Dr. Weisman will not be attending the meeting; thus, this waiver is null and void.

Waiver to Allow Participation in a Food and Drug Administration Advisory Committee

DATE: April 13, 2023

TO: Russell Fortney
Director, Advisory Committee Oversight and Management Staff
Office of the Chief Scientist

FROM: Byron Marshall
Director, Division of Advisory Committee and Consultant Management
Office of Executive Programs
Center for Drug Evaluation and Research

Name of Advisory Committee Meeting Temporary Voting Member: **David Weisman, M.D**.

Committee: Peripheral and Central Nervous System Drugs Advisory Committee

Meeting date: June 9, 2023

Description of the Particular Matter to Which the Waiver Applies:

David Weisman, M.D., is a temporary voting member of the Peripheral and Central Nervous System Drugs Advisory Committee. The committee's function is to review and evaluate data concerning the safety and effectiveness of marketed and investigational human drug products for use in the treatment of neurologic diseases and make appropriate recommendations to the Commissioner of Food and Drugs.

On June 9th, the committee will discuss supplemental biologics license application 761269/s-001, for Leqembi (lecanemab) solution for intravenous infusion, submitted by Eisai, Inc., for the treatment of early Alzheimer's disease. Biogen is jointly developing and commercializing lecanemab with Eisai. This product was approved under 21 CFR 314.500 (subpart H, accelerated approval regulations) for the treatment of Alzheimer's disease. Confirmatory studies are studies to verify and describe the clinical benefit of a product after it receives accelerated approval. The committee will discuss the confirmatory study, BAN2401-G000-301, conducted to fulfill post-marketing requirement 4384-1 detailed in the January 6, 2023, approval letter, available at https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2023/761269Orig1s000ltr.pdf.
The topic of this meeting is a particular matter involving specific parties.

Type, Nature, and Magnitude of the Financial Interest:

Dr. Weisman's employer, Abington Neurological Associates (ANA), is participating in a study titled *A Phase 3b/4 Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study to Verify the Clinical Benefit of Aducanumab (BIIB037) in Participants With Alzheimer's Disease (NCT05310071),* sponsored by Biogen. The study population overlaps with the indication coming before the advisory committee. The study began on October 10, 2022, with an anticipated end date of October 31, 2026. ANA anticipates receiving a total of between $ (b) (4) . Dr. Weisman serves as Site Principal Investigator of the study and receives between $5,000 and $15,000 per year in salary support from the study funding.

In addition, his employer is participating in a study titled *A Placebo-Controlled, Double-Blind, Parallel-Group, Bayesian Adaptive Randomization Design and Dose Regimen-finding Study With an Open-Label Extension Phase to Evaluate Safety, Tolerability and Efficacy of BAN2401 in Subjects With Early Alzheimer's Disease* [BAN2401-G000-201] (NCT01767311)], sponsored by Eisai. Although this study is on the product at issue for the indication coming before the committee, this is a Phase 2 study which is not up for discussion at this meeting. The advisory committee meeting discussion will focus on the data from the Phase 3 clinical trial to determine whether the drug has clinical benefits. The study began in April 2019, with an anticipated end date of early 2025. ANA anticipates receiving between (b) (4) per year. Dr. Weisman serves as Site Principal Investigator of the study and receives between $0 and $5,000 per year in salary support from the study funding.

Basis for Granting the Waiver:

Dr. David Weisman has unique qualifications and specialized expertise needed for this particular matter.

Dr. David Weisman is a neurologist at ANA, where he is also Founder and Director of the Clinical Research Center. Dr. Weisman received his medical degree from Pennsylvania State College of Medicine. After an internship at St. Mary's Hospital in San Francisco, he completed neurology residency at Yale New Haven Hospital, where he served as Chief Resident for neurology. He then went to the University of California, San Diego for fellowship training in Alzheimer's disease and other dementias.

Dr. Weisman founded the Clinical Trial Center at ANA in 2008. While serving as the site's director, Dr. Weisman has conducted numerous clinical trials in mild cognitive impairment and Alzheimer's disease and has become a leading Alzheimer's disease trialist nationwide. Under Dr. Weisman's direction, the ANA Clinical Trial Center has become nationally recognized, and he was honored as an investigator for the Alzheimer's Disease Cooperative Study.

Dr. Weisman has 23 years of service, and his research focuses on clinical trials for the prevention and treatment of Alzheimer's disease, mild cognitive impairment, and other dementias. Dr. Weisman delivers lectures on dementia and is a proponent of an early diagnosis and better therapies for Alzheimer's disease. He has devoted his research career towards advancing new therapies in Alzheimer's disease and has published numerous scientific articles and abstracts.

With Dr. Weisman's extensive experience and background in Alzheimer's disease and the conduct of clinical trials, his participation in the committees' discussions is necessary to provide expert advice and recommendations to the Agency.

The particular matter is considered sensitive.

This topic is considered to be sensitive, as the FDA Division with responsibility for the review of this product expects the matter coming before the committee to garner significant public interest.

Dr. David Weisman's expertise in this particular matter is necessary in the interest of public health.

Alzheimer's disease is a fatal illness that causes progressive decline in memory and other aspects of cognition. Dementia due to Alzheimer's disease is the most common form of dementia, accounting for 60 to 80 percent of all cases. Alzheimer's disease involves parts of the brain that control thought, memory, and language and can seriously affect a person's ability to carry out daily activities. Alzheimer's disease is the most common cause of dementia among older adults, one of the top 10 leading causes of death in the United States, and the 5th leading cause of death among adults aged 65 years or older. The number of people living with the disease doubles every 5 years beyond age 65. In 2010, the costs of treating Alzheimer's disease were projected to fall between $159 and $215 billion. By 2040, these costs are projected to jump to between $379 and more than $500 billion annually. There's no cure for Alzheimer's, but certain medications and therapies can help manage symptoms temporarily. Lecanemab is the second approval for a new class of medications that target the fundamental pathophysiology of Alzheimer disease, instead of only treating the symptoms. It has a novel mechanism of action in amyloid-targeting therapies and works by blocking the formation of amyloid plaques in the brain.

In the interest of public health, it is important that the Agency has available the unique set of expertise that Dr. Weisman will provide for the discussion of the particular matter before the committee.

Any potential for a conflict of interest is greatly outweighed by the strong need for Dr. Weisman's expertise in this matter.

The FDA would like to obtain the committee's input on the adequacy of the efficacy and safety data from the confirmatory phase 3 study, BAN2401-G000-301, that is intended to serve as confirmatory evidence for full approval. Dr. Weisman is highly respected internationally for his deep insights and broad perspectives, and he has been highly valued as a member of the Peripheral and Central Nervous System Drugs Advisory Committee. Few neuropsychiatrists possess his combination of broad perspectives, clinical acumen, public health focus, and wealth of experience in clinical trial design and analysis, and few individuals would be as able to disentangle the difficult issues raised by this supplemental biologics license application. For these reasons, the expertise of Dr. Weisman will be invaluable to a robust and productive discussion on the application coming before the committee.

Accordingly, I recommend that you grant Dr. David Weisman, a temporary voting member of the Peripheral and Central Nervous System Drugs Advisory Committee, a waiver from the conflict-of-interest prohibitions of 18 U.S.C. § 208(a).

Certification:

✓ The individual may participate, pursuant to 18 U.S.C. 208(b)(3) – The need for the individual's services outweighs the potential for a conflict of interest created by the financial interest involved.

Limitations on the Regular Government Employee's or Special Government Employee's Ability to Act:

_____ Non-voting

_____ Other (specify):

_____

_____

_____ Denied – The individual may not participate.

Russell Fortney -S Digitally signed by Russell Fortney -S Date: 2023.05.18 08:56:23 -04'00'

Russell Fortney
Director, Advisory Committee Oversight and Management Staff
Office of the Chief Scientist

May 18, 2023
Date