ALZHEIMER’S ASSOCIATION AWARDS LARGEST EVER RESEARCH GRANT ($8 MILLION) TO EXPAND THE A4 ALZHEIMER’S PREVENTION TRIAL

LEARN Project will Track Cognitive Change in a Comparison Group of Older Individuals, and Initiate the First Tau Imaging Study in a Longitudinal Prevention Trial

CHICAGO, March 5, 2014 – The Alzheimer’s Association today announced its largest ever research grant – $8 million over four years – to support the Longitudinal Evaluation of Amyloid Risk and Neurodegeneration (LEARN) study as a companion study to the Anti-Amyloid Treatment in Asymptomatic Alzheimer’s Disease (A4) Study, a pioneering Alzheimer’s prevention trial that is starting this year.

The grant was awarded to Reisa Sperling, M.D., M.M.Sc., professor of neurology at Harvard Medical School, director of the Center for Alzheimer Research and Treatment at Brigham and Women’s Hospital and Massachusetts General Hospital, and co-principal investigator of the A4 Trial (with Paul S. Aisen, M.D., professor of neurosciences at University of California San Diego, and director of the Alzheimer’s Disease Cooperative Study).

“The Alzheimer’s Association’s goal with this award, with our colleagues at A4, is to jump-start the development of new detection methods, treatments, and prevention strategies for Alzheimer’s disease and other dementias,” said Maria Carrillo, Ph.D., Alzheimer’s Association vice president of medical and scientific relations. “These groundbreaking studies may help us distinguish people with normal cognition in the general population who are at highest risk to eventually develop Alzheimer’s, and identify treatments – and when best to administer them - to slow or prevent this terrible disease.”

“With this $8 million venture, the Alzheimer’s Association is continuing our leadership and leveraging a unique opportunity to build an expansion study onto the clinical infrastructure of the A4 Study and magnify the impact of our investment, and A4’s,” Carrillo said. “For example, we may eventually be able to develop Alzheimer’s risk profiles – similar to the Framingham Heart Risk profiles – to help determine if and under what circumstances early screening may be appropriate.”

The $4 million lead gift that made this landmark grant possible was from a private family foundation that is a member of the Alzheimer’s Association Zenith Society, which comprises the Association’s highest and most involved level of philanthropy.

LEARN – Longitudinal Evaluation of Amyloid Risk and Neurodegeneration

A first of its kind study, one objective of LEARN is to determine causes of cognitive decline besides buildup of an abnormal protein called amyloid beta in the brain; amyloid beta “plaques” are a hallmark brain lesion of Alzheimer’s disease discernable during life by specialized PET imaging, and also at
autopsy. To that end, a subset of study participants will have an innovative PET scan of the brain for buildup of tau protein, which makes up neurofibrillary tangles, the other hallmark Alzheimer’s brain lesion.

LEARN was developed in complement to the A4 Study, which is investigating whether treatments that block amyloid beta protein build up in the brain can slow or prevent Alzheimer’s in those people who do not yet have memory and thinking problems. A4 is unique because it will specifically look at individuals who are cognitively normal and have no known Alzheimer’s-related genetic mutations, but are thought to be at risk to develop the disease because of buildup of the amyloid beta protein in their brains. A4 will test if giving this asymptomatic population an anti-amyloid treatment will not only change this amyloid buildup, but more importantly slow or prevent Alzheimer’s disease.

The A4 Study is separately funded with significant support from the federal National Institutes of Health (NIH), pharmaceutical and philanthropic organizations. The A4 Study is coordinated by the Alzheimer's Disease Cooperative Study, formed through a cooperative agreement between the National Institute on Aging at NIH and the University of California San Diego, to facilitate the testing of promising drugs for the treatment of Alzheimer’s.

“The A4 Study is the ultimate test, to date, of the notion of early intervention in treatment of late onset Alzheimer’s disease,” Carrillo said.

The LEARN subcomponent of A4 will follow over time individuals who do not have elevated amyloid and determine what biological changes are related to cognitive decline, including possible later amyloid buildup as well as increases in tau levels, helping to shed light on the perplexing individual variation in disease progression.

“Although research suggests that older people with elevated amyloid-beta build-up are at increased risk of cognitive decline, there is a critical need to demonstrate a differential rate of clinical decline between amyloid positive and amyloid negative individuals on a standardized set of clinical outcomes,” said Sperling. “LEARN will attempt to confirm the important expectation that the cognitive outcomes used in the A4 Study’s treatment arms do, in fact, manifest amyloid-related cognitive decline at a faster rate. We will also learn a great deal about the non-amyloid drivers of cognitive decline to facilitate future trials aimed at other age-related brain processes.”

“We also need to ‘test the tests,’” Sperling continued. “There are some novel cognitive measures that have been developed for A4 to detect very subtle memory and thinking changes in people in the earliest stages or preclinical stages of Alzheimer’s disease, including computerized memory tests and self-assessment of memory function that are administered on an iPAD. These new tests need to be verified in large, real-world populations.”

“This timely and critically important grant from the Alzheimer’s Association to A4 will greatly enhance an already powerful study and provide valuable information that will be freely available to the field,” Sperling said.

All data generated through LEARN will be made publicly available and accessible to scientists though the Global Alzheimer’s Association Interactive Network (GAAIN™). (www.gaain.org)

The A4 Study will screen 3,000 older individuals (ages 65-85) with PET amyloid imaging to identify 1,000 people with elevated levels of amyloid-beta in their brains. This group will then be randomized into A4’s two treatment arms (active treatment n=500; placebo n=500). As a result, 2,000 highly motivated, older volunteers will not be eligible for the A4 Study. Through the Alzheimer’s Association grant, 500 of
these individuals will be matched as closely as possible to the two treatment arms, and followed in the natural history LEARN observational cohort.

The LEARN study will follow participants for 36 months with identical clinical and cognitive testing performed every six months running parallel to the A4 treatment study. The baseline PET imaging, cognitive testing, and blood work is already funded through A4. The LEARN funding is for the clinical and cognitive assessments, MRI scans at baseline and 36 months, brain PET amyloid scans at the 36 month mark, CSF lumbar punctures in 50 percent of subjects, and blood biomarker tests.

Cutting Edge Tau Imaging Substudy

To complement these studies, the Alzheimer’s Association grant will also fund the use of a cutting-edge new tau imaging agent for PET scans in the A4 Study and LEARN cohort to allow the scientists to follow the development and progress of tau protein “tangles” – which is the other important hallmark brain lesion of Alzheimer’s. Pilot studies, conducted by Keith Johnson, M.D., at Massachusetts General Hospital, suggest that tau imaging may help determine where the neurodegenerative disease process begins and how it progresses to cause the symptoms that are so devastating to people with Alzheimer’s and their families.

The PET tau imaging pilot substudy will include 150 individuals – 100 participating in the A4 Study (50 active treatment, 50 placebo) and 50 in the LEARN study. One of the goals of the A4 and LEARN studies is to determine if anti-amyloid treatment can delay the progression of the neurodegeneration as measured by tau imaging and other biomarkers, including amyloid PET, volumetric MRI, functional connectivity, and CSF markers. The study also hopes to clarify the role of tau in tracking progression towards Alzheimer's disease dementia, in particular if tau is suitable as a biological marker of disease progression from the preclinical to the early symptomatic stages of Alzheimer’s, and investigate whether the build-up of tau in the brain is altered in response to anti-amyloid treatments.

The study has yet to determine which of the several promising PET agents will be used for the tau imaging. The research team will conduct an assessment of potential applications from organizations and researchers to determine the most advantageous tau imaging agent for use in the A4 and LEARN studies.

Massachusetts General Hospital

Massachusetts General Hospital (www.massgeneral.org), founded in 1811, is the original and largest teaching hospital of Harvard Medical School. The MGH conducts the largest hospital-based research program in the United States, with an annual research budget of more than $775 million and major research centers in AIDS, cardiovascular research, cancer, computational and integrative biology, cutaneous biology, human genetics, medical imaging, neurodegenerative disorders, regenerative medicine, reproductive biology, systems biology, transplantation biology and photomedicine.

Brigham and Women's Hospital

Brigham and Women's Hospital (BWH) is a 793-bed nonprofit teaching affiliate of Harvard Medical School and a founding member of Partners HealthCare. BWH has more than 3.5 million annual patient visits, is the largest birthing center in New England and employs nearly 15,000 people. The Brigham’s medical preeminence dates back to 1832, and today that rich history in clinical care is coupled with its national leadership in patient care, quality improvement and patient safety initiatives, and its dedication to research, innovation, community engagement and educating and training the next generation of health care professionals.
Alzheimer’s Association

The Alzheimer’s Association is the world’s leading voluntary health organization in Alzheimer's care, support and research. Our mission is to eliminate Alzheimer’s disease through the advancement of research, to provide and enhance care and support for all affected, and to reduce the risk of dementia through the promotion of brain health. Our vision is a world without Alzheimer’s. Visit www.alz.org or call 800.272.3900.

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