January 20, 2021

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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

> broadest flexibility in applying the statutory standards, while preserving appropriate guarantees for safety and effectiveness. These procedures reflect the recognition that physicians and patients are generally willing to accept greater risks or side effects from products that treat life-threatening and severely-debilitating illnesses, than they would accept from products that treat less serious illnesses. These procedures also reflect the recognition that the benefits of the drug need to be evaluated in light of the severity of the disease being treated."

Aducanumab should not and, in fact, does not promise to cure Alzheimer's disease or end the scourge of dementia. Aducanumab, by the FDA's own assessment, does provide patients with MCI due to AD or early-stage Alzheimer's disease dementia a clinically significant and meaningful delay in disease and symptom progression and consequently in quality of life with an acceptable safety profile. Any person who lives with MCI due to AD or early-stage dementia or who cares about those persons as family, friend or clinician would agree that these quality-of-life outcomes are deeply precious and valuable. For years and across many settings, the FDA has heard directly from people living with MCI or early-stage dementia that having no disease-modifying treatment is a crushing death sentence and that any safe and effective therapy delivering improved quality of life in early stages would be a veritable Godsend. Their expectations for a first-in-class therapy are measured and their benefit-risk tolerance is entirely reasonable. They recognize – perhaps better than those of us who do not have MCI or dementia – that a first-in-class therapy offers them precious albeit limited additional time. They understand – as we ought to appreciate more fully – that halting disease and symptom progression, even temporarily, provides an enormous opportunity. People living with MCI or early-stage dementia hold dear that opportunity for extended quality of life just as much as people living with cancer, heart failure, HIV/AIDS, or respiratory disease. We have absolute confidence that the FDA guarantees a level playing field for all reviews without regard to disease, patient population, sponsor, or external pressures.

We are grateful for the robust review process and appreciate the substantive questions and concerns raised by members of the Peripheral and Central Nervous System Drugs Advisory Committee (Ad Comm). The Ad Comm is an essential part of the review process; rightly, the Ad Comm is neither the beginning nor the end of the FDA's process. Months of FDA work preceded the Ad Comm meeting and determined that aducanumab is both safe and effective. Months more of the FDA's work will follow the Ad Comm during which time we expect that the FDA will thoroughly, meticulously and impartially analyze both the Ad Comm's input and the responses from aducanumab'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),[i] ikremer@leadcoalition.org or (571) 383-9916.

Sincerely,

Abe's Garden Alzheimer's Center of Excellence

ActivistsAgainstAlzheimer'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)

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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

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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

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Chronic Disease Coalition

ClergyAgainstAlzheimer'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

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Faith United Against Alzheimer's Coalition

Family Caregiver Alliance

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Global Alzheimer's Platform Foundation

Global CEO Initiative on Alzheimer's Disease

Global Coalition on Aging

Global Neurosciences Institute

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HealthMatters Program

HealthyWomen

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David P Hoffman DPS CCE (Maria College*)

Home Instead Senior Care

William Hu MD, PhD, FAAN (Rutgers University*)

ICAN, International Cancer Advocacy Network

Infusion Access Foundation (IAF)

Iona Senior Services

Kathy Jedrziewski, PhD (University of Pennsylvania*)

Katherine S. Judge, PhD (Cleveland State University*)

Justice In Aging

Latino Alzheimer’s and Memory Disorders Alliance

LatinosAgainstAlzheimer’s

LeadingAge

Lewy Body Dementia Association

Life Molecular Imaging

Linked Senior, Inc

Livpact Inc.

Lupus and Allied Diseases Association, Inc.

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David X. Marquez, PhD (Department of Kinesiology and Nutrition, University of Illinois at Chicago*)

Metropolitan Area Agency on Aging/ACT on Alzheimer’s

Michigan State University Alzheimer's Alliance

Minnesota Association of Area Agencies on Aging

Minnesota Brain Aging Research Collaborative

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Darby Morhardt, PhD, LCSW (Northwestern University Feinberg School of Medicine*)

Mount Sinai Center for Cognitive Health

Catherine Mummery, MBBS PhD (University College London*)

National Alliance for Caregiving

National Association of Activity Professionals

National Association of State Long-Term Care Ombudsman Programs (NASOP)

National Certification Council for Activity Professionals

National Consumers League

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

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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

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ResearchersAgainstAlzheimer's

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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

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University of Rochester Alzheimer's Disease Care, Research and Education Program (AD-CARE)

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VeteransAgainstAlzheimer's

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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.*

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[i] 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.