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RESEARCH ADVANCES FROM THE ALZHEIMER'S ASSOCIATION INTERNATIONAL CONFERENCE 2011

- New Reports Highlight Advances in Early Detection and Global Collaborations -**
- French President Sarkozy Addresses Researchers on National Alzheimer's Plan -**

July 20, 2011 – This week, more than 5,000 scientists from around the world gathered in Paris to report the latest advances in Alzheimer's research at the Alzheimer's Association® International Conference 2011 (AAIC 2011). Scientists presented and discussed early detection, medical intervention and global standardization for the health epidemic of the 21st century – Alzheimer's disease and other dementias.

“Alzheimer's is growing at an alarming rate in the United States and around the world,” said William Thies, PhD, Alzheimer's Association Chief Medical and Scientific Officer. “The good news out of the Alzheimer's Association International Conference this year is that we are making advances toward earlier detection of Alzheimer's, often as a result innovative global scientific collaborations.”

“These advances are critical to helping people live longer, healthy lives free of the disability and death caused by Alzheimer's. Identifying the disease early in its process – even before symptoms start to become evident – and treating it early is how we will accomplish that. Therefore, what's really important is for everyone to join the fight against Alzheimer's disease. In the U.S., the Alzheimer's Association is leading the public effort to inform and implement the recently passed National Alzheimer's Project Act. A series of public input sessions are upcoming in August around the county. To learn more and get involved, go to www.alz.org,” Thies said.

French President Sarkozy Addresses Alzheimer's Scientists From Around the World

French President Nicolas Sarkozy addressed AAIC 2011 attendees about development and implementation of the French National Alzheimer's Plan. Launched in 2008, the French plan has three pillars: (1) improving the quality of life for people with dementia and their families; (2) mobilizing French society in the fight against Alzheimer's; and (3) advancing Alzheimer's research.

According to the Alzheimer's Association, the French National Alzheimer's Plan can be a model for the creation of similar plans in other nations around the world. It is an example of national leadership deciding that Alzheimer's is a critical issue that must be addressed because of the health and financial impact it will have on the nation as the populations ages – leadership that says we must plan for the future, invest in critical research and provide resources to all affected people.

Research Highlights from AAIC 2011

- Research from two studies presented at AAIC 2011 focused on clarifying the relationship between brain injury and mild cognitive impairment (MCI). Older veterans who experienced traumatic brain injury (TBI) showed a more than two-fold increase in the risk of developing dementia. Over a seven-year period, the risk of getting a dementia diagnosis was a little more than 15% in those who had a traumatic brain injury compared with just under 7% in those without TBI.

In another more preliminary study, researchers compared cognitive test results for a group of former American NFL football players to those of two other groups: (1) 41 similar adults with no cognitive changes and (2) a sample of 81 people diagnosed with mild cognitive impairment (MCI). The researchers found that former football players were at elevated risk for MCI compared with non-athletes. The athletes with MCI had test results similar to the other group with MCI, except the athletes were slightly less impaired and were significantly younger.

The relationship between brain injury and risk of dementia remains unclear, with some studies suggesting an increased risk and others finding no association. It is an important topic that deserves more research attention. To learn more about current knowledge of brain health and Alzheimer's risk, visit www.alz.org.

- Scientists at AAIC 2011 reported on a study suggesting that falls are more common among individuals with the earliest brain changes of Alzheimer's. They measured the rate of falls among seemingly cognitively healthy older adults with and without preclinical Alzheimer's, as determined by a brain PET scan looking for deposits of a toxic protein called amyloid. Those people with amyloid deposits had twice the risk of falls. These study results suggest that, in some people, changes in gait and balance may appear as early indicators of Alzheimer's, even before memory changes.
- Previous research has identified a number of potentially modifiable risk factors for Alzheimer's. However, it remains unclear whether changing these mostly lifestyle-based risk factors would result in fewer cases of Alzheimer's. At AAIC 2011, researchers presented a new mathematical model of global Alzheimer's risk suggesting that reducing the prevalence of well-known, lifestyle-based, chronic disease risk factors by 25 percent could potentially prevent 3 million cases of Alzheimer's worldwide, including nearly one half million in the U.S.

Scientists used mathematical modeling to calculate the percentage of Alzheimer's cases that may be attributable to diabetes, mid-life hypertension, mid-life obesity, smoking, depression, low educational attainment and physical inactivity. The researchers caution that these estimates make an assumption that has not yet been proven – that there is a causal relationship

between the risk factors examined and Alzheimer's disease, and that modifying the risk factors may lower Alzheimer's risk.

- Researchers at the AAIC 2011 in Paris reported initial findings of characteristics of a group of older adults who have maintained normal cognitive functioning over time. The scientists reported that, in their study group, the most significant factors related to maintaining healthy cognition included low scores on measures of stress, anxiety, depression and trauma – despite participants' experiencing life-threatening illnesses, violence, or living with addicted parents and spouses. The investigators hypothesize that resilience in the face of distressing life events is likely related to positive coping styles and the personality trait of "conscientiousness."
- Bapineuzumab (Pfizer, Janssen Alzheimer's Immunotherapy) is a passive immunotherapy being tested for mild to moderate Alzheimer's disease. Initial reports of Phase II study results of bapineuzumab raised concerns due to side effects of vasogenic edema (VE). Two studies presented at AAIC 2011 described (1) a re-evaluation of the Phase II safety results, and (2) the first report of long-term safety data for bapineuzumab treatment beyond 78 weeks.

Long-term safety results were reported at AAIC 2011 from an ongoing, open-label, Phase II extension study. Eighty-six (86) people received bapineuzumab treatment for at least three years and 43 for at least four years at the time of this interim analysis. Overall, bapineuzumab was generally well-tolerated and side-effects tended to be mild. The most encouraging finding from these studies is that VE (now referred to as ARIA-E) seems to occur less frequently as time goes on. The risk of developing ARIA-E diminished with an increasing number of infusions of the drug; from 6.7 percent for infusions 1-3 to 2.7 percent for infusions 4-10.

Two neuroradiologists independently reviewed more than 2000 MRI images from 262 participants in Phase II bapineuzumab studies. The scientists found that risk factors for ARIA-E included both APOE-ε4 (a genetic risk factor for Alzheimer's) and a higher dose of bapineuzumab, consistent with previous observations. According to the researchers, the risk factors identified in this study suggest that these imaging abnormalities may be related to accumulation and clearance of amyloid from blood vessels in the brain.

- One important goal in Alzheimer's research is to prevent damage and loss of brain cells by intervening early in the disease process – even before outward symptoms are evident, because by then it may be too late to effectively treat the disease. In 2008, the U.S. National Institute on Aging funded the establishment of the Dominantly Inherited Alzheimer's Network (DIAN) study, conducted by an international network of 11 leading research centers and directed at Washington University in St. Louis. The DIAN study is investigating young-onset familial Alzheimer's caused by rare genetic mutations. DIAN now has the largest and most extensive worldwide research network investigating dominantly inherited Alzheimer's. By studying Alzheimer's in rare individuals destined to get the disease because of their genes, we can learn more about the vast majority of people with Alzheimer's.

At AAIC 2011, the DIAN researchers presented the clinical, cognitive, MRI, PET, cerebrospinal fluid (CSF), and blood biomarkers from the first group of DIAN participants. The DIAN registry will eventually total 400 individuals; at AAIC, the scientists reported data from the initial 150 enrollees. The results suggest that brain chemistry and imaging changes

can be detected at least 10 years, and perhaps up to 20 years, before the expected age of onset of Alzheimer's. According to the researchers, the results demonstrate the feasibility and promise of performing Alzheimer's prevention studies in this special population.

- As the Alzheimer's field moves closer to new and earlier tests for the disease, innovative global research initiatives are taking the first important steps to confirm and standardize Alzheimer's biomarkers. A biomarker is something that can be objectively measured as an indicator of disease processes or the body's response to therapy. For example, blood pressure is a biomarker for heart disease. Two studies presented at AAIC 2011 show the importance of global standardization of biomarkers for Alzheimer's and sharing international data.

Data from three multi-center studies of Alzheimer's compared, for the first time, results of brain amyloid imaging and the impact of genetics and ethnicity on those results across countries on three different continents. The three studies are: the Alzheimer's Disease Neuroimaging Initiative (US-ADNI), Australian Imaging Biomarker and Lifestyle Flagship Study of Aging (AIBL), and Japanese Alzheimer's Disease Neuroimaging Initiative (J-ADNI). They found that the effect of age and APOE-ε4 on amyloid deposition in the Japanese population is similar to Caucasians, despite a lower ε4 allele frequency in the Japanese. Most importantly for the Alzheimer's research field, the results suggest that the three multi-national ADNI data sets are feasible for combined analysis. Combined analysis increases the power of the results, decreases ethnicity effects and makes the findings more broadly applicable. This is one of the first demonstrations of the value of open data sharing in the worldwide ADNI initiative, spearheaded by the Alzheimer's Association.

The earliest Alzheimer's related brain changes are usually seen in the hippocampus, the "control center" of memory-related activity in the brain – which often is one of the first brain areas affected by Alzheimer's. A variety of published protocols now exist for assessing hippocampal volume. As a first phase of the standardization process, researchers surveyed the various available protocols to identify underlying reasons why they result in different volume estimates. This work was funded by the Alzheimer's Association. The next step will be to create, test and verify a single protocol for MRI-based evaluation of Alzheimer's disease-related hippocampal shrinkage.

- A person with mild cognitive impairment (MCI) has problems with memory, language, or another mental function that are severe enough to be noticeable to themselves or to other people and to show up on tests, but not serious enough to interfere with daily life. Not everyone diagnosed with MCI goes on to develop Alzheimer's disease. However, research has shown that individuals with MCI have an increased risk of developing Alzheimer's over the next few years, especially when their main problem is memory. Identification of factors that predict progression from MCI to Alzheimer's dementia has emerged as an important Alzheimer's research priority. A global perspective on MCI including data from six countries (Australia, France, Germany, Sweden, United Kingdom, and the United States), presented for the first time at AAC 2011, found that a number of common factors emerge as indicators of the progression from MCI to Alzheimer's, including: depression, apathy, anxiety, age, loss of ability in activities of daily living, cardiovascular factors (including stroke and diabetes), and low levels of education. The studies also call for doctors to pay more attention to subjective memory complaints in otherwise healthy individuals as possible indicators of Alzheimer's.

- It is believed that build-up of a toxic molecule known as beta amyloid in the brains of people with Alzheimer's occurs prior to cognitive decline. An accurate measurement or indicator of increased amyloid deposits in the brain could possibly provide an earlier diagnosis compared to current methods of cognitive testing, and also possibly indicate the progression or severity of the disease. Two studies reported at AAIC 2011 investigated new methods for possible use in early detection of Alzheimer's, tracking progression of the disease, identifying participants for research trials and measuring the impact of therapies. One study uses blood measurements for estimating the amount of a toxic substance known as beta amyloid deposited in the brain. The other study suggests that abnormal levels of certain proteins in cerebrospinal fluid (including beta amyloid) in people with mild cognitive impairment may indicate who will develop Alzheimer's within the next 10 years.
- A small pilot study presented at AAIC 2011, researchers explored whether characteristics of blood vessels in the back of the eye might serve as possible biomarkers for Alzheimer's disease. The researchers found that the width of certain blood vessels in the back of the eye were significantly different for people with Alzheimer's compared with healthy people, and that this correlated with brain imaging that is indicative of Alzheimer's. While most Alzheimer's-related pathology occurs in the brain, the disease has also been reported to create changes in the eye, which is closely connected to the brain and more easily accessible for examination in a doctor's office. The study is very preliminary, but encouraging.
- Results of a survey of people in France, Germany, Poland, Spain and the U.S. reported that while people fear Alzheimer's second only to cancer, the overwhelming majority say they would go to the doctor if they saw symptoms of memory loss and confusion. The poll was supported by a grant to Alzheimer Europe from Bayer, and was conducted by the Harvard School of Public Health. However, many of the respondents believe there is now an effective medical treatment to slow the progression of Alzheimer's; and many also said there is a reliable test currently available to determine if a person is in the early stages of Alzheimer's. Neither of these statements is true. The scientists say better public education about Alzheimer's is needed.

About AAIC

The Alzheimer's Association International Conference (AAIC) is the world's largest conference of its kind, bringing together researchers from around the world to report and discuss groundbreaking research and information on the cause, diagnosis, treatment and prevention of Alzheimer's disease and related disorders. As a part of the Alzheimer's Association's research program, AAIC serves as a catalyst for generating new knowledge about dementia and fostering a vital, collegial research community.

About the Alzheimer's Association

The Alzheimer's Association is the world's leading voluntary health organization in Alzheimer 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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