ACT-AD
Accelerate Cure/Treatments for Alzheimer's Disease

Advisory Council

Alliance for Aging Research

Alzheimer's Foundation of America

American Society on Aging

National Alliance for Caregiving

National Association of Area Agencies on Aging

National Consumers League

Research!America

Society for Women's Health Research

May 30, 2014

The Honorable Fred Upton
Chairman
U.S. House of Representatives
Committee on Energy and Commerce
2125 Rayburn House Office Building
Washington, DC 20515

The Honorable Diana DeGette
U.S. House of Representatives
2368 Rayburn House Office Building
Washington, DC 20515

RE: Comments on 21st Century Cures: A Call to Action White Paper

Dear Chairman Upton and Representative DeGette,

The coalition to Accelerate Cure/Treatments for Alzheimer's Disease (ACT-AD) is comprised of more than 50 national organizations representing patients, caregivers, researchers, health professionals, and other health advocates. For the past nine years we have supported efforts to expedite the development, review, and approval of transformational therapies for Alzheimer's disease (AD). On behalf of ACT-AD, we would like to thank you for your leadership in announcing the 21st Century Cures Initiative. We understand all too well that many of the discoveries made today will not provide relief in time to reach the millions Americans expected to suffer from the devastating effects of Alzheimer's in the next decade. Thank you for your desire to provide hope to these patients and their families by endeavoring to shorten the time it takes to bring new treatments to market. ACT-AD appreciates the opportunity to comment on the Committee's first white paper about what could improve treatment discovery, development and delivery for Alzheimer's disease.

As you are well aware, more than 5 million Americans currently live with Alzheimer's disease. By the middle of this century that number is expected to double. Without more meaningful treatment options that allow for improved quality of life for those with the disease or interventions that halt, delay or reverse progression of AD in its earliest stages, the human and economic burdens associated with this disease will continue to advance at unsustainable rates. In recent years several late-phase therapeutic development programs for Alzheimer's disease were discontinued due to marginal or negative results. In response to challenges faced in these programs, the U.S. Food and Drug Administration (FDA) became a more active partner in the development process for Alzheimer's disease by routinely participating in meetings and conferences with patient advocates, the scientific community, and industry focused on improving AD clinical trials and issuing draft guidance for industry further clarifying requirements for testing early-stage Alzheimer's treatments. The National Institutes of Health (NIH) has also recently elevated the importance of Alzheimer's disease research by advancing three clinical trials targeting earlier intervention in the disease course and specific gene mutations that predispose a person to develop Alzheimer's disease. By forming the Accelerating Medicines Partnership, NIH will be able to leverage resources and data from the public and private sectors to make more rapid advances in identifying Alzheimer's biomarkers

that predict a treatment outcomes. We applaud the FDA and NIH for making these commitments that prioritize Alzheimer's disease based solely on the societal threats this disease poses despite a lack of commensurate resources to offset their involvement in these research and regulatory activities.

Several years ago, we and our colleagues in the advocacy community called on Congress to create the National Center for Advancing Translational Sciences (NCATS) at NIH because of its unique ability to aid in the translation of basic scientific discoveries into treatments for diseases like Alzheimer's. One approach taken by NCATS is drug repurposing under its "Discovering New Therapeutic Uses for Existing Molecules" program. Repurposing has had very promising results in treating difficult diseases including HIV/AIDS and certain cancers. We hope for similar success in repurposing drugs for the treatment of Alzheimer's disease. One NCATS project was started in 2013 to use a repurposed drug to block activity of a certain Alzheimer's-linked protein in mice. The results of this study have not been released and the effects of this treatment in humans are not yet known. However, this week NCATS put out a call for applications to "New Therapeutic Uses" program. This round of funding provides the added incentive of an additional year of support for researchers looking to study available drugs for pediatric indications. Given that the study of drugs for age-related disease like Alzheimer's in geriatric populations (of mice and humans) pose many complexities as do trials in pediatric populations, and drug repurposing was one of six major themes identified by the NIH at the Alzheimer's disease research summit it held in 2012, we would ask that the Committee consider making a recommendation that Alzheimer's disease applications to the "New Therapeutic Uses" program be considered for added incentives in future solicitations put out by NCATS.

In 2012 and 2013, at the suggestion of the former head of the Neurological Products Division at FDA, ACT-AD co-convened two pivotal meetings looking at the potential for a combination approach to treating Alzheimer's disease. Participants at the meetings discussed the possible benefits and challenges associated with combining treatments for AD, from basic mechanisms through regulatory approval. Advocates, industry, the scientific community, and regulators have coalesced around AD combination therapy in theory but it is slow to take root in reality. A lack of research into what Alzheimer's targets should be pursued in combination, difficulties in navigating a company's rights to different treatments that would make up a drug combination, and issues of antitrust linked to drug pricing are barriers to moving combination therapy to the forefront of AD drug development. We believe combination therapy should be more explicitly considered as part of research, regulatory and reimbursement strategy discussions related to Alzheimer's. The 21st Century Cures Initiative could be a vehicle for proposing mechanisms to remove these barriers. Without easing these restrictions, we stand to lose many years in capitalizing on an opportunity that was crucial to the success in turning lethal diseases like HIV/AIDS, forms of cancer and tuberculosis into treatable conditions.

Lastly, we welcomed the FDA's draft guidance on early Alzheimer's drug development in 2013 because it expressed the conditions under which they would consider the use of Accelerated Approval for an AD treatment, however the guidance also included a requirement for some patients that fall in the early stages of the disease to improve their cognition and function when on a drug in a clinical trial. This is problematic because at least one study has shown that cognitive decline precedes functional symptoms. Looking ahead to the future, there may be sensitive enough instruments developed to measure both cognition in function in these early patients but at this point emerging research shows that using what is available today these early and mild patients are not able to demonstrate functional improvement with existing ways of measuring function in current trials. In

situations like these, we would ask that the FDA retain the ability to remain flexible to alternative approaches in deciding whether or not an improvement in cognition alone is meaningful enough for patients to warrant approval. Any changes to the regulatory process proposed by the Committee as part of this 21st Century Cures Initiative should be sensitive to evolving challenges of ongoing trials and not unintentionally disruptive to a therapeutic area.

Thank you for your careful consideration of the views expressed above. We hope the Committee will contemplate provisions that advance these important and promising areas for improving Alzheimer's drug development when it moves to legislative action. Please feel free to contact Cynthia Bens at cbens@agingresearch.org or (202) 293-2856 with any questions.

Sincerely,

Daniel Perry
Chairman

Cynthia Bens
Vice President, Public Policy