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Ranking Member Baldwin and distinguished Senators, thank you for inviting me to be here today. On behalf of the University of Wisconsin's School of Medicine & Public Health, I am honored to participate in today's forum. My name is Sterling Johnson. I hold a PhD in Clinical Neuropsychology, and I am the Jean R. Finley Professor of Geriatrics and Dementia in the Department of Medicine's Division of Geriatrics and Gerontology at the University of Wisconsin School of Medicine and Public Health. I have been a scientific researcher for over twenty years.

I am honored to be representing an institution with such a deep, rich history in scientific research, and a lasting commitment to advancing research training and community service. University of Wisconsin School of Medicine and Public Health has over 6500 faculty and staff, the majority of which contribute to scientific research, as well as faculty who are currently training more than 660 medical students, 85 MD-PhD students, and 772 PhD students. We have nearly 400 scientists leading or co-leading NIH funded grants.

Medical research is the cornerstone of progress in healthcare. In fact, research is the only way we can make progress – learning what causes disease, how to detect and diagnose disease earlier and more accurately, and the effectiveness of new treatments. Without consistent and reliable investment in medical research, led by the National Institutes of Health (NIH), our health outcomes as a country would stagnate. The impact of NIH investment on some of the most common diseases is clear. For example, the absolute number of deaths from heart disease – the number one cause of death in the US – is on the decline, even though older adults are the fastest growing segment of our population. We are seeing similar progress in breast and prostate cancer death rates. These gains are a direct result of NIH investments in these diseases over the past 30 years.

These kinds of breakthroughs take time- progress is not always linear. The NIH has shown perseverance in areas where it would have been easier to simply give up, and that has made the difference for millions of patients in America. Since the 1940s and 1950s, federal investment in scientific research led by the NIH has ensured that America is the global leader in biomedical research. We are the envy of the world in this regard. Each year, NIH awards over 60,000 grants that directly support over 300,000 researchers at more than 2,500 different institutions, working every single day to advance our collective scientific

knowledge. This continued investment has ensured that some of the most impactful research being done globally happens here in the United States, and we must continue those investments to ensure we are not outpaced by our adversaries.

It took almost twenty years from the first discovery related to immunotherapy to assurance that it could beat back cancer. Cancer immunotherapy, or the utilization of components of the immune system to target and eliminate cancer, is now a lifesaving cure for many kinds of cancers.

Today, in the Alzheimer's disease field, we are experiencing something similar. As we've gotten better at treating many common diseases, deaths from Alzheimer's and related dementias have greatly increased over time. In response, the NIH began investing consistently in the early 2010s. The impact is substantial. New therapies that slow the disease and new simple diagnostic tools such blood tests make it easier for doctors to diagnose Alzheimer's especially in its early stages and even prior to symptoms. Without consistent NIH investments over time, this could not have happened.

Other exciting new discoveries are also making a difference for Alzheimer's patients. Immunotherapy approaches are being used to robustly remove amyloid plaques from the brain and slow down symptom progression, and two drugs have received full approval from the Food and Drug Administration. More drugs are being tested—and some of these clinical trials are being funded by the NIH. There is a long way to go to get to a cure, but the path is now clear.

We knew previously that Alzheimer's disease is defined biologically by abnormal collections of two proteins, beta-amyloid and tau. These cause plaques and tangles in the brain that are hallmarks of Alzheimer's disease. When Alzheimer first described this in 1906, it was by looking at a slice of brain tissue through a microscope. In 2004, with NIH funding and support, researchers at University of Pittsburgh developed a medical imaging procedure for seeing amyloid plaques in living patients. This effectively opened the modern era of research and discovery. Soon a medical imaging technique was invented to visualize tangles which happen inside brain cells and are so closely tied to symptoms. As a result of NIH investment, private companies such as GE and others have begun significant investments to further the research supported by NIH, directly impacting Wisconsin, and other states across the nation.

At the University of Wisconsin, we've shown that amyloid plaques are detectable with imaging about 20 or more years prior to the dementia stage of Alzheimer's. That gives us quite a window of opportunity to intervene, resulting in a more cost-effective delivery of care, expanded treatment choices for patients, and improved patient quality of life. We

know from our research that health and lifestyle optimization won't necessarily stop plaques and tangles from forming, but it may slow down the development of symptoms, which is empowering for patients and their families.

We have also used NIH funding to look at how Alzheimer's disease is interrelated with other diseases. For example, we now know that people living with Down syndrome are at exceptionally high risk for Alzheimer's disease. In fact, nearly all individuals who have Down syndrome will develop the plaques and tangles from Alzheimer's disease if they live to an advanced age. Understanding the biological underpinnings of the relationship between these diseases is the first step toward identifying ways to help patients.

NIH grants are essential to researchers like me to fund our work at the level that is needed to do definitive studies. I have a highly trained professional workforce. Many of these team members have trained for years to develop the skills necessary to advance our research. I am very fortunate to have the support of the National Institute of Aging, which offers extraordinary infrastructure for Alzheimer's Disease research across the field. They have developed this infrastructure in accordance with the National Alzheimer's Project Act (NAPA), which was mandated by Congress on a bipartisan basis. My ongoing projects include:

The Wisconsin Registry for Alzheimer's Prevention (WRAP), a long-term observational study that provides information on individuals' cognition, lifestyle, physical activity, biomarkers, genetics and metabolism. WRAP volunteers have generously agreed to be tested repeatedly for years starting at midlife. The data are made available to other researchers studying Alzheimer's disease. Findings from the project include:

- The insight that Alzheimer's is detectable using imaging or blood biomarkers two decades before a clinical diagnosis of mild cognitive impairment or dementia. Our work has shown that the presymptomatic stage of AD lasts at least as long as the cognitively impaired stage, offering us new ways to prevent disease.
- Insights on health and lifestyle factors that provide some measure of protection to cognitive decline.
 - Discoveries that pathologies including vascular disease can co-exist with Alzheimer's and hasten cognitive decline

Wisconsin Alzheimer's Disease Research Center (ADRC), which provides infrastructure and support for researchers in their pursuit of answers that will lead to improved diagnosis and care for patients while, at the same time, focusing on the program's long-term goal — finding a way to prevent and effectively treat Alzheimer's disease. The center was established in 2009 with funding from the National Institute on Aging (NIA) and is one of 35

federally funded, [NIA-designated Alzheimer's Disease Research Centers](#) across the United States.

- ADRC is an efficient engine that accelerates Alzheimer's disease research. The Wisconsin ADRC [maintains a pool](#) of research volunteers, a repository of cognitive test data, samples of cerebral spinal fluid, serum, DNA and blood, brain scans, and brain tissue samples that donors have generously agreed to provide after death. Scientists from UW-Madison, or anywhere in the world, can [apply](#) to access this information and use it in their research. At any one time, we are supporting work on about 50 different research studies at the University of Wisconsin-Madison.

The ADRC consortium for CLARITY in AD and Related Disorders Through Imaging: I'm proud to help lead CLARiTI, a multi-site imaging observational study that will occur at the ADRC sites to examine how the several causes of cognitive impairment interact.

This project aims to understand what else may be going on in the brain besides Alzheimer's that may be contributing to cognitive decline. Neuropathologists have shown that what we presume to be Alzheimer's disease is, over 65% of the time, a mix of causes - but we don't yet have the tools to identify all of them. Such knowledge would greatly inform clinical trial participant selection, improve diagnosis and prognosis, and accelerate biomarker and treatment discovery.

In the development and execution of the scientific projects I have just described, my colleagues and I support hundreds of well-paying jobs in the state of Wisconsin at all levels of education and experience.

Every grant dollar has impacts far beyond the lab. In fiscal year 2023, every \$1 of NIH funding generated approximately \$2.46 of economic activity. In Wisconsin, NIH grants support state of the art equipment including imaging facilities, clinical space at the medical center and other buildings where we see our patients for their research visits, and a highly skilled ancillary workforce to make those research visits successful including accountants who manage the grants, nurses who monitor patients, and many others.

Reducing funding will lead to interruptions and negative consequences that go far beyond an individual grant. The research suffers, but so do the staff and communities. By reducing investments in research, you not only slow the discovery of new treatments, but you slow economic growth as well.

In my work, I have already begun to see the impacts of current NIH cuts and delays. I mentioned that we are launching a study with multiple ADRC sites to examine how the causes of cognitive impairment interact – this is absolutely an essential next step into understanding the progression of Alzheimer's, and if other ADRCs do not have their funding

renewed, the work will likely stop. It is disruptive and even professionally devastating to early-career scientists who are at the cusp of launching their careers, and it discourages promising young students from pursuing a future in biomedical research.

We are also seeing impacts on the current researcher workforce, and future pipeline. Without consistent and dependable NIH support, researchers will have to make difficult choices about where to spend their careers. If you were a young researcher, would you choose to enter a public institution at risk of being defunded each year, or go to a private organization or pharmaceutical company with a guaranteed commitment to your project? So far, one researcher at my lab has chosen to leave, in part due to the uncertainty of NIH funding to pursue another option. If the delays continue, I expect to see more key researchers and trainees make different choices, creating a workforce gap. My institution trains 2,380 medical and research professionals every year, but that number will decline dramatically with reductions in our NIH support.

Ranking Member Baldwin and distinguished Senators: this is a critical moment for families across America facing the unimaginable burden of Alzheimer's Disease. We are closer than ever to effective therapies and prevention strategies, as researchers increase momentum developed from the individual discoveries supported by the NIH. The progress in the past 20 years especially has been remarkable. We must stay the course. For these patients –our loved ones – the clock is ticking. All they want is time, and we have the opportunity to give them that. But it can only be done with full support by the NIH.