Testimony Before the FDA's Peripheral and Central Nervous System Drugs Advisory Committee Regarding Lecanemab

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I am Nina Zeldes, a Health Researcher at Public Citizen's Health Research Group. Public Citizen's Health Research Group has no financial conflicts of interest and I have no financial conflicts of interest.

Public Citizen strongly opposes FDA approval of the supplemental biologics license application of lecanemab for the treatment of Alzheimer's disease, because the evidence for the drug's benefits does not outweigh its significant risks.

The evidence of lecanemab's efficacy is based on Study 301.[1] Although the primary endpoint, the change from baseline in the Clinical Dementia Rating-Sum of Boxes (CDR-SB) at 18 months of treatment, was statistically significant, the treatment difference between lecanemab and placebo was -0.45, on a scale that ranges from 0 to 18.[2]

In fact, a *New England Journal of Medicine*[3] article by lecanemab investigators on the results of this study verified that "a definition of clinically meaningful effects in the primary end point of the CDR-SB score has not been established."

Secondary endpoint measures similarly yielded treatment effects that were small compared to the range of values for the instruments, suggesting the effects of the drug on function may not be clinically meaningful.[4]

Despite all the spin and lobbying for drug approval, the FDA has not been provided with evidence of clinical benefit for lacanemab that is clearly compelling. The new information highlights the concerning patient safety data, which include ARIA (amyloid-related imaging abnormalities), cerebral hemorrhage and infusion-related reactions.[5]

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[1] Food and Drug Administration. FDA Briefing document, sBLA# 761269/s-001, drug name: lecanemab-irmb; Peripheral and Central Nervous System (PCNS) Drugs Advisory Committee Meeting. June 9, 2023. https://www.fda.gov/media/169263/download. Accessed June 9, 2023.
[2] *Id.* PDF p. 8
[3] Van Dyck CH, Swanson CJ, Aisen P, et al. Lecanemab in early Alzheimer's disease. *New England Journal of Medicine*. 2023;388(1):9-21.
[4] Food and Drug Administration. FDA Briefing document, sBLA# 761269/s-001, drug name: lecanemab-irmb; Peripheral and Central Nervous System (PCNS) Drugs Advisory Committee Meeting. June 9, 2023. https://www.fda.gov/media/169263/download. Accessed June 9, 2023.
[5] *Id.* PDF p. 8.

For example, ARIA occurred in 21% of subjects treated with lecanemab, compared to only 9% in the placebo arm and infusion related reactions were 3.7 times as likely with lecanemab.[6]

Lecanemab was also associated with a decrease in brain volume and cortical thickness, which may - as FDA noted - be indicators of atrophy or neurodegeneration, making it necessary to "collect longer-term data in a large number of patients to further understand the clinical implications."[7]

A first step towards providing the necessary additional data was Study 301's open-label extension, 301 OLE. The results reinforced the serious safety concerns, such as ARIA, and showed that treatment with lecanemab was associated with 3 deaths.[8]

Based on the available evidence about efficacy and safety, we urge the committee to vote "No" on the voting question and recommend to the FDA that the supplemental biologics license application not be approved.

[6] *Id.* PDF p. 29, p. 32.
[7] *Id.* PDF p. 22.
[8] *Id.* PDF p. 25.