

Written Remarks of David Morgan, PhD

Thank you, Congressman Bilirakis, for your leadership in convening this roundtable focused on the very important issue of speeding the delivery of therapies and treatments to patients in need. I also thank you and your colleagues on the Energy & Commerce Committee, particularly Chairman Upton, for undertaking the 21st Century Cures Initiative.

My name is Dr. David Morgan. I am the CEO of the Byrd Alzheimer's Institute at the Morsani College of Medicine at the University of South Florida. The Byrd Institute is a Translational Research Center, combining patient clinics, drug trials, caregiver education and laboratory research in a single location. I also serve as lead representative of ResearchersAgainstAlzheimer's, a coalition of more than 400 Alzheimer's researchers who believe it is possible to achieve our national goal of preventing and effectively treating Alzheimer's by 2025. However, critical to achieving this goal is obtaining additional resources – both public and private – and establishing changes in the regulatory environment to facilitate these discoveries.

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Alzheimer's and related dementias are devastating not only to the 5 million victims and their families, but also health care budgets and infrastructure. New data published earlier this year attributes more than a half-million deaths annual to Alzheimer's, rivaling heart disease and cancer. The total annual medical costs of the disease exceed \$200 billion, more than for cancer or heart disease. The major risk factor for Alzheimer's is old age. As we see continued gains in longevity (because of success in treating other diseases) and the baby boom generation reaches the age of risk, the financial impact of Alzheimer's on Medicare and Medicaid will overwhelm our country's capacity to maintain these programs.

There exists not a single disease-modifying therapy for Alzheimer's, and the most recent medication was approved 10 years ago. Available drugs only treat the symptoms...like treating pneumonia with aspirin. We need a disease modifying agent... like penicillin for pneumonia. We need a prevention agent... like statins for heart disease.¹ Unfortunately, of 413 Alzheimer's trials conducted between 2002 and 2012, only one agent advanced to the Food and Drug Administration and was approved, giving us a success rate of 0.4 percent.² These failures and the immense costs associated with them have chilled industry interest in the sector.

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But, as a scientist, I and others perceive a much brighter future. Congress recognized the threat of Alzheimer's and it passed a law creating the National Alzheimer's Project Act (NAPA). In 2012, a plan was issued with the absolutely necessary objective of preventing and effectively treating Alzheimer's by 2025 – 11 years from today. The last 5 years have seen major advances in our scientific understanding of the disease, to the point that pathways leading to prevention, initially, and, later, effective treatments can be readily envisioned. We do not need breakthroughs to achieve this goal; we need the resources and improved regulatory environment to do the very hard work of proving the science is right.

Congress and the Administration have also been supportive of the need for additional public resources to support Alzheimer's research at the National Institutes of Health. To reach this goal we will need at

¹ See: http://www.alz.org/research/science/alzheimers_disease_treatments.asp

² See: <http://alzres.com/content/6/4/37>

least \$2 billion per year for research, about 4 times more than is being spent today. Two billion is still less than what we spend on cancer, on AIDs or on heart disease. This is not an expense, it is an investment to avoid the major future costs that are otherwise inevitable.

However, beyond providing robust and stable funding for the NIH to support Alzheimer's research, Congress can – and must – remove impediments within current law or practice, particularly when it comes to how we develop drugs and conduct clinical trials, how we review and evaluate drugs at the FDA and how we reimburse for treatments and therapies in the Medicare program.

I will now offer a few specific ideas for your consideration:

Additional Exclusivity

The dismal success rate of candidate Alzheimer's therapies that I mentioned earlier has dampened industry interest in the sector. While even the most appealing incentives will not crack the scientific challenges, adequate incentives could attract and retain industry interest. A major concern in the Alzheimer's space is that clinical trials simply take too much time and consume too much money. A trial to slow disease progression can take 4 years from the first enrollee to the final data analysis. The most promising approaches using "prevention" trials to greatly delay or completely avoid the disease may take up to 8 years. With the patent clock ticking, these studies are too long for industry to take the financial risk when the period of exclusivity is so short.

Beginning with the Orphan Drug Act more than 30 years ago and continuing more recently to disorders in pediatrics and infectious disease, Congress has provided **additional periods of exclusivity** to drugs for indications where the need was great but the markets were limited. These incentives of varying timeframes succeeded in attracting industry participation to a field and, ultimately, producing treatments for patients in need. I would strongly encourage Congress to recognize the barriers in the Alzheimer's space and provide a similar additional exclusivity period and potentially other incentives for disease-modifying treatments for Alzheimer's and dementia, particularly for drugs developed through very lengthy and costly prevention trials. Additional exclusivity is a proven success and one that we should consider for this challenge.

Dormant Therapies & Repurposing

I would also urge Congress to focus on incentives for the immense potential that may exist, particularly in therapeutic areas like Alzheimer's, in repurposing existing drugs used to treat other conditions. Additionally, there have been candidate drugs that were abandoned during development, largely because the sponsor concluded that inadequate patent protection existed to warrant continued development. Legislation known as the **MODERN Cures Act**, which the Congressman is cosponsoring, would address the latter concern with such "dormant" therapies, and should be enacted into law. Additionally, the NIH through the National Center for Advancing Translational Sciences or NCATS, is doing some exciting work to screen existing drugs to determine potential use to treat other diseases. While this work at NIH should be encouraged, policymakers need to also explore appropriate incentives that would motivate industry to take on the task of developing such drugs.

21st Century Clinical Trials

As noted earlier, trials for Alzheimer's therapies are too lengthy and too costly. All stakeholders – academia, industry, investors, foundations, patient organizations and government – must work to reduce the time and cost of this important phase of the discovery pipeline. A report issued late last year by RTI International found that reengineering our system of conducting trials could reduce considerably the time and cost of Alzheimer's drug development. They estimated this would prevent about 7 million new cases from the years 2025 to 2040. Innovations such as a standing **network of high-performing Alzheimer's clinical trials sites**, a **global registry** of well-characterized and willing trial participants and **centralized Institutional Review Boards (IRBs)** can all help us achieve this goal. Congress must drive the FDA to embrace more innovative trial designs (fewer placebo groups and more treatment arms) and to communicate its thinking on these important issues through clear and current guidances. Additionally, we must all strive to develop and qualify **Alzheimer's biomarkers** so those that are validated can be used with confidence as surrogate endpoints in Alzheimer's trials to further accelerate the process.

Patient Access

Finally, I want to note that the job is far from over once FDA approval for a drug is granted. In order for patients to benefit, they must have access to these hoped for new therapies and treatments. This means that payers, particularly Medicare, must recognize the immense potential benefits of a treatment or therapy, particularly disease-modifying treatments that can prevent, lessen or delay the debilitating symptoms of the disease, reducing healthcare costs and improving the lives of patients.

Such a policy should also extend to diagnostics. Unfortunately, a year ago the Center for Medicare and Medicaid Services (CMS) failed to approve reimbursement for the use of an imaging agent that could help physicians rule out Alzheimer's in patients without a clear diagnosis. Recent studies indicate that about 20 percent of all Alzheimer's diagnoses do not have Alzheimer's at autopsy or by use of imaging biomarkers. Misdiagnosis of Alzheimer's is a real risk to patients, particularly those with more treatable forms of dementia that go improperly treated because of this error. Encouraging the Center for Medicare and Medicaid Services to reconsider its refusal to accept reimbursement of the Alzheimer's imaging agent based upon the Appropriate Use Criteria developed by the Alzheimer's Association and the Society for Nuclear Medicine³ will significantly benefit the lives of patients and families misdiagnosed with Alzheimer's disease and may lead to diagnosis of another more treatable cause for the memory impairment.

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Thank you, again, for convening this session.

3. Update on appropriate use criteria for amyloid PET imaging: dementia experts, mild cognitive impairment, and education. Johnson KA, et al. J Nucl Med. 2013 Jul;54(7):1011-3