

January 19, 2021

Patrizia Cavazzoni, MD
Director (Acting) Center for Drug Evaluation and Research
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Peter Stein, MD
Director, Office of New Drugs
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Billy Dunn, MD
Director (Acting) Office of Neuroscience
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Dear Drs. Cavazzoni, Stein, and Dunn,

With not a single disease-modifying therapy on the market to help any of the hundreds of thousands of Americans getting sicker every year due to Alzheimer's disease, UsAgainstAlzheimer's has watched closely the evaluation of the safety and efficacy of aducanumab.

We urge the FDA to approve aducanumab and put in place a platform to assess the real-world experience with the drug by persons in the early stages of Alzheimer's disease. We note that the FDA has considerable discretion in making this decision, and that it regularly exercises this discretion in favor of approval of early therapies for other diseases.¹ People staring into the abyss of Alzheimer's deserve no less.

The unmet medical need is huge, and the human suffering from delay in therapeutic innovation in Alzheimer's is staggering. Starting this month, Baby Boomers will begin to turn 75 at the rate of ten thousand a day. The hundreds of thousands experiencing early AD will only grow. And, of course, we know the inevitable course of this disease. Mortality is 100%. For every person who progresses to mild and moderate and then late-stage disease, there are three or more caregivers who devote increasing and then full-time care. Every year, every month, every week which extends functional ability—keeps a person at an independent functional status and delays that inevitable slide—is a blessing.

¹ Drugs Intended to Treat Life-threatening and Severely Debilitating Illnesses. 21 CFR §312.80 (2020).

Even were the FDA analysis a close call, you should decide in favor of giving families and their loved ones with mild cognitive impairment and early Alzheimer’s disease a treatment option where today there is none. The people we serve cannot wait years for “the perfect drug” while they are getting sicker. Every single day of delayed progression of their disease matters.² We want and deserve to make a personal risk/benefit decision together with our physicians and should not, with this set of facts, have this choice taken from us.

An Advisory Committee meeting—including the public comments from patients—is no doubt an important input to that evaluation process. We agree with the FDA guidance that: “The discussion, together with the votes, helps inform the agency’s own deliberations on scientific and regulatory matters.”³ The November 6, 2020 meeting of the Peripheral and Central Nervous System Advisory Committee did not have adequate time for a full discussion of the issues raised prior to the Committee’s voting. We encourage FDA to focus during its continuing analysis on answering the unanswered questions rather than on the vote itself.

We ask for this focus because important questions were raised during the Advisory Committee meeting, but the timing and format left open many questions when it came time for the Committee to vote.⁴

At the same, the public comments from patients were unanimously and unambiguously in favor of approval, and those comments also went 100% unaddressed and unexplored. As patients and patient-advocates, we experienced a process that was designed to enlighten but, instead, proved confusing and incomplete.

Some have suggested that the FDA staff and the sponsor worked too closely in examining the results of aducanumab’s clinical trial results. That this was the first time that the FDA and a sponsor produced a joint briefing document may have influenced the view of the Advisory Committee and others. But existing FDA guidance contemplates that the FDA staff and drug sponsors are to consult over the course of a drug’s development process. And we believe that COVID taught the world that the FDA and drug sponsors working together in their different roles (with the FDA maintaining its independent role) speeds up response to urgent, unmet health needs.

UsAgainstAlzheimer’s has been heartened by the FDA’s thorough clinical review to date, and we ask for that process to continue with thoughtful recognition of all of the evidence and seeking answers to the unanswered questions which emerged from the Advisory Committee meeting. We have high confidence in the review team—their experience, their independence, their ability to address statistical

² DiBenedetti, D, et al (2020). Assessing what matters most to patients with or at risk for Alzheimer’s and care partners: a qualitative study evaluating symptoms, impacts, and outcomes. *Alzheimer’s Research and Therapy*. 12 (90)

³ United States Food and Drug Administration. Guidance for FDA Advisory Committee Members and FDA Staff: Voting Procedures for Advisory Committee Meetings. p.4. (2008).

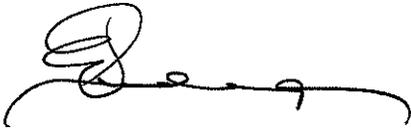
⁴ United States Food and Drug Administration. Meeting of the Peripheral and Central Nervous System Drugs Advisory Committee, November 6, 2020. Recording at 1:00:29, 1:03:02, 1:16:02, 1:19:00, 1:21:49, 1:23:27, 1:25:13, 1:28:03, 2:29:23, 2:30:15, 2:33:05, 3:35:13, 3:37:53, 3:41:38, 3:43:08, 3:44:26, 3:48:20, 3:55:58, 3:58:45, 4:02:38, 4:04:29, 4:09:47, 4:11:25, 4:32:01, 4:44:45, 4:53:41, 4:56:21, 5:11:25, 5:18:03, 5:22:16, 5:23:14, 5:25:55, 5:44:34, 5:46:59, 5:50:11.

matters in clinical context. Post-marketing collection of real-world evidence will help us all understand the effectiveness and safety of aducanumab, and we stand ready to support any such efforts.

Our spouses, parents, friends, and neighbors with mild cognitive impairment and mild Alzheimer's are seeing their disease progress every day. Every day they lose is a day they will never get back. We need a first-in-class drug before we can have any hope of a best-in-class drug. And, we believe, that the approval of aducanumab will produce a burst of innovation and accelerate the day we can enjoy a best-in-class drug.

If we can be of any help in your important work, we stand ready to do so.

Respectfully,

A handwritten signature in black ink, appearing to read "George Vradenburg". The signature is fluid and cursive, with a long horizontal stroke at the end.

George Vradenburg
Executive Chairman and Co-Founder

A handwritten signature in black ink, appearing to read "Russ Paulsen". The signature is cursive and somewhat stylized.

Russ Paulsen
Chief Operating Officer