P1-16 Sun, Jul 31, 2022, 12:30 - 2:15 pm	Abstract # 69429 Subcutaneous Dose Selection of Lecanemab for Treatment of Subjects with Early Alzheimer's Disease Authors: S. Hayato, et al
Lecanemab Session P2-16 Mon, Aug 1, 2022, 12:30 - 2:15 pm	Abstract # 69438 Absolute Bioavailability of a Single, Fixed Subcutaneous Dose of Lecanemab in Healthy Subjects Authors: S. Rawal, et al
Lecanemab Virtual poster Sun, Jul 31, 2022, 7:00 am - 11:55 pm	Abstract #65104 Analysis of Interaction Characteristics Between Amyloid β and Lecanemab by HDX-MS Authors: E. Yamauchi, et al
Lecanemab Session P4-28 Wed, Aug 3, 2022, 12:30 - 2:15 pm	Abstract # 69405 Lifetime Clinical Benefits of Lecanemab in Early Alzheimer's Disease Using Simulation Modeling Authors: A. Monfared, et al
Lecanemab/elenbecestat Session P1-16 Sun, Jul 31, 2022, 12:30 - 2:15 pm	Abstract # 69198 Diversity in Phase 2 and Phase 3 Placebo-Controlled, Double-Blind Lecanemab and Elenbecestat Early Alzheimer's Disease Studies Authors: J. Grill, et al
E2511 Virtual poster Sun, Jul 31, 2022, 7:00 am- 11:55 pm	Abstract # 62590 E2511, A Novel Small Compound TrkA Biased Positive Allosteric Modulator, Reinnervates Cholinergic Neuron and Activates Cholinergic Functions in Non-Clinical Studies Authors: T. Tomioka, et al
E2511 Virtual platform (on-demand)	Abstract # 66208 First-in-Human (FIH), Single- and Multiple-Ascending-Dose (SAD/MAD) Studies in Healthy Subjects of E2511, a Novel Tropomyosin receptor kinase A (TrkA) Positive Allosteric Modulator (PAM) Authors: P. Aceves, et al
General AD Session P1-10 Sun, Jul 31, 2022, 12:30 - 2:15 pm	Abstract # 65661 Healthcare Resource Utilization (HCRU) Among Veterans with Alzheimer's Disease Authors: B. Aguilar, et al

General AD Session P1-06 Sun, Jul 31, 2022, 12:30 - 2:15 pm	Abstract # 67811 Derivation and Evaluation of Signatures using Plasma Beta-Amyloid and pTau-181 for Brain Amyloid-β Detection Presenter: V. Devanarayan, et al
General AD Session P2-09 Mod, Aug 1, 2022, 12:30 - 2:15 pm	Abstract # 65606 Concordance and Disconcordance in Disease Severity Classification Between Clinician Judgments and Cognitive Testing Scores for Alzheimer's Disease in the United States Veterans Affairs Healthcare System Authors: M. Li, et al
General AD Session P2-07 Mon, Aug 1, 2022, 12:30 - 2:15 pm	Abstract # 68231 Development and Validation of AI-Based Tools for Brain Amyloid-β Detection using MRI Authors: V. Devanarayan, et al
General AD Session P4-01 Wed, Aug 3, 2022, 12:30 - 2:15 pm	Abstract # 59971 Development of Clinical Trial Simulation Tools for Alzheimer's Disease through the Critical Path for Alzheimer's Disease (CPAD) Consortium Authors: S. Sivakumaran, et al
General AD Session P4-07 Wed, Aug 3, 2022, 12:30 - 2:15 pm	Abstract # 68154 Baseline Regional Tau Distribution Predicts Fast Cognitive Decline in Subjects with Mild Cognitive Impairment Authors: A. Charil, et al
General AD Virtual platform (on-demand)	Abstract # 63148 Understanding the Impact of Social Stigma on the Patient Journey in Alzheimer's Disease through Social Media Narratives Authors: A. Tahami Monfared, et al

■ Sysmex and Eisai Collaboration Research Poster

Asset in Development, Session, Time (Pacific Time)	**Abstract Number, Title, Authors**
General AD Session P4-21 Wed, Aug 3, 2022, 12:30 - 2:15 pm	Abstract # 68727 Highly Specific Plasma β-Amyloid Assays on the Fully Automated Platform Predict Brain β-Amyloid Pathology Determined by a Centiloid Threshold of Amyloid PET Authors: K. Yamashita, et al

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.

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[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 (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. With regard to the results from pre-specified analysis at 18 months of treatment with lecanemab 10 mg/kg IV biweekly, Study 201 demonstrated reduction of brain Aβ accumulation ($P<0.0001$) and slowing of disease progression measured by ADCOMS* ($P<0.05$) in early AD patients. 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 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 Alzheimer's disease (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.

* 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 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 Elenbecestat

Elenbecestat is Eisai's in-house discovered and developed BACE (beta-site amyloid precursor protein cleaving enzyme) inhibitor. Phase 3 clinical studies (MISSION AD1, AD2) for elenbecestat aimed at early AD were discontinued in September 2019.

4. 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.

5. 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.

6. 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.

7. About the 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 regular monitoring of the effects of treatment for dementia.