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

DATE: April 19, 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 Voting Member: **Robert C. Alexander, 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:

Robert C. Alexander, M.D., is a standing 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. 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. Alexander reported a financial interest in stocks in [redacted] (b) (6), all competing firms. The value of his stock holdings in these competing firms is between $100,000 and $150,000.

Under a regulatory exemption (5 CFR § 2640.202(b)(2)) issued by the Office of Government Ethics, an employee may participate in any particular matter involving specific parties in which the disqualifying financial interest arises from the ownership by the employee, his spouse, or minor children of securities issued by one or more entities that are not parties to the matter but that are affected by the matter if the aggregate market value of the holdings of the employee, his spouse and minor children in the securities of all the affected entities does not exceed $25,000. Because Dr. Alexander's financial interest in stocks in competing entities exceeds that amount, he has a disqualifying financial interest.

In addition, Dr. Alexander's employer, Banner Health (Banner), is participating in a study titled *A* [redacted] (b) (4), sponsored by [redacted] (b) (4), a competing firm. The study population overlaps with the indication coming before the advisory committee. The study began in [redacted] (b) (4) 2023, with an anticipated end date of [redacted] (b) (4) 2025. Dr. Alexander serves as an academic collaborator for the study and does not have a direct role in the study. Banner receives between [redacted] (b) (4) per year from [redacted] (b) (4) for its participation in this study. Dr. Alexander receives between $50,000 and $100,000 per year in salary support from this funding.

Basis for Granting the Waiver:

Dr. Robert C. Alexander has unique qualifications and specialized expertise needed for this particular matter.

Dr. Robert C. Alexander is a psychiatrist and the Chief Scientific Officer of the Alzheimer's Prevention Initiative, at the Banner Alzheimer's Institute, a sub-component of Banner Health. Dr. Alexander is also the Research Professor at the Department of Psychiatry at the University of Arizona College of Medicine.

Dr. Alexander received his undergraduate and medical degrees from the University of Chicago. He completed an internal medicine internship at the New England Deaconess Hospital and a residency in Adult Psychiatry at McLean Hospital/Harvard Medical School. Following residency, Dr. Alexander was a fellow in the Neuropsychiatry Branch of the National Institute of Mental Health (NIMH) and then at Columbia University (in Medical Genetics). He has been in medical practice for more than 20 years. In recent years, he has focused on neurodegeneration in both Alzheimer's and Parkinson's disease. He also has extensive experience in both early-and late-stage drug development and medical governance. Dr. Alexander was the medical leader of the AstraZeneca team that developed the beta-secretase inhibitor that delivered the phase 1 package and started phase 2/3 in only 21 months – the fastest development time in the class.

Since then, he guided the early clinical development of a number of treatments targeted toward Alzheimer's disease and other neurodegenerative disorders, including small molecules, antibodies, antisense oligomers and gene therapies. Dr. Alexander is uniquely qualified due to his specialized knowledge and experience with treating Alzheimer's Disease and other neurodegenerative disorders. His participation in the committee's discussion is essential to providing 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. Robert C. Alexander'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 combination of expertise that Dr. Alexander 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. Alexander's expertise in this matter.

Dr. Alexander 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 broad perspectives, clinical acumen, public health focus, and wealth of experience in clinical trial design and analysis, required to disentangle the difficult issues raised by this supplemental biologics license application. For these reasons, the expertise of Dr. Alexander will be invaluable to a robust and productive discussion on the application coming before the committee.

Accordingly, I recommend that you grant Dr. Robert C. Alexander, a standing 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 08:54:25 -04'00'

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

May 18, 2023
Date