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**TWO NEW ALZHEIMER'S DISEASE STUDIES SHOW ADVANCES AGAINST
DIFFERENT TREATMENT TARGETS**

**- Plus, Higher than Expected MCI Prevalence Shows
Urgent Need for Better Therapies -**

Chicago, July 28, 2008 – Two studies related to experimental Alzheimer's therapies reported positive results today at the 2008 Alzheimer's Association International Conference on Alzheimer's Disease (ICAD 2008) in Chicago.

One Phase II trial, of a compound called AL-108, targeted early abnormal brain changes in a protein called "tau" in a condition related to Alzheimer's called mild cognitive impairment (MCI). The researchers saw improvement on various measures of memory. Another study examined brains of people with Alzheimer's half of whom had diabetes, and half did not. The researchers found that people in the study who took a combination of insulin and oral anti-diabetes medications had fewer Alzheimer's-related brain changes (amyloid plaques) than all the others in the study. This could be a pathway for developing new treatments.

Plus, a new study from the Mayo Clinic showed higher than expected rates of MCI in a large, older population. People with MCI have ongoing memory problems, but they do not have other losses such as confusion, attention problems, and difficulty with language. People with MCI are much more likely to get Alzheimer's than the general population.

"We are making progress. It is very important that we have as many drugs as possible in the pipeline for Alzheimer's, and that we explore every available avenue for treatments," said Ralph Nixon, MD, PhD, of the Alzheimer's Association's Medical and Scientific Advisory Council. "However, the population is aging, and we need to make significant advances soon in treatment and prevention of Alzheimer's or it will become an overwhelming epidemic, wiping out our healthcare resources and devastating Medicare."

Dr. Nixon is Professor of Psychiatry and Cell Biology, Vice Chairman of Research in the Department of Psychiatry, and Director of the Silberstein Institute at New York University School of Medicine. Dr. Nixon is also Director of Research and the Center for Dementia Research at the Nathan S. Kline Institute for Psychiatric Research.

Rates of Cognitive Impairment Higher Than Anticipated

As the field of Alzheimer's research moves toward earlier treatment and ultimately prevention, it becomes necessary to identify patients at the earliest point in the disease. Mild Cognitive Impairment (MCI) is the term used to describe the intermediate state between normal aging and the very earliest features of Alzheimer's, but its frequency in the population is not known.

Ronald C. Petersen, MD, PhD, and colleagues at Mayo Clinic, Rochester, MN, are conducting the Mayo Clinic Study of Aging, which is a longitudinal study of people ages 70 to 89 from Olmsted County, Minnesota. One of the goals of the Study is to follow healthy subjects over time to detect the earliest point of cognitive impairment. In 2004, the researchers recruited 1,786 people who were found to be cognitively normal, and reevaluated them a year later. All subjects underwent a baseline evaluation including an interview of the subject and their study partner by a nurse, a cognitive assessment, and a neurological exam by a physician.

Individuals in the study developed MCI at a rate of about 5.3 percent per year, and this rate was higher with advanced age – about 3.5 percent per year for 70-79 year olds and about 7.2 percent per year for 80-89 year olds. Men were nearly twice as likely to develop MCI as women.

“The rate of new MCI cases in this group was considerably higher than anticipated,” Petersen said. “If we extrapolate Alzheimer's incidence rates to MCI, we would expect perhaps 1 to 2 percent per year, but our findings were substantially higher than that.”

“These results underscore the urgency of developing new and better strategies to create disease modifying therapies for Alzheimer's. In addition, for public health purposes, we need to know how many people are cognitively impaired and potentially on the road to Alzheimer's,” Petersen added.

AL-108 Trial (Phase IIa) Shows Promise of Tau-Targeted Therapies in MCI

MCI can be divided into two broad subtypes. Amnesic MCI (aMCI) significantly affects memory, while nonamnesic MCI does not. Other functions, such as language and attention span, may be impaired in either subtype. Persons with aMCI convert to Alzheimer's at a much higher rate than the normal aging population.

Donald Schmechel, MD, Adjunct Professor of Medicine (Geriatrics), Professor of Psychiatry, and Associate Professor of Neurobiology of Duke University Medical Center, Durham, NC, and colleagues conducted a Phase IIa clinical trial of AL-108 (Allon Therapeutics), an experimental therapy designed to combat neurofibrillary tangles (NFT). NFT are one of the early key abnormal brain changes in aMCI and Alzheimer's. AL-108 is a nasal spray formulation of an eight amino acid peptide, known as NAPVSIPQ, derived from the neuroprotective protein Activity-Dependent Neuroprotective Protein.

The trial was a double-blind, randomized, placebo-controlled study to evaluate the safety, tolerability and effect of two doses of AL-108 after 12 weeks of treatment (low dose=5 mg daily, high dose=15 mg twice daily). The study was open to men and women, age 55-85 years (inclusive, mean age=69.4) with Mini-Mental State Exam scores ≥ 24 , self-reported memory complaint corroborated by spouse or companion, and Wechsler Memory Scale III (WMS-III) age-adjusted Logical Memory II score ≤ 5 . One hundred forty-four (144) subjects were randomized at 16 centers in the U.S. Cognitive tests were conducted four weeks prior to drug administration, and then at baseline, four, eight, 12, and 16 weeks.

The primary endpoint is a change from baseline at Week 12 in a composite score that focuses on measures of memory. Secondary efficacy endpoints include analysis of the change in the individual cognitive tests as a function of both treatment and length of treatment.

High dose AL-108 gave a statistically significant improvement in the delayed match-to-sample test (DMTS 12s). After four weeks, a 34.2 percent change from baseline ($p=0.067$, versus placebo) was seen; by Week 16, a 62.4 percent improvement from baseline was observed ($p=0.038$, versus placebo), showing a durable response four weeks after treatment ended.

An improvement on the digit span forward test of the high dose group became statistically significant at Week 8, with an 11.2 percent change from baseline ($p=0.032$, versus placebo), and remained significant at Week 16 with an 11.7 percent change from baseline ($p=0.052$, versus placebo).

The low dose AL-108 was not different from placebo. AL-108 was well tolerated with similar rates of adverse events (AEs) in placebo and AL-108 treated subjects. The most common AE was headache which occurred at a rate expected in this patient population. No serious AEs were associated with AL-108.

“Twelve weeks of AL-108 treatment given intranasally by spray resulted in a statistically significant, dose-dependent and durable improvement on measures of short-term memory, including visual, verbal, and auditory working memory, which is a type of memory function that deteriorates throughout the progression of Alzheimer’s,” Schmechel said.

“This makes AL-108 the first drug to validate in humans the importance of the ‘tangle’ or ‘tau’ pathway in Alzheimer’s. Based on these results in MCI, there are plans for further development of AL-108 in Alzheimer’s,” Schmechel added.

Insulin and Diabetes Drugs May Reduce Alzheimer’s Brain Lesions

Several large-scale studies have shown that people with diabetes have a higher risk of developing Alzheimer’s than persons without diabetes. At the same time, previous research showed that some people with diabetes had fewer Alzheimer’s-associated brain lesions than non-diabetics.

Michal Schnaider Beeri, PhD, of the Mount Sinai School of Medicine, New York, and colleagues hypothesized that the treatment of diabetes with insulin and other drugs may have helped reduce the observable brain damage attributed to Alzheimer’s. At ICAD 2008, they reported the results of a study examining the brains of 124 persons with diabetes and 124 without diabetes, of comparable age, sex, and dementia severity, from the Mount Sinai School of Medicine Brain Bank.

Diabetic subjects were classified according to their recorded lifetime anti-diabetic medications: none ($n=29$), insulin only ($n=49$), diabetes medications other than insulin only ($n=28$), or concomitant use of both insulin and any oral anti-diabetic medications ($n=18$). Densities of Alzheimer’s-associated brain lesions, known as amyloid plaques and neurofibrillary tangles, were assessed in several brain regions.

The researchers found that diabetic subjects who were treated with both insulin and oral hypoglycemic agents had significantly fewer amyloid plaques (as much as 80 percent) than people in all the other categories. These other groups of subjects did not differ from each other in their Alzheimer’s-related brain characteristics.

“These results suggest that the combination of insulin and oral anti-diabetes medications may beneficially influence Alzheimer’s-related brain changes,” Beeri said. “This also points to biological pathways in the brain, such as insulin signaling, that might be a focus for developing new treatment strategies.”

About ICAD

The 2008 Alzheimer's Association International Conference on Alzheimer's Disease (ICAD 2008) is the largest gathering of international leaders in Alzheimer research and care ever convened. At ICAD 2008, more than 5,000 researchers from 60 countries will share groundbreaking information and resources on the cause, diagnosis, treatment and prevention of Alzheimer's and related disorders. As a part of the Association's research program, ICAD serves as a catalyst for generating new knowledge about dementia and fostering a vital, collegial research community. ICAD 2008 will be held in Chicago at McCormick Place, Lake Side Center from July 26–31.

About the Alzheimer's Association

The Alzheimer's Association, the nonprofit world leader in Alzheimer's research and support, is the first and largest U.S. voluntary health organization dedicated to finding prevention methods, treatments and an eventual cure for Alzheimer's. For more than 25 years, the donor-supported Alzheimer's Association has provided reliable information and care consultation; created supportive services for families; increased funding for dementia research; and influenced public policy changes. For more information, call (800) 272-3900 or visit www.alz.org.

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- Ronald C. Petersen, "The Mayo Clinic study of aging: Incidence of mild cognitive impairment." (Funders: National Institute on Aging; Robert H. and Clarice Smith and Abigail Van Buren Alzheimer's Disease Research Program of the Mayo Clinic)
- Donald E. Schmechel. "A phase 2, double-blind, placebo-controlled study to evaluate the safety, tolerability, and effect on cognitive function of AL-108 after 12 weeks of intranasal administration in subjects with mild cognitive impairment." (Funder: Allon Therapeutics)
- Michal Schnaider Beerli. "Combination of insulin with other diabetes medication is associated with lower Alzheimer's neuropathology." (Funder: National Institute on Aging)

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