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Robert Califf, M.D.
Commissioner, Food and Drug Administration
U.S. Department of Health and Human Services
10903 New Hampshire Avenue
Silver Spring, MD 20993

Patrizia Cavazzoni, M.D.
Director, Center for Drug Evaluation and Research
Food and Drug Administration
U.S. Department of Health and Human Services
10903 New Hampshire Avenue
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Dear Dr. Califf and Dr. Cavazzoni,

Despite the unacceptable June 6, 2021, Food and Drug Administration (FDA) approval of aducanumab with almost unanimous opposition from the FDA's advisory committee, this Friday (the Prescription Drug User Fee Act [PDUFA] deadline for a decision on lecanemab) the FDA appears likely to repeat its mistake by approving lecanemab, unaccompanied by an advisory committee meeting.

We urge a postponement of the PDUFA date so the drug can be discussed before an advisory committee meeting, rather than being perceived as yet another Biogen/FDA done deal.

A November article by lecanemab investigators found a significant slowing of the rate of progression of cognitive impairment with lecanemab compared with placebo. But amyloid-related imaging abnormalities with microhemorrhages or hemosiderin deposits occurred in 126 (14.0%) of subjects in the lecanemab group and only 69 (7.7%) of subjects in the placebo group. The authors concluded that "Longer trials are warranted to determine the efficacy and safety of lecanemab in early Alzheimer's disease."[1]

Science magazine has "obtained medical records showing a 79-year-old Florida woman participating in an ongoing trial of the antibody died in mid-September after experiencing extensive brain swelling and bleeding, as well as seizures."

Three deaths thought to be related to the drug have now occurred in lecanemab subjects. "Eric Smith, a neurologist at the University of Calgary who also reviewed the case materials [of the

[1] van Dyck CH, Swanson CJ, Aisen P, et al. Lecanemab in early Alzheimer's disease. *NEJM*. 2022.

latest death], agrees the drug likely caused the death. He previously consulted for Eisai partner Biogen and was an investigator for the two companies' other anti-amyloid drug aducanumab."[2]

This Friday's scheduled FDA expedited approval of lecanemab, absent any advisory committee input, would demonstrate that the agency is unwilling or unable to learn from its worst approval mistake — aducanumab — I have ever seen in 50 years of FDA watching. It seems the unprecedented aducanumab FDA/Biogen axis is still in place.

Sincerely,

Sidney Wolfe, M.D.
Founder, Senior Advisor
Public Citizen's Health Research Group

[2] *Science*. Scientists tie third clinical trial death to experimental Alzheimer's drug. December 21, 2022. https://www.science.org/content/article/scientists-tie-third-clinical-trial-death-experimental-alzheimer-s-drug. Accessed January 4, 2023.