Statement of Richard J. Hodes, M.D.
Director, National Institute on Aging
Senate Special Committee on Aging

Good afternoon, Chairman Collins, Ranking Member McCaskill, and distinguished members of the Committee. I am Richard J. Hodes, M.D., Director of the National Institute on Aging (NIA), which is one of the 27 Institutes and Centers of the National Institutes of Health (NIH). It is an honor to be here today to discuss NIH's efforts to stem the rising tide of Alzheimer's disease, a devastating condition and a public health issue of increasing relevance and urgency, both in the United States and globally.

First, however, I would like to thank you, Chairman Collins, as well as your colleagues on the Committee, for your unflagging championship of

The **Study of Nasal Insulin to Fight Forgetfulness (SNIFF)** will test an insulin nasal spray to see if it improves or preserves memory in adults with memory-related mild cognitive impairment or mild Alzheimer's disease. This trial is ongoing.

The **Dominantly Inherited Alzheimer's Network Trials Unit (DIAN-TU)** trial will assess the safety, tolerability, and biomarker efficacy of two experimental drugs, gantenerumab and solanezumab, in people who are genetically at high risk for the disease. Recruitment recently began for this trial.

The **Alzheimer's Prevention Initiative APOE4 (API APOE4)** trial will test two anti-amyloid drugs, an active vaccine and a beta-secretase inhibitor, in cognitively normal older volunteers who are at increased risk of developing late-onset Alzheimer's because they have two copies of the APOE4 gene. We anticipate beginning recruitment for this study later this year.

The **Alzheimer's Prevention Initiative Autosomal Dominant Alzheimer's Disease (API ADAD)** study is a five-year clinical trial to determine if an antibody treatment, crenezumab, designed to bind to and possibly clear away abnormal amounts of amyloid protein in the brains of people with Alzheimer's, can prevent decline in cognitive function. Crenezumab will be tested among members of a unique and large family population in Colombia sharing a genetic mutation known to cause observable signs of Alzheimer's disease at around age 45. This study is ongoing.

In addition, NIH supports over 70 projects aiming to discover and develop new therapeutics for Alzheimer's, including a major ongoing initiative supporting studies that lead to the submission of an Investigational New Drug (IND) application to the Food and Drug Administration, a prerequisite for beginning human trials of potential new therapies. NIH also supports over 35 clinical trials, including both pilot and large scale trials, of a wide range of interventions to prevent, slow, or treat Alzheimer's, mild cognitive impairment (MCI), and/or cognitive decline.

As we move toward identifying at-risk individuals earlier in the disease course, we are also identifying more effective ways to gauge treatment efficacy more quickly and efficiently. For example, although we have made tremendous strides in the development of measures that can alert physicians and researchers to subtle cognitive declines in healthy older people, the best way to detect changes in people's everyday function is less clear. Researchers with the NIA-supported

international study supported in part by the NIH. As of today there are 35 identified regions in

drive the changes in molecular networks leading to the clinical signs and symptoms of the disease.

The next frontier in research involves the integration of genetic, biomarker, and clinical information. Even as genetic studies such as the previously-discussed IGAP study may be of considerable utility in identifying potential pathways of interest and biomarkers of disease, biomarkers can also guide genetic studies in both early- and late-onset forms of the disease.[7] For example, using neuroimaging and cerebrospinal biomarkers as *endophenotypes* – markers that are associated with, but not direct symptoms of, a condition – investigators have identified several novel Alzheimer's-related genetic variants.

We hope to expand our knowledge of the gene/biomarker interface through a major new initiative supported by the NIA and the National Human Genome Research Institute which was announced in July 2014. Five newly-awarded projects will analyze how genome sequences—the order of chemical letters in a cell's DNA—may contribute to increased risk or protect against Alzheimer's disease. The NIH awarded grants for using innovative new technologies and computational methods for the analyses. The scientists also will seek insights into why some people with known risks do not develop the disease. The investigators will analyze the genome sequencing data generated during the first phase of the ongoing Alzheimer's Disease Sequencing Project (ADSP), and will use the data to identify rare genetic variants that protect against, or contribute to, Alzheimer's disease, explore differences in data from different racial/ethnic groups, and examine how brain images and other biomarkers are associated with genome sequences. This wou01 Tu9(t(-300484005700573004005 70eoy)20 0 0 170054h-5000sC4840057005 170h3ds)

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will be useful for determining the efficacy of new therapies, as well as a program project to further understand the cellular disease processes by which certain genetic mutations lead to FTD.

Through an interdisciplinary workshop, NIH recently brought together diverse groups of researchers to address issues related to research on small blood vessels in the brain and other organ systems, which will inform research on the underlying causes of vascular contribution to cognitive decline and dementia. Finally, as mentioned earlier, NIH has released an initiative to encourage interdisciplinary research to understand the interaction of vascular disease and Alzheimer biology. These are just a few examples of the many NIH-supported studies, initiatives, and workshops aimed at understanding the causes of and finding treatments for these devastating diseases.

Supporting Caregivers of Patients with Dementia

Finally, NIH-supported research on interventions and strategies to support individuals who face the often overwhelming challenge of caring for a loved one with dementia has produced some welcome results. We now know that some of these interventions, many of them developed and tested by NIH-supported researchers, can reduce caregiver depression and anxiety, improve the caregiver's knowledge about dementia and how to cope with it, reduce

health representatives and ACL's Native American Family Caregiver programs to train and support caregivers of frail elders.