November 1, 2012

Theresa M. Mullin, Ph.D
Director, Office of Planning and Informatics
Center for Drug Evaluation and Research
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

RE: [Docket No. FDA-2012-N-0967] Input on Implementation of PDUFA V Patient-Focused Drug Development Activities

Dear Dr. Mullin:

The undersigned organizations representing a cross-section of Alzheimer's disease stakeholders are writing to urge the Food and Drug Administration (FDA) to continue making Alzheimer's disease (AD) a priority at the agency. We have long supported the inclusion of patient-focused drug development enhancements in the user fee agreement and we applaud the FDA for pursuing this endeavor. However, we hope that the FDA continues to represent the needs of individuals with Alzheimer's disease as the agency charts its course for conducting these activities over the next five years. This letter includes our recommendations for building on the FDA's successes of the last several years.

The National Institute on Aging (NIA) reports that as many as 5.1 million Americans have AD and the numbers of Americans who will be diagnosed with the disease are projected to increase dramatically in the coming years. It is estimated that more than 10 million baby boomers will develop Alzheimer's in addition to today's patients. The growing numbers of people with Alzheimer's and the rapidly-rising costs associated with the disease will put a heavy burden on families, businesses and government. To address these public health and fiscal challenges, our organizations have been supporting initiatives with the potential to accelerate the discovery of therapies to slow, stop, or reverse AD.

There are no approved treatments for Alzheimer's that can alter its fatal course. It takes upwards of 13 years to bring a treatment to market for this disease, with more failing than succeeding in the traditional drug development process. Since 2006, the FDA has worked with organizations in the Alzheimer's community to advance a dialogue between regulators, researchers, drug developers and patients to tackle and actively overcome specific roadblocks to the development of therapies for this complex disease. These interactions have successfully led the agency to:

- expand its Patient Consultant Program to AD patients and caregivers for the first time, giving them a voice during FDA advisory committee meetings;
- establish a trans-agency "Neurology Across FDA" Working Group that allows all centers involved in Alzheimer's disease therapy review an opportunity to meet regularly and discuss neurological issues; and
- participate in regular workshops for FDA leadership and in-line reviewers to learn about the science of the disease and discuss issues of importance—including clinically meaningful outcomes, patient selection and endpoint use in clinical trials, and acceptable toxicity at various stages of intervention.

These successes have helped both the FDA and the stakeholders gain a better understanding of gaps in knowledge that need to be filled by the research community and industry. They have also opened the door to ways the FDA can provide a higher degree of clarity on what it will take to get a new treatment approved.

We are fortunate that solid work is being done by the National Institutes of Health (NIH) and consortia efforts to further uncover novel ways to intervene earlier in the Alzheimer's disease course; to pursue qualification of proven biomarkers for the disease; to develop reliable patient reported outcome measures; and to advance disease modeling that will expedite clinical trials. However, there are still

areas where further input from the Alzheimer's community can provide valuable patient perspectives to the agency on disease burden, quality of life issues, and unmet need.

One particular area where more work can be done is in understanding acceptable risk of toxicity in people with early-stage disease and in a pre-symptomatic population. As was raised at the October 25th public meeting on implementation of the patient-focused drug development activities included in PDUFA V, FDA officials can articulate with certainty that they would be willing to accept a fairly high degree of risk with new Alzheimer's therapies if the benefits of those therapies were far beyond those provided by existing symptomatic treatments. It is also known that FDA would consider a certain level of known risk for therapies intended to treat people with the dominantly inherited form of AD, as well as those who are highly likely to convert to disease because of another genetic predisposition. There are still gray areas in how FDA would approach the question of risk in people with no known genetic risk for Alzheimer's. As more treatments are developed to delay the onset or progression of the disease, the question of acceptable risk when treating an asymptomatic person will be of critical importance. We are encouraged by signals provided by you and others in various centers on how the patient advocacy community can begin to provide data to the agency that is useful in answering these questions.

We understand that there are statutory limits on the number of meetings that can be held and the amount of funding that can be devoted to the patient-focused drug development process during this reauthorization period. Groups that have regularly participated in the stakeholder negotiations around the user fee agreements are already collaborating to maximize the impact of the patient engagement process by clustering and jointly pursuing common objectives. In addition to being helpful to patient groups in building out these clusters, FDA can also help by providing input on other considerations that went into selecting the diseases published in the September 24th *Federal Register* notice so that we can continue our involvement in those specific patient-focused meetings to inform our external activities.

Thank you for your leadership and for considering our views. We look forward to continuing to work collaboratively with the FDA to find solutions to problems that are hampering access to new treatments for complex diseases, like Alzheimer's. If you have any questions, please contact Cynthia Bens, Vice President of Public Policy at the Alliance for Aging Research and Accelerate Cure/Treatments for Alzheimer's Disease (ACT-AD) coalition, at (202) 293-2856 or cbens@agingresearch.org.

Sincerely,

Accelerate Cure/Treatments for Alzheimer's Disease (ACT-AD)
Alliance for Aging Research
Alzheimer's & Dementia Alliance of Wisconsin
Alzheimer's Foundation of America
Alzheimer's Research and Prevention Foundation
American Academy of Neurology
American Association for Geriatric Psychiatry (AAGP)
American Health Assistance Foundation
American Medical Directors Association (AMDA)
Assisted Living Federation of America (ALFA)
B.A.B.E.S. "Beating Alzheimer's by Embracing Science"
Critical Path Institute
Cure Alzheimer's Fund
Janssen Alzheimer's Immunotherapy
Linked Senior
National Alliance for Caregiving
National Association of States United for Aging and Disabilities (NASUAD)
National Family Caregivers Association
RetireSafe
Sage Bionetworks
USAgainstAlzheimer's
Volunteers of America

CC. Janet Woodcock, MD, Director, Center for Drug Evaluation and Research
John Jenkins, MD, Director, Office of New Drugs
Russell Katz, MD, Director, Division of Neurology Products
Robert Yetter, PhD, Associate Director for Review Management, Office of the Director, Center for Biologics Evaluation and Research
Patrick Frey, Director, Office of Planning and Analysis
Andrea Tan, Operations Research Analyst, Center for Drug Evaluation and Research