PUBLICCITIZEN
1600 20th Street, NW • Washington, D.C. 20009 • 202/588-1000 • www.citizen.org

July 13, 2021

The Honorable Christi A. Grimm
Principal Deputy Inspector General
Office of Inspector General
U.S. Department of Health and Human Services
330 Independence Avenue SW
Washington, DC 20201

RE: Inspector General investigation of the FDA's inappropriately close collaboration with Biogen regarding aducanumab for treatment of Alzheimer's disease must examine the role played by Acting FDA Commissioner Janet Woodcock

Dear Principal Deputy Inspector General Grimm:

Public Citizen welcomes Acting Food and Drug Administration (FDA) Commissioner Janet Woodcock's July 9 belated request to you to investigate the "interactions between Biogen and the FDA during the process leading to the decision to approve" aducanumab for treatment of Alzheimer's disease. We hope that you are now convinced of the urgent need for an independent investigation by your office of the unprecedented, inappropriately close collaboration between the FDA and Biogen that occurred before and after the submission of Biogen's biologics license application (BLA) for aducanumab for treatment of Alzheimer's disease, as we previously requested in our December 9, 2020, and June 30, 2021, letters to you.[1]

Your investigation must be broad-based and examine all aspects of the FDA's interactions with Biogen before and after the company submitted its BLA for aducanumab and of the agency's review and decision-making process.

That Dr. Woodcock herself has called for an investigation by your office should not dissuade you from examining *her* role in this matter. Your investigation should, among other things, determine when Dr. Woodcock first became aware of the collaboration between FDA staff and Biogen and whether she ever specifically endorsed or facilitated it in any way. Perhaps most importantly, your office also must examine how Dr. Woodcock fostered a culture within the agency's Center for Drug Evaluation and Research (CDER) that permitted and encouraged such an inappropriate collaboration with regulated industry. We note that under her leadership of CDER over the past three decades, the relationship between the FDA and the pharmaceutical industry has grown ever cozier — resulting in industry's regulatory capture of the agency.

On January 28, we shared with Dr. Woodcock a copy of our December 9, 2020, letter to you and urged her to endorse our call for an Office of Inspector General (OIG) investigation of the

[1] https://www.citizen.org/wp-content/uploads/2560.pdf and https://www.citizen.org/wp-content/uploads/2592.pdf.

unprecedented, inappropriately close collaboration between the FDA and Biogen.[2] At that time, as we explained in our December 9, 2020, letter to you, there already were clear indicators of this inappropriately close collaboration, which had been made fully transparent in press releases and presentation documents issued by Biogen in 2019 — when Dr. Woodcock was still Director of CDER — and in the unprecedented joint briefing document prepared by the FDA and Biogen for the FDA's November 6, 2020, meeting of its Peripheral and Central Nervous System (PCNS) Drugs Advisory Committee.

Because the inappropriately close FDA-Biogen collaboration had dangerously compromised the independence and objectivity of senior staff and clinical reviewers in CDER's Office of Neuroscience (ON) during the agency's review of Biogen's BLA for aducanumab, we urged Dr. Woodcock on January 28 to take the following additional actions, among others: (1) assign all further review and decision-making related to the BLA for aducanumab to CDER staff who were not involved in the inappropriately close collaboration with Biogen; and (2) temporarily remove Dr. Billy Dunn from his position as ON Director until the requested OIG investigation was completed, given that he supervised the FDA team reviewing the BLA for aducanumab and likely played a key role in the close collaboration with Biogen (a role that was laid bare according toa detailed exposé published on June 29 by STAT[3]).

But our January 28 requests to Dr. Woodcock fell on deaf ears.

In a disdainful February 11 response letter[4] to our January 28 letter, Dr. Woodcock reflexively defended the close collaborations between the FDA and the pharmaceutical industry that she had fostered over many years, extolling their purported benefits and failing to acknowledge the potential for such collaborations to dangerously undermine the integrity of the agency's review process for new drugs, as occurred in the case of her agency's review of aducanumab. In her letter to us, she asserted that "FDA scientists thoroughly, ***and independently***, analyze [primary study data submitted in new drug applications], developing their own interpretations—which at times align with and at other times differ from the sponsor's" [emphasis added].

However, senior staff and clinical reviewers in CDER's ON apparently did *not* "independently" review data from the phase 3 clinical trials of aducanumab. According to the June 29 exposé by STAT, "After the June 14, 2019, meeting [between Biogen and the FDA], Biogen and the FDA established a 'working group collaboration' consisting of company employees and agency review staff. The group met or communicated almost daily in June, July, and August of 2019, working to collect and analyze Aduhelm data for inclusion in the planned marketing submission."[5]

FDA Mathematical Statistician Tristan Massie — one of the few FDA staff involved in the review of Biogen's BLA of aducanumab who did not succumb to the regulatory capture that compromised the independence and objectivity of the FDA's overall review of Biogen's BLA — in a prerecorded presentation to the PCNS Drugs Advisory Committee characterized the *post hoc* analyses of clinical trial data that had been jointly conducted by Biogen and FDA ON staff

[2] https://www.citizen.org/wp-content/uploads/2566.pdf.
[3] https://www.statnews.com/2021/06/29/biogen-fda-alzheimers-drug-approval-aduhelm-project-onyx/.
[4] https://www.citizen.org/wp-content/uploads/2566_FDA-Response_February-11-2021.pdf.
[5] https://www.statnews.com/2021/06/29/biogen-fda-alzheimers-drug-approval-aduhelm-project-onyx/.

overall as "unscientific, statistically inappropriate and misleading."[6] Such an assessment of the non-independent ON review of aducanumab clinical trial data that was conducted jointly with Biogen could not be more damning.

In her July 9 letter to you, Dr. Woodcock declared that she has "tremendous confidence in the integrity of the staff and leadership of CDER involved in the aducanumab review and their commitment to unbiased and science-based decision-making." Her blind confidence is unjustified given the currently available evidence of the inappropriately close collaboration between agency staff and Biogen, information that has been known to her for at least several months, if not longer.

Public trust in the FDA has been severely damaged by the agency's review and approval process for aducanumab. The first steps toward restoring that trust must include an expeditious, independent investigation by your office of the unprecedented, inappropriately close collaboration between the FDA and Biogen, and that investigation must thoroughly examine the role played by Dr. Woodcock in this troubling matter.

We look forward to your prompt confirmation that such an investigation is underway.

Sincerely,

Michael A. Carome, M.D.
Director
Public Citizen's Health Research Group

cc: The Honorable Xavier Becerra, Secretary of Health and Human Services

[6] https://www.fda.gov/media/143505/download. PDF page 25.