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Alzheimer's Clinical Trials Consortium (ACTC)
Eisai Co., Ltd.

Alzheimer's Clinical Trials Consortium Selects Elenbecestat and BAN2401 for Upcoming Clinical Studies on Prevention of Alzheimer's Disease

The Alzheimer's Clinical Trials Consortium (ACTC) and Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") announced today that the investigational oral BACE (beta amyloid cleaving enzyme) inhibitor elenbecestat (development code: E2609) and the investigational anti-amyloid beta (Aβ) protofibril antibody BAN2401, which are currently being evaluated as treatments for early Alzheimer's disease (AD), have been selected by the ACTC as treatments to be evaluated in upcoming clinical studies targeting primary prevention (A3 Study) and secondary prevention (A45 Study) of AD. These studies will be conducted with funding from various sources including the United States National Institute on Aging (NIA), part of the National Institutes of Health, and Eisai.

The ACTC, which is an NIA-funded clinical trial network with 35 primary clinical study sites across the United States, aims to accelerate and expand studies for therapies in AD and related dementias across the spectrum from pre-symptomatic to more severe stages of disease. ACTC was established with grant funding from the NIA in December 2017. The A3 and A45 Studies are led by three academic principal investigators: Dr. Paul Aisen from University of Southern California, and Drs. Reisa Sperling and Keith Johnson from Brigham and Women's Hospital and Massachusetts General Hospital, Harvard Medical School.

"The A3 and A45 Studies should provide critically important answers about the optimal time to intervene with anti-amyloid therapy, with the hope that starting treatment much earlier in the disease process may be advantageous in preventing future cognitive decline", said Dr. Sperling, Director, Center for Alzheimer Research and Treatment at Brigham and Women's Hospital and co-Principal Investigator, ACTC.

Dr. Aisen, Director of the University of Southern California Alzheimer's Therapeutic Research Institute, which serves as the coordinating center for the ACTC, noted that "The mission of the ACTC includes the development of public-private partnerships to conduct trials of promising candidate therapies. This

collaboration with Eisai will allow us to test two promising therapies in innovative studies that may advance the field".

The A3 Study aims to get closer to the goal of primary prevention of AD, through preventing amyloid build-up in the brain. The study targets cognitively normal individuals who are currently below the threshold for amyloid elevation on amyloid PET but are at high risk for further Aβ accumulation. The A3 study will be a global, multicenter, double-blind, randomized trial to compare the effects of two doses of elenbecestat vs. placebo, to test whether a BACE inhibitor can slow brain amyloid accumulation at this very early stage of disease. The A3 Study will also measure accumulation of tangle pathology using tau PET and exploratory cognitive outcomes.

The A45 study will target the preclinical (pre-symptomatic) stage of AD. The study will enroll clinically normal participants (no/minor cognitive impairment) who have elevated levels of amyloid in brain and are at high risk for progression to mild cognitive impairment and AD dementia. The A45 study will be a global, multicenter, double-blinded, placebo-controlled, randomized trial of a treatment regimen consisting of an anti-Aβ antibody and a BACE inhibitor to prevent cognitive decline and delay biomarkers of pathological progression versus placebo. In the active arm, individuals will be provided first with BAN2401 with the goal to clear amyloid deposits and Aβ protofibrils from the brain, after which they will be maintained on elenbecestat with the aim of decreasing the production of Aβ and preventing the reaccumulation of amyloid plaques and protofibrils.

"We are excited to partner with the ACTC group with trials focusing on therapies for earlier stages of AD and will thus allow us to understand the benefit of BAN2401 and elenbecestat across a broader spectrum of the disease" said Lynn Kramer, MD, Chief Clinical Officer and Chief Medical Officer, Neurology Business Group, Eisai.

Discovered by Eisai, elenbecestat is an investigational next-generation oral candidate for the treatment of AD that inhibits BACE. By inhibiting BACE, a key enzyme in the production of Aβ, elenbecestat reduces Aβ production, which reduces amyloid aggregates in the brain. In this regard, elenbecestat is thought to exert disease modifying effects and may have potential to slow the progression of AD. Currently, a global Phase III clinical study program (MISSION AD) of elenbecestat in early AD is underway.

Discovered through a strategic research alliance between Eisai and BioArctic AB (Headquarters: Sweden), BAN2401 is a humanized monoclonal antibody for AD. BAN2401 selectively binds to neutralize and eliminate soluble, toxic Aβ aggregates (protofibril) that are thought to be a causative factor for AD. This suggests that BAN2401 may exert disease modifying effects and may have potential to slow the progression of AD. Currently, a global Phase III clinical study (Clarity AD) of BAN2401 in early AD is underway.

Eisai and Biogen Inc. (Nasdaq: BIIB) (Headquarters: Cambridge, Massachusetts, United States) are collaborating on the joint development and commercialization of AD treatments.

Trials will be starting early 2020. Individuals who may be interested in participating in these trials may sign up for additional information at **www.A3A45.org**.

<table>
<tr><td colspan="2">Media Inquiries</td></tr>
<tr><td>Public Relations Brigham and Women's Hospital
CONTACT:
Lori Schroth
Office: 617-525-6374 | Mobile: 617-459-2111
lschroth@bwh.harvard.edu</td><td>Public Relations University of Southern California
CONTACT:
Leigh Hopper
USC Central Communications
Media Relations Specialist
310-308-0405
http://pressroom.usc.edu/</td></tr>
<tr><td colspan="2">Public Relations Department
Eisai Co., Ltd.
TEL: +81-(0)3-3817-5120</td></tr>
</table>

<Notes to editors>

1. About The Alzheimer's Clinical Trials Consortium (ACTC)

The ACTC, funded by the National Institute on Aging at the National Institutes of Health, provides the infrastructure for academic clinical trials in Alzheimer's Disease and related dementias. The consortium, based at the University of Southern California, Harvard University and the Mayo Clinic, includes expert units to support clinical trials design, biostatistics, informatics, medical safety, regulatory oversight, recruitment, clinical operations, data management, site monitoring, a biomarker laboratory and repository, and neuroimaging. The ACTC includes 35 primary clinical sites across the United States.

2. About Eisai Co., Ltd.

Eisai Co., Ltd. is a leading global research and development-based pharmaceutical company headquartered in Japan. We define our corporate mission as "giving first thought to patients and their families and to increasing the benefits health care provides," which we call our *human health care* (*hhc*) philosophy. With approximately 10,000 employees working across our global network of R&D facilities, manufacturing sites and marketing subsidiaries, we strive to realize our *hhc* philosophy by delivering innovative products to address unmet medical needs, with a particular focus in our strategic areas of Neurology and Oncology.

Leveraging the experience gained from the development and marketing of Aricept®, a treatment for Alzheimer's disease and dementia with Lewy bodies, Eisai has been working to establish a social environment that involves patients in each community in cooperation with various stakeholders including the government, healthcare professionals and care workers, and is estimated to have held over ten thousand dementia awareness events worldwide. As a pioneer in the field of dementia treatment, Eisai is striving to not only develop next generation treatments but also to develop diagnosis methods and provide solutions.

For more information about Eisai Co., Ltd., please visit www.eisai.com.