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Good morning, Chairman Collins, Ranking Member Casey, and distinguished members of the Committee. I am Richard 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 update you on our progress addressing a public health issue of considerable urgency: the need for compassionate care and effective treatment for men and women with Alzheimer's disease or a related form of dementia (AD/ADRD). I look forward to telling you about some of the many ongoing initiatives and exciting scientific advances in dementia treatment and care supported by the over one billion dollars in additional funding for AD/ADRD--including frontotemporal dementia, vascular cognitive impairment/dementia, Lewy body dementia, and mixed dementias--NIH has received since 2014.

### **An Issue of Widespread Concern**

As you know, Alzheimer's disease is a progressive brain disease that slowly destroys memory and thinking skills and eventually even the ability to carry out the simplest tasks of daily living. Other forms of dementia are characterized by different brain pathologies and may initially present with different symptoms, but all forms of dementia share a common, devastating trait: Although treatment can help manage symptoms in some people, these diseases cannot, at present, be cured or even adequately controlled.

In the United States alone, as many as 5.6 million people age 65 and older are living with Alzheimer's disease.<sup>1</sup> Although several large epidemiological studies suggest that the percentage of older people with dementia, including Alzheimer's disease, has been declining, absolute numbers of persons with dementia continue to rise as<sup>2</sup> the number of "oldest old" – those over 85 and at highest risk of dementia – climbs. The growth of this age group is expected to accelerate in the coming decades, and will increase from approximately 5.8 million in 2010 to some 19 million in 2050.<sup>3</sup> Health conditions that often emerge at midlife and are known risk factors for

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<sup>1</sup> Hebert LE et al. Alzheimer disease in the United States (2010-2050) estimated using 2010 census. *American Academy of Neurology* 80: 1778-1783, 2013. See Table 1.

<sup>2</sup> Larson EB, Yaffe K, and Langa KM. New Insights into the Dementia Epidemic. *New England Journal of Medicine* 369: 22-25-2277, 2013.

<sup>3</sup> Vincent, Grayson K. and Victoria A. Velkoff. The Next Four Decades, The Older Population in the United States, 2010-2050. Current Population Reports, P25-1138. U.S. Census Bureau, Washington, D.C., 2010.

later development of dementia, such as hypertension and diabetes, also remain common.<sup>4</sup> For these reasons, unless we identify a way to prevent or effectively treat dementia, the number of affected Americans will rise dramatically within the lifetime of many of us here today.<sup>5</sup>

Family caregivers provide the majority of care for people with dementia in the community, and the support that is typically required for a person with dementia as the condition progresses can profoundly impact the caregiver's well-being. While many dementia caregivers report satisfaction with caregiving and find the experience deeply rewarding, they may also feel exhausted, overwhelmed, isolated, and distressed at the mental, emotional, and behavioral changes these diseases can cause in their loved ones, as well as the unceasing labor involved in physical care. NIA-supported investigators estimate that family caregivers spend an average of around 92 hours—the equivalent of over two full workweeks—per month on in-home caregiving of adults ages 65 and older with dementia. For spouses of persons with dementia, that figure rises to some 145 hours per month.<sup>6</sup>

In addition to the severe medical and psychological costs to patients and their families, AD and related forms of dementia impose significant economic costs in many forms. In a recent NIA-funded study, economists found in the last five years of life, total health care spending for people with dementia was more than a quarter-million dollars per person, some 57 percent greater than costs associated with death from other diseases, including cancer and heart disease. This analysis estimates that total health care spending was \$287,000 for those with probable dementia and \$183,000 for other Medicare beneficiaries in the study.<sup>7</sup>

Acknowledging the magnitude of this public health crisis, in 2010 Congress passed the National Alzheimer's Project Act (NAPA), and in 2012 then-Secretary Sebelius of the Department of Health and Human Services (DHHS) released the groundbreaking and ambitious National Plan to Address Alzheimer's Disease.<sup>8</sup> One goal articulated in the National Plan is to prevent and/or effectively treat AD/ADRD by 2025. Another goal, and one that we consider at

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<sup>4</sup> Barnes DE and Yaffe KY. The Projected Effect of Risk Factor Reduction on Alzheimer's Disease Prevalence. *Lancet Neurology* 10: 819-828, 2011.

<sup>5</sup> Hebert, op cit.

<sup>6</sup> Kasper JD et al. The Disproportionate Impact of Dementia on Family and Unpaid Caregiving to Older Adults. *Health Aff (Millwood)* 34: 1642-1649, 2015.

<sup>7</sup> Kelley AS et al. The Burden of Health Care Costs for Patients with Dementia in the Last Year of Life. *Ann Intern Med* 163: 729-736, 2015.

<sup>8</sup> The National Plan included other AD-related dementias, including frontotemporal, Lewy Body, vascular, and mixed dementias, from its establishment.

NIA to be of similarly critical importance, is to expand supports for people with AD/ADRD and their families and caregivers.

### **Back to Basics**

Thanks to the efforts of an expanding community of scientists, we have important progress to report on our understanding of the disease and more promising paths to prevention and effective treatment. Our hope for a cure has never been stronger, as new resources and initiatives are allowing the scientific community to redouble their efforts to understand the basic biology of AD/ADRD, prevent the development of these diseases, and possibly even reverse the most intractable symptoms.

An area in which we have made remarkable progress is in the complex genetics of AD/ADRD. Initiatives such as the Alzheimer’s Disease Sequencing Project, the Alzheimer’s Disease Genetics Consortium, the Late-Onset Alzheimer’s Disease Family Study, and many others continue to provide important insights into the etiology of these diseases. For example, we now know from our studies of genetics in combination with clinical and pathological studies that AD is not a single entity, but rather has several different complex phenotypes—underscoring the fact that a “one-size-fits-all” approach to treating the disease may not be appropriate, and highlighting the need for personalized diagnosis and treatment. Individuals’ AD-related genes can also be used in the research setting to calculate a “polygenic risk score” that estimates the likelihood of developing the disease across time.

A number of genes implicated in the pathogenesis of these diseases have been identified, and new discoveries are constantly being made. Just last month, an NIA-supported analysis of genetic data from more than 94,000 individuals revealed five new risk genes for AD and confirmed 20 known others. The international research team also reported for the first time that mutations in genes specific to tau, a protein that is abnormal in AD, may play an earlier role in the development of the disease than originally thought.

These new findings also support developing evidence that groups of genes associated with specific biological processes, such as cell trafficking, lipid transport, inflammation and the immune response, are “genetic hubs” that play an important role in the disease process; this in turn suggests that interventions that target one process may have broad effects on other processes

and diseases. Some genes are observed in more than one pathway, leaving open the possibility that individuals with multiple affected pathways may be more vulnerable to the pathophysiology associated with AD/ADRD. This knowledge may provide an avenue to identify highly targeted therapeutic approaches for AD/ADRD.

Even beyond the realm of genetics, NIH remains at the forefront of discovery related to the basic biology of neurological disease, and right now we are revisiting and re-exploring the implications of the most fundamental fact about AD/ADRD: These are diseases that, for the most part, occur in people ages 65 and older. They are diseases of aging. What does this mean, at the cellular level, and how can we leverage this information to better understand and even intervene against these diseases?

Answers are beginning to emerge from the growing field of geroscience, which is built upon the hypothesis that slowing aging processes will delay the appearance or severity of many different chronic diseases. Supporting this hypothesis is data from the NIA-supported Interventions Testing Program and a number of other projects and initiatives, through which researchers have identified behavioral, genetic and pharmacological approaches to extend lifespan in a variety of model systems. Importantly, interventions that extend lifespan often result in significant delays in the appearance of pathology and frailty. Conversely, when lifespan is shortened, diseases and frailty occur earlier.

Geroscience approaches are already producing exciting and promising results and opening new avenues for translational research. For example, last year NIA-supported investigators found that senescent cells, which are alive but no longer divide or function normally, in the mouse brain play a role in the neurodegeneration associated with AD/ADRD, and that eliminating these cells before they cause damage to neurons appears to preserve cognition. Future research questions include whether these findings apply to other mouse models of AD/ADRD or to humans, and whether treatments to destroy or inhibit senescent cells can reverse cognitive damage that has already occurred.

Last month NIA released a pair of funding opportunity announcements (FOAs) to support independent research teams that will use established approaches that manipulate the rate of aging in model systems to advance our understanding of the role of aging in the development and etiology of AD/ADRD. We anticipate that these studies will provide key information about how

aging processes result in vulnerability to dementia, and may also uncover new targets for prevention and treatment.

### **Translational Medicine in the Era of Big Data**

Translation of basic findings into effective treatment has traditionally been a slow process. However, we have been able to speed that process significantly in recent years, building on basic science and with the support of an expanded foundational “infrastructure for discovery”. NIA is increasingly turning to massive data sets containing de-identified information on millions of people in order to speed discovery, and to facilitate diagnosis and treatment based on highly specific individual data. These “big data” approaches are facilitating discovery even as they help usher in the era of precision medicine.

An NIH flagship Big Data initiative related to AD/ADRD, the Accelerating Medicines Partnership-Alzheimer’s Disease (AMP-AD), is a precompetitive public-private partnership including government, industry, and nonprofit organizations that focuses on discovering novel, disease relevant therapeutic targets and on developing biomarkers to help validate existing therapeutic targets. AMP-AD is transforming the way new therapeutic targets and biomarkers are discovered through the use of powerful molecular profiling and advanced information technologies and by providing an infrastructure for rapid and broad sharing of valuable and robust datasets.

The Target Discovery component of the AMP-AD Program applies a systems biology approach to the discovery and validation of new therapeutic targets in an open science research model. Since its inception in 2014, the research teams within the AMP-AD Target Discovery Consortium have established a centralized data resource/infrastructure, the AMP-AD Knowledge Portal, for rapid and broad data sharing; generated human data from over 2000 brains and over 1000 plasma samples (across all stages of AD) and made them widely available to researchers; developed network models of disease pathways/targets; and nominated over 100 novel candidate targets. In addition, the newly nominated targets and associated data and analyses have also been made broadly available through the AGORA web-based interactive platform. This groundbreaking program was renewed in 2018.

One intriguing finding using brain banks and cohort studies participating in the AMP-AD consortium provides new evidence that viral species, particularly herpesviruses, may have a role in AD biology. Although these findings do not prove that the viruses cause the onset or progression of Alzheimer's, they do demonstrate how viral DNA sequences and activation of biological networks—the interrelated systems of DNA, RNA, proteins and metabolites—may interact with molecular, genetic and clinical aspects of Alzheimer's. NIA is planning a new initiative, to which the National Advisory Council on Aging has given concept approval, to encourage studies to answer whether microbial pathogens in AD represent a causal component of the disease and to invite research across a broad range of topics on mechanisms underpinning neurodegeneration in AD associated with microbial pathogens in the central nervous system.

### **New Biomarkers for Detection, Diagnosis, and Treatment Monitoring**

Another area in which NIA has made tremendous progress is the identification and use of clinical, imaging, genetic, and biochemical biomarkers for early detection and tracking of AD/ADRD and for use tracking treatment efficacy in clinical trials. 2019 will mark the fifteenth anniversary of the establishment of the Alzheimer's Disease Neuroimaging Initiative (ADNI), a landmark public-private partnership. ADNI investigators have made major contributions to AD research, particularly in the areas of early detection and progression monitoring. For example, ten years ago, Alzheimer's disease could only be definitively diagnosed after the patient had died, because the only fully reliable diagnostic tool we had was examination of post-mortem brain tissue for the disease's characteristic amyloid plaques and tau tangles. Today, however, due in large measure to the work of ADNI scientists, we can diagnose Alzheimer's in living subjects using sophisticated neuroimaging techniques or by detecting tau and amyloid in the cerebrospinal fluid. These breakthroughs have had and will continue to have important implications on researchers' ability to counsel patients with symptoms of dementia, help them manage their symptoms, and recommend appropriate clinical trials. A critical aspect of this initiative is its innovative data-access policy, which provides all data without embargo to all scientists in the world. More than 53 million data downloads from ADNI servers have been executed by investigators around the world, and ADNI also makes biosamples available to scientists globally.

Although groundbreaking and undeniably effective, brain imaging and cerebrospinal fluid analysis are both cumbersome and expensive. NIA-supported researchers are currently working to develop blood tests that detect amyloid- $\beta$ , a pathological hallmark of Alzheimer's, and other AD-related entities in the blood and plasma. In one study, NIA-supported investigators found that measuring the ratio of A $\beta$ 42/A $\beta$ 40 (subtypes of amyloid  $\beta$ ) in blood plasma may be one such inexpensive, minimally invasive test. Elsewhere, investigators with the NIA Intramural Research Program developed a novel framework to identify brain and blood metabolites associated with disease pathology and progression in prodromal and preclinical AD as potential disease biomarkers.

### **From Target to Treatment**

NIA supports a number of initiatives to make the often fraught journey from target or biomarker identification to compound development to animal testing to evaluation in humans as seamless as possible. For example, one of the major reasons for the high failure rate of AD drugs in the clinic is the poor predictive power of studies in AD transgenic mouse models. To address this obstacle, NIA launched the MODEL-AD Consortium, which aims to develop some 50 new transgenic models based on genetic risk factors for late-onset AD and make them available to researchers from academia and industry for use in basic research and therapy development. The Consortium has already created models incorporating some of the most common genetic mutations found in sporadic late-onset disease. Researchers supported by the NIA are also using human induced pluripotent stem cells—stem cells that are generated directly from adult cells and that can be induced to develop into different types of cells—to define the molecular function of identified risk genes for AD and to build 3-dimensional tissue models of brain cell interactions. These assays are also being used to screen large numbers of potential therapeutic compounds in a remarkably short period of time.

As potential treatments and treatment targets emerge from laboratory and model studies, it can be challenging for scientists to decide which compounds to test—and how to test them. NIA is investing in bringing to light data from preclinical efficacy testing studies (published and unpublished) by creating the Alzheimer's Disease Preclinical Efficacy Database (AlzPED). AlzPED is a publicly available and searchable data resource designed to improve transparency in



reporting and reproducibility and translatability of animal model efficacy testing studies. The database hosts curated summaries of published studies (over 600 published studies curated to date) and provides easy access to information on: study design methods and outcomes, animal models, therapeutic agents, therapeutic targets, patents and related clinical trials. It also provides a platform for creating citable reports/preprints of unpublished studies, including studies with negative findings. In addition to being a valuable resource for academic and industry researchers and data scientists, AlzPED also provides NIH and other funding organizations with a tool for enforcement of requirements for transparent reporting and rigorous study design.

New challenges arise when a compound is ready to move from animal into human testing. Basic researchers may lack the resources or know-how to move promising compounds into clinical trials; biopharmaceutical companies may be reluctant to invest in neurotherapeutics development because there are few clinically validated targets or strategies, there is a long track record of failure, and many nervous system disorders affect relatively small populations.

To help meet these challenges, NIA participates in the NIH Blueprint Neurotherapeutics Network (BPN), which provides support for small molecule drug discovery and development. Through this and other initiatives, NIA supports a robust preclinical-early clinical drug development program for AD/ADRD. Over 30 novel AD/ADRD drug candidates are currently in different stages of late preclinical and early clinical development for over a dozen different targets (non-A $\beta$ ; non-tau). From 2012- 2016 NIA and BPN supported the biotech firm Tetra Discovery Partners for a program aimed at developing BPN14770, which is designed to treat behavior and cognition in Fragile X Syndrome, and memory loss in early-to-moderate AD patients. The compound has successfully completed Phase 1 testing, is now in Phase 2 clinical testing for Fragile X Syndrome and is poised enter Phase 2 testing for early AD in 2019.

At present, over 40 compounds are currently under study for the prevention and treatment of AD, mild cognitive impairment, and age-related cognitive decline. NIH also supports approximately 140 clinical trials, including both pilot and large-scale trials, of a wide range of interventions to prevent/slow/treat AD and/or cognitive decline. Over 60 of these studies are testing non-pharmacological interventions, including but not limited to diet, exercise, and cognitive training.

Other investigators are exploring the application of treatments already in use for other conditions. For example, one researcher recently conducted a small clinical trial of deep brain

stimulation (DBS), an effective therapy in the treatment of Parkinson's disease, in patients with AD. Although this study failed to show benefit in individuals under 65, additional analyses in individuals over the age of 65 showed a potential slowing of cognitive decline. These results indicate that DBS may be beneficial in late-, but not early-onset AD. The National Advisory Council on Aging (NACA) recently granted concept approval for an FOA supporting research on other noninvasive brain stimulation approaches to treat AD/ADRD. Elsewhere, NIA-supported investigators found that a form of vitamin B3 prevented neurological damage and showed cognitive benefits in a mouse model of AD; other investigators found that people with mild cognitive impairment (MCI), often a precursor to AD, who took metformin, a safe and commonly-used diabetes drug, performed better on some cognitive tests (although not others) than MCI patients who did not take the drug—results that justify further study of this widely-used agent.

To ensure that the benefits of participation in AD/ADRD clinical trials are broadly available to diverse populations, last year NIA established its National Strategy for Recruitment and Participation in Alzheimer's and Related Dementias Clinical Research. The National Strategy was developed with facilitation by the Alzheimer's Association and the expertise and insights of government, private, academic, and industry stakeholders, as well as individuals, caregivers, and study participants. It represents the culmination of more than two years of dedication and work to outline practical, proactive approaches to help study sites engage a wider, more diverse number of volunteers. In another NIA-supported initiative, the Global Alzheimer's Platform Trial-Ready Cohort for Preclinical/Prodromal Alzheimer's Disease, NIA is working with the Global Alzheimer's Platform Foundation to recruit a large number of "trial-ready" potential participants at high risk of developing AD/ADRD. Investigators anticipate that this approach will markedly shorten recruitment timelines, potentially from years to months.

A new, NIA-funded Alzheimer's Clinical Trial Consortium (ACTC) will help investigators harness best practices and latest methods for Alzheimer's trials. The ACTC includes 35 sites in the United States and will address the complexity, time, and expense of participant recruitment and site activation to find new and effective ways to treat or prevent these devastating disorders. It will also provide needed infrastructure in areas such as imaging, biostatistics, and data management.

## **“Until There Is a Cure, There Is Care”**

I would also like to report on progress toward the equally compelling goal of expanding research on care and caregiving interventions in the area of Alzheimer’s and related dementias. This field of research has grown tremendously over the past several years, and some programs have already begun to be disseminated into more widespread use. For example, the REACH II (Resources for Enhancing Alzheimer’s Caregiver Health) caregiver intervention, originally supported by the NIA, has been demonstrated to be effective in an ethnically diverse population and is currently being translated more broadly through the Department of Veterans Affairs. Centers in fifteen states are participating in this effort, and modifications are underway to extend the intervention to caregivers of veterans with traumatic brain and spinal cord injury. The Indian Health Service (IHS) is also pilot testing the program with several Tribal Nations sites through the IHS and Administration for Community Living.

Other care-related interventions exist for which additional data and evaluation are needed. To provide a comprehensive assessment of evidence for effectiveness of interventions studied to date, including REACH II, the NIA has entered into an interagency agreement with the Agency for Healthcare Research and Quality to support an Evidence-based Practice Center (EPC) in conducting a systematic review of the relevant science and issuing findings on these topics. The NIA has also contracted with the National Academies of Sciences, Engineering, and Medicine to establish a committee of experts that will assess the EPC’s evidence review in the context of a range of other data, identify research gaps, and issue recommendations that will inform future research and practice.

Although some progress has been made in these areas, the critical need for further research around care and services for persons with dementia and their caregivers led NIA, along with the DHHS Office of Women’s Health and Office of the Assistant Secretary for Planning and Evaluation and several private organizations, to convene the first National Research Summit on Dementia Care in October 2017. The goal of this seminal meeting was to identify research directions for accelerating improvements in comprehensive care, services, and supports for persons with dementia, families, and other caregivers. The Summit yielded 58 final recommendations across multiple areas of research. NIA has used those recommendations to set

milestones for future research focus and priority-setting, and leads an NIH-wide effort to address these milestones through funding initiatives targeting specific research priorities.

For example, FOAs directed at the small business community soliciting applications for research on socially assistive robots and other assistive technologies for persons with dementia and their caregivers have led to the ongoing development of home technologies to sustain the ability of persons with dementia to dress themselves; a non-invasive sensor that both detects difficulty swallowing and helps re-train the person with dementia to swallow safely, reducing the individual's risk of food aspiration; and a friendly robotic "coach" that encourages people with MCI to exercise.

Other investigators are testing the ability of web-based and distance learning interventions to improve the health and well-being of dementia caregivers, who may be isolated by geography or circumstance. And this year the NIA will expand the Edward R. Roybal Centers for Translational Research in the Behavioral and Social Sciences of Aging to include 6-8 new Centers focused on translation of interventions to improve dementia care and support for caregivers.

Recently, NIA released a new FOA aiming to improve care for persons with dementia and their caregivers through health systems. Through the Alzheimer's Disease and Alzheimer's Disease-Related Dementias Health Care Systems Research Collaboratory, NIA will support a center for collaborative research within and among health and long-term care systems to encourage pragmatic trials of innovative dementia care. The Collaboratory will build investigator capacity, support AD/ADRD pragmatic trial design, and maintain the resource and knowledge base for AD/ADRD pragmatic trials.

Another upcoming NIA initiative, recently approved in concept by NACA, is an FOA on Home and Community-Based Services (HCBS). Community-based services—that is, services obtained in the community versus nursing homes or other residential long-term care facilities—can provide needed assistance and respite to overwhelmed family members of persons with dementia, but significant barriers to their use may exist. For example, a caregiver may lack the resources to pay for community-based services, or be unable to transport a loved one with dementia to an adult day program, or be subject to insurance caps limiting how long or how often a service may be used. This FOA will address gaps in our understanding of these barriers and the degree to which they affect use of non-residential services. Research funded under this FOA will

also help us to better understand what services are being utilized in the community, as well as outcomes associated with varied use of services accounting for needs of diverse populations, including those who live alone.

In addition, in September 2018, NIA launched the Improving Care for People with Alzheimer's Disease and Related Dementias Using Technology (iCare-AD/ADRD) Challenge. This Eureka prize competition seeks to spur the development of technology applications to improve dementia care coordination and/or care navigation, as part of the implementation of the 21st Century Cures Act. Up to \$400,000 in cash prizes may be awarded to teams or individuals that successfully complete in the challenge. Entries will be accepted through June 30, 2019.

### **Recruiting New Talent**

A final point that I'd like to make is that the explosion in research opportunities has required us to reach out to the best and brightest scientific minds in the nation and motivate them to turn their considerable talents to the challenges of AD/ADRD. We have been particularly successful in encouraging young investigators as well as established investigators not previously focusing on AD/ADRD to apply for AD/ADRD-related research funding. An internal NIA analysis showed that between 2015 and 2018, over a quarter of the Institute's Research Project Grant (R01) equivalent AD/ADRD awardees were either NIH-designated New Investigators (i.e., this was their first competitive NIH grant) or Early-Stage Investigators (not only was this their first competitive NIH grant, but they were also within 10 years of their terminal degree). Over a third of the R01 AD/ADRD awardees had not previously applied for AD/ADRD funding from NIH – half of whom were established investigators previously pursuing other lines of research. We anticipate that the success of these investigators in securing funding will ensure an active pipeline of energetic researchers looking at AD/ADRD from new perspectives for years to come.

NIA also released a notice in 2018 inviting researchers holding non-AD/ADRD grants from other NIH Institutes and Offices to apply for supplemental funding for new research that was relevant to both AD/ADRD and the topic of their research grant. The response was tremendous. Over 300 supplements were awarded to investigators representing some 25 NIH Institutes, Centers, and Offices, broadening the spectrum of research and inspiring investigators

to think creatively about how their area of study could interface successfully with research on AD/ADRD. A few of these research topics included:

- A study to evaluate the effects of alcohol drinking on AD-linked neural and behavioral pathologies in a mouse model (National Institute on Alcohol Abuse and Alcoholism)
- A gene-environment study of the association between early-life exposure to air pollutants and later-life development of AD-related pathology (National Institute of Environmental Health Sciences)
- A study examining the interrelationships among psychosocial stress due to discrimination, markers of vascular risk, and cognitive function in early middle-aged African-American women (National Heart, Lung, and Blood Institute)
- A study to identify trends in infection management and palliative care in facility-bound AD/ADRD patients at the end of life (National Institute of Nursing Research)
- Validation of a novel biomarker—changes in blood flow, as determined by neuroimaging—to measure AD initiation and progression (National Institute of Neurological Disorders and Stroke)

This highly successful program has been repeated in FY 2019.

The past five years have been an era of unprecedented growth and discovery for AD/ADRD. The most highly-anticipated discovery of all—an effective treatment or preventive intervention for these diseases—remains in the future. This future can't arrive quickly enough for the millions of Americans who are afflicted today, but I believe that working together in partnership, the scientific, advocacy, patient, and legislative communities will get there.

This concludes my testimony, and I welcome your questions.