January 20, 2021

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Interim Commissioner
Director, Center for Drug Evaluation and Research
U.S. Food and Drug Administration
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Patrizia Cavazzoni, MD
Director (Acting) Center for Drug Evaluation and Research
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Peter Stein, MD
Director, Office of New Drugs
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Billy Dunn, MD
Director (Acting) Office of Neuroscience
U.S. Food and Drug Administration
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Submitted electronically to: Janet.Woodcock@fda.hhs.gov, Patrizia.Cavazzoni@fda.hhs.gov, Peter.Stein@fda.hhs.gov, Billy.Dunn@fda.hhs.gov

Re: FDA review of Biologics License Application (BLA) 761178, for aducanumab solution for intravenous infusion, submitted by Biogen Inc., for the treatment of Alzheimer’s disease

Dear Drs. Woodcock, Cavazzoni, Stein and Dunn:

We write to urge the FDA to utilize its regulatory flexibility in rendering a decision on biologics license application (BLA) 761178, for aducanumab solution for intravenous infusion, submitted by Biogen Inc., for the treatment of Alzheimer’s disease. Should FDA approve the application, we also recommend that a post-marketing surveillance study (also known as a Phase IV or confirmatory trial) be conducted to provide additional information about aducanumab’s benefits, risks and best use.

We have complete confidence in the FDA Office of Neuroscience. Under Dr. Dunn’s remarkable leadership, we know there is relentless commitment to the best interests of people living with neurodegenerative conditions and unwavering fidelity to the FDA’s scientifically rigorous process. People living with mild cognitive impairment due to Alzheimer’s disease (MCI due to AD) or early-stage Alzheimer’s disease dementia are depending on the FDA’s impartial evaluation of aducanumab’s safety and efficacy to deliver their first, best and only opportunity to bend the curve of disease and symptom progression. In that context, the FDA’s own guidances (e.g. Demonstrating Substantial Evidence of Effectiveness for Human Drug and Biological Products and Expedited Programs for Serious Conditions—Drugs and Biologics) provide for regulatory flexibility particularly in the case of products intended for serious and life-threatening conditions, such as Alzheimer’s disease, where no satisfactory alternative therapy exists. The Expedited Programs Guidance document specifically references 21CFR 312.80:

*"The Food and Drug Administration (FDA) has determined that it is appropriate to exercise the
illuminating the regulatory approval pathway for safe and effective products. Thank you for your consideration of these comments and for FDA’s consistent commitment to therapeutic development a
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ducanumab’s sponsor to that input. Ultimately, the FDA will make an application decision that is fair, objective, and solely governed by the confluence of scientific rigor and merit to serve the best interests of people living with MCI or early-stage dementia in need of and entitled to a safe and effective therapy offering them an extended quality of life that nothing else offers.

Under the best of circumstances, there are no ‘slam dunk’ submissions to the FDA and no product under review promises a panacea to the affected patient population. This is particularly true for potential first-in-class therapies. The FDA’s review criteria do not demand that a first-in-class therapy provide a cure. The standard, as it should be, is that the product be safe and effective. Patients and clinicians do not have the luxury of waiting for a best-in-class drug, but they are in the best position to make decisions about whether to use aducanumab as a first-in-class medication. As with any first-in-class product, there is much to be learned from how aducanumab is used by a larger and more diverse population of clinicians and patients. A robust post-marketing surveillance study will provide invaluable additional data about aducanumab’s safety and efficacy along with practical, real world evidence to inform and catalyze future therapeutic development along with modernization of our country’s health care infrastructure.

Thank you for your consideration of these comments and for FDA’s consistent commitment to illuminating the regulatory approval pathway for safe and effective products. For any questions or
additional information, please contact Ian Kremer, Executive Director of Leaders Engaged on Alzheimer's Disease (the LEAD Coalition), ikremer@leadcoalition.org or (571) 383-9916.

Sincerely,

Abe’s Garden Alzheimer’s Center of Excellence
Activists Against Alzheimer’s Network
ADvancing States
African American Network Against Alzheimer’s
AgeneBio
Aging and Memory Disorder Programs, Howard University
Aging Life Care Association®
Alliance for Aging Research
Alzheimer's & Dementia Alliance of Wisconsin
Alzheimer's Los Angeles
Alzheimer's New Jersey
Alzheimer's Orange County
Alzheimer's San Diego
Alzheimer's Tennessee
Alzheimer's Texas
American Association for Geriatric Psychiatry
American Brain Coalition
American Medical Women's Association
American Society of Consultant Pharmacists (ASCP)
Brian S. Appleby, M.D. (Case Western Reserve University School of Medicine*)
Argentum | Expanding Senior Living
The Balm In Gilead, Inc.
David M. Bass, PhD (Benjamin Rose Institute on Aging*)
Benjamin Rose Institute on Aging
Soo Borson MD (Minnesota Brain Aging Research Collaborative*)
The Brain Donor Project
Bridge Builder Strategies
BrightFocus Foundation

Christopher M. Callahan, MD (Indiana University Center for Aging Research*)
Caregiver Action Network
Caregiver Voices United
CaringKind, The Heart of Alzheimer's Caregiving
Center for BrainHealth at The University of Texas at Dallas
Chambers-Grundy Center for Transformative Neuroscience, Department of Brain Health, UNLV
Sandra Bond Chapman, PhD (Center for BrainHealth at The University of Texas at Dallas*)
Chronic Disease Coalition
Clergy Against Alzheimer's Network
Coalition of Wisconsin Aging and Health Groups
Cognitive Dynamics Foundation
Creutzfeldt-Jakob Disease Foundation
Jeffrey Cummings, MD, ScD (University of Nevada Las Vegas*)
Darrell K. Royal Fund for Alzheimer's Research
Walter Dawson, Dphil (Oregon Health & Science University*)
Dementia Alliance International
Dementia Alliance of North Carolina
Drexel University College of Nursing and Health Professions
The Emory Goizueta Alzheimer’s Disease Research Center
Gary Epstein-Lubow, MD (Alpert Medical School of Brown University*)
Faith United Against Alzheimer's Coalition
Family Caregiver Alliance
National Hispanic Council On Aging (NHCOA)
National Infusion Center Association (NICA)
National Minority Quality Forum
National Prion Disease Pathology Surveillance Center
National Task Group on Intellectual Disabilities and Dementia Practices
NFL Neurological Center
Noah Homes
Thomas O. Obisesan, MD, MPH (Howard University Hospital*)
The Ohio Council for Cognitive Health
Monica W. Parker, MD (Goizueta Alzheimer’s Disease Research Center, Emory University*)
Patients Rising
Pat Summitt Foundation
Richard Perry MD FRCP (Imperial College, London*)
Planetree International, Inc.
Anton P. Porsteinsson, M.D. (University of Rochester School of Medicine and Dentistry*)
Daniel C. Potts, MD, FAAN (University of Alabama College of Community Health Sciences*)
Prevent Alzheimer's Disease 2020
Vanessa Raymont, MBChB, MSc, MRCPsych (University of Oxford*)
ResearchersAgainstAlzheimer’s
Craig W Ritchie, MD, PhD (University of Edinburgh*)
Theresa Rohr-Kirchgraber, MD, FACP, FAMWA (Indiana University National Center of Excellence of Women’s Health*)
Marwan Sabbagh, MD, FAAN (Lou Ruvo Center for Brain Health*)
Stephen Salloway, M.D., M.S. (The Warren Alpert Medical School of Brown University*)
Sanford Health
Second Wind Dreams, Inc./ Virtual Dementia Tour
The Evangelical Lutheran Good Samaritan Society
The Youth Movement Against Alzheimer's
Geoffrey Tremont, Ph.D., ABPP-CN (Alpert Medical School of Brown University*)
R. Scott Turner, MD, PhD (Georgetown University Memory Disorders Program*)
University of Rochester Alzheimer's Disease Care, Research and Education Program (AD-CARE)
UsAgainstAlzheimer’s, LEAD Coalition co-convener
VeteransAgainstAlzheimer’s
Anand Viswanathan, MD, PhD (Massachusetts General Hospital and Alzheimer’s Disease Research Center*)
Volunteers of America, LEAD Coalition co-convener
David A. Weidman, MD, FAAN (Banner Alzheimer's Institute*)
Carol J. Whitlatch, PhD (Benjamin Rose Institute on Aging*)
Nancy Wilson, MA LCSW (Baylor College of Medicine*)
Jennifer Wolff, PhD (Johns Hopkins Bloomberg School of Public Health*)
WomenAgainstAlzheimer’s
Women's Brain Health Initiative
World Molecular Imaging Society
*Affiliations of individual researchers are for identification purposes only and do not necessarily represent the endorsement of affiliated institutions.

[1] http://www.leadcoalition.org Leaders Engaged on Alzheimer’s Disease (the LEAD Coalition) is a diverse national coalition of member organizations including patient advocacy and voluntary health non-profits, philanthropies and foundations, trade and professional associations, academic research and clinical institutions, and home and residential care providers, large health systems, and biotechnology and pharmaceutical companies. The LEAD Coalition works collaboratively to focus the nation’s strategic attention on dementia in all its causes – including Alzheimer’s disease, vascular disease, Lewy body dementia, and frontotemporal degeneration – and to accelerate transformational progress in detection and diagnosis, care and support, and research leading to prevention, effective treatment and eventual cure. One or more participants may have a financial interest in the subjects addressed.