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Advisory Committee Management Branch (ACMB), DFO Team 1
Division of Advisory Committee and Consultant Management (DACCM)
Center for Drug Evaluation and Research
Office of Executive Programs
U.S. Food and Drug Administration
10903 New Hampshire Ave.
Silver Spring, MD 20993–0002

Re: FDA-2023-N-1114: Peripheral and Central Nervous System Drugs Advisory Committee; Notice of Meeting; Establishment of a Public Docket; Request for Comments

Dear Dr. Seo and members of the Peripheral and Central Nervous System Drugs Advisory Committee:

Signatories to this public comment letter do not take a formal position on the merits of the supplemental biologics license application for Leqembi (lecanemab) for the treatment of mild cognitive impairment (MCI) and early dementia due to Alzheimer's disease. Instead, we write to urge the Advisory Committee to consider the perspectives of people living with early Alzheimer's, family and other care partners, researchers, long-term care and healthcare providers, and advocates as you discuss transition of the accelerated approval label to a traditional FDA approval.

The development of safe and effective therapies to prevent, delay, slow, and better manage Alzheimer's disease and related dementia (ADRD) is one of the most pressing and complex public health challenges facing our nation. One in three older adults who die have ADRD,[1] and over six million Americans have dementia due to Alzheimer's disease.

Lecanemab does not promise to cure Alzheimer's disease or end the scourge of dementia, but it does address otherwise high unmet need by providing substantial clinical benefits. Lecanemab, as borne out by the phase III trial results published in the *New England Journal of Medicine* last year,[2] slows progression of early Alzheimer's by 27% over an 18-month trial. This delay is

[1] Alzheimer's Association. 2023 Alzheimer's Disease Facts and Figures https://www.alz.org/media/Documents/alzheimers-facts-and-figures.pdf
[2] Van Dyck, Christopher H, et al. Lecanemab in Early Alzheimer's Disease. New England Journal of Medicine. 5 Jan 2023. https://www.nejm.org/doi/full/10.1056/NEJMoa2212948.

accompanied by a meaningfully prolonged ability to perform a range of activities at home and in the community as observed by caregivers, including actions such as being able to find personal belongings (72.6% less decline), speak about current events (46.7% less decline), dress oneself (50.9% less decline), clean laundry (53.5% less decline), make a meal (31.5% less decline), and be left on his/her/their own (32.3% less decline), among others. In short, these effects prolong the amount of real time an individual extends their independence and quality of life – time where cognition, personality, and the ability to care for oneself remain largely intact – and reduces caregiver burden.[3] Many individuals who live with MCI or early-stage dementia due to AD or who care about those persons as family, friend or clinician, believe these quality-of-life outcomes are deeply precious and valuable. People living with MCI or early-stage dementia due to Alzheimer's hold dear that opportunity for extended quality of life just as much as people living with other serious and life-threatening diseases such as cancer, heart failure, HIV/AIDS, or respiratory disease. As more treatments bear positive clinical results, there is hope that these initial successes will be followed by even greater advances. The community's expectations for first-in-class therapies are measured and the benefit-risk tolerance is seen as reasonable in conjunction with recommended monitoring and management of potential side effects.

For clinicians, the Phase III trial results indicate lecanemab as a viable and important treatment option for individuals with MCI or early-stage dementia due to AD who meet FDA label indications. There is general consensus among neurologists "who have reviewed the phase III data that the CLARITY AD trial was well-designed, and its findings are clinically and statistically significant," according to a February 2023 American Academy of Neurology letter to CMS.[4] While additional post-market research on subpopulations that may be especially vulnerable to ARIA is warranted, for the majority of individuals ARIA risk is low, and decisions on the appropriateness of treatment with lecanemab should be made by individuals in consultation with their physicians. The signatories of this letter have full confidence in the FDA's impartial, rigorous, and expert review based on the merits of the Phase III data findings.

Thank you for your consideration of these comments and for FDA's consistent commitment to illuminating the regulatory pathway for safe and effective products. For any questions or additional information, please contact Sue Peschin, President & CEO, Alliance for Aging Research, at speschin@agingresearch.org or Ian Kremer, Executive Director of Leaders Engaged on Alzheimer's Disease (the LEAD Coalition), at ikremer@leadcoalition.org.

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[3] Cohen, Sharon. "Context of Clarity AD Results." Presentation at Clinical Trials in Alzheimer's Disease Conference, Nov. 29, 2022.

[4] American Academy of Neurology. RE: Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease [CAG-00460N]. 2 Feb 2023. https://www.aan.com/siteassets/home-page/policy-and-guidelines/advocacy/comment-letters/lecanemab-ncd-reconsideration-request.pdf

Sincerely,

Alliance for Aging Research
American Academy of Neurology
LEAD Coalition
National Minority Quality Forum
Healthcare Leadership Council
Partnership to Fight Chronic Disease
Neelum T. Aggarwal, MD; American Medical Women's Association*
Alzheimer's Disease Resource Center
Alzheimer's New Jersey
Alzheimer's Tennessee
Alzheimer's Drug Discovery Foundation
Alzheimers Orange County
American Federation for Aging Research
American Society of Consultant Pharmacists
Autistic Women & Nonbinary Network
Benjamin Rose Institute on Aging
Bridge Builder Strategies
BrightFocus Foundation
Caregiver Action Network
CaringKind, The Heart of Alzheimer's Caregiving
Center for BrainHealth, University of Texas at Dallas
Chambers-Grundy Center for Transformative Neuroscience, Department of Brain Health, UNLV
CNS Innovations
Cognitive Dynamics Foundation
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Dementia Alliance International
Dementia Alliance of North Carolina
Genetic Alliance
Gerontological Advanced Practice Nurses Association
Global CEO Initiative on Alzheimer's Disease
HFC
Hypertrophic Cardiomyopathy Association
ICAN, International Cancer Advocacy Network
International Association for Indigenous Aging
Iona Senior Services
Latino Alzheimer's and Memory Disorders Alliance
Allan Levey, MD, PhD ; Emory University School of Medicine*

Lewy Body Dementia Association
Linked Senior, Inc.
Livpact
LuMind IDSC Foundation
Lupus and Allied Diseases Association, Inc.
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National Alliance for Caregiving
National Association of Activity Professionals
National Association of State Long Term Care Ombudsman Programs (NASOP)
National Indian Council on Aging
National Task Group on Intellectual Disabilities and Dementia Practices
Noah Homes
Ohio Council for Cognitive Health
Pat Summitt Foundation
Patients Rising Now
Planetree International
Positrigo
RetireSafe
Second Wind Dreams
The Balm In Gilead, Inc
The Brain Donor Project
TimeSlips Creative Storytelling
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** Affiliations of individual researchers are for identification purposes only and do not necessarily represent the endorsement of affiliated institutions.*