PORTAL
Program On Regulation, Therapeutics, And Law

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Dear Acting Commissioner of Food and Drugs Janet Woodcock, M.D.,

I am hereby resigning from the FDA's Peripheral and Central Nervous System Advisory Committee. I was honored to have served the Committee since 2015 because I believed in the value of Advisory Committees to provide a way for outside experts to provide science-based guidance to the agency on its drug approval decisions. But after my experience on this Advisory Committee for both the eteplirsen and now the aducanumab discussions, it is clear to me that FDA is not presently capable of adequately integrating the Committee's scientific recommendations into its approval decisions.

With eteplirsen, the AdComm and FDA's own scientific staff reported that there was no convincing evidence that the drug worked; both groups were overruled by FDA leadership, which approved the drug based on considerations (including concerns about the sponsor's finances) that were not part of the Advisory Committee's discussions. This week, the aducanumab decision by FDA administrators was probably the worst drug approval decision in recent U.S. history. At the last minute, the agency switched its review to the Accelerated Approval pathway based on the debatable premise that the drug's effect on brain amyloid was likely to help patients with Alzheimer's disease. But this pivotal question was not discussed at the Advisory Committee meeting, and its premise was specifically excluded from discussion, as the FDA said: "We're not using the amyloid as a surrogate for efficacy." At our public meeting, concerns about trial data from one of the FDA's own reviewers were not given adequate time for discussion, and some of the questions FDA asked the Committee to answer were worded in a way that seemed slanted to yield responses that would favor the drug's approval.

For both eteplirsen and aducanumab, the decisions by FDA administrators to ignore the Advisory Committee's clear recommendations led to their approval of two highly problematic drugs that offered little evidence that they would meaningfully benefit patients suffering from these devastating conditions. This will undermine the care of these patients, public trust in the FDA, the pursuit of useful therapeutic innovation, and the affordability of the health care system.

For these reasons, I feel I can no longer make a useful contribution as a member of this Advisory Committee. The aducanumab and eteplirsen debacles demonstrate that the agency needs to reassess its decision-making processes, including how drug candidates are selected for AdComm review, which questions are put to the Committee and how those questions are worded, how anecdotal patient experience with drugs is presented to the committee, and how Committee recommendations are used (or ignored) by FDA officials. When clear AdComm recommendations against a drug are overruled by FDA administrators, as occurred in both these instances, the agency owes it to the nation to provide a detailed justification.

In the future, reforms in these areas could allow outside experts to be better able to provide meaningful input into the FDA approval process. Should this occur, I would look forward to the possibility of rejoining a committee if and when it becomes clear that our input as experts will be fairly sought and help support appropriate decision-making that is truly in patients' best interests.

Sincerely,

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Cc: Nathan Fountain, Xavier Becerra