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

DATE: March 8, 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 Member: **David Weisman, M.D.**

Committees: Psychopharmacologic Drugs Advisory Committee and Peripheral and Central Nervous System Drugs Advisory Committee

Meeting date: April 14, 2023

Description of the Particular Matter to Which the Waiver Applies:

Dr. David Weisman is a temporary voting member of the joint meeting of the Psychopharmacologic Drugs Advisory Committee and the Peripheral and Central Nervous System Drugs Advisory Committee.

The Psychopharmacologic Drugs Advisory 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 practice of psychiatry and related fields and make appropriate recommendations to the Commissioner of Food and Drugs.

The Peripheral and Central Nervous System Drugs Advisory 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 April 14, 2023, the committees will discuss supplemental new drug application (sNDA) 205422 s009, efficacy supplement for REXULTI (brexpiprazole) tablets, submitted by Otsuka Pharmaceutical Company, Ltd., and Lundbeck, Inc., for the proposed treatment of agitation associated with Alzheimer's dementia. The topic of this meeting is a particular matter involving specific parties.

Type, Nature, and Magnitude of the Financial Interest:

Dr. Weisman's institution, Abington Neurological Associates (ANA), was awarded the study titled *Escitalopram for Agitation in Alzheimer's Disease (S-CitAD) (NCT03108846),* sponsored by unaffected entities, the Johns Hopkins Bloomberg School of Public Health Center for Clinical Trials in collaboration with the National Institute on Aging. The study began in April 2017, with an anticipated end date in 2025. ANA anticipates receiving between $5,000 and $15,000 per year for the study. Dr. Weisman is Founder of the Clinical Research Center at Abington Neurological Associates and serves as a Site Principal Investigator of the study. He anticipates receiving between $0 and $5,000 per year in salary support for his work on the study.

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 the Pennsylvania State University College of Medicine. After an internal medicine internship at St. Mary's Hospital in San Francisco, he completed a neurology residency at Yale New Haven Hospital, where he served as Chief resident for neurology. He later joined 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's research focuses on clinical trials for the prevention and treatment of Alzheimer's disease, mild cognitive impairment, and other dementias. Dr. Weisman 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 experiences 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 sensitive.

The FDA Division responsible for review of REXULTI (brexpiprazole) expects the matter coming before the committees to garner public interest and non-trade press interest.

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

Alzheimer's disease is the most common cause of dementia. The first symptoms of Alzheimer's disease are typically memory, language, and thinking problems. Alzheimer's disease is progressive and results in worsening cognitive function over time and reduced ability to carry out activities of daily living independently. According to the 2022 Alzheimer's Disease Facts and Figures, published by Alzheimer's Association, Alzheimer's disease remains the fifth leading cause of death among individuals aged 65 years and older. Alzheimer's disease is also a leading cause of disability and poor health in older adults. In 2021, family members and friends provided more than $271 billion in unpaid care to people living with Alzheimer's disease and other dementias.

According to the National Institute on Aging, experts suggest that more than 6 million Americans aged 65 years or older may have Alzheimer's disease. Many individuals under age 65 years also have the disease, although prevalence estimates vary. Although treatments are available to alleviate some of the illness's symptoms, there is no cure for the disease.

Neuropsychiatric symptoms in Alzheimer's disease are common and often more acutely troubling than cognitive symptoms. These symptoms include agitation, aggression, delusions, hallucinations, paranoia, wandering, depression, apathy, disinhibition, and sleep disturbances. One or more of these symptoms are observed in 60 to 90 percent of patients with dementia; the prevalence increases with disease severity. The presence of neuropsychiatric symptoms leads to greater functional impairment in patients with dementia and cognitive impairment. These behaviors often accelerate or lead to nursing home placement.

There are currently no FDA approved medications for the proposed indication, agitation associated with Alzheimer's dementia. Prescription drug labels for antipsychotic medications, including brexpiprazole, contain a boxed warning to alert healthcare professionals about an increased risk of mortality associated with the use of atypical antipsychotics in elderly patients with dementia-related psychosis. If approved for the indication under review, brexpiprazole would be a "first-in-class" product for the treatment of agitation associated with Alzheimer's dementia.

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

Alzheimer's disease is a neurological condition, as such specific expertise is required. Dr. Weisman has a wealth of experience in clinical trials in Alzheimer's disease, and is a leading Alzheimer's disease trialist nationwide. His expertise in both Alzheimer's disease generally and in agitation associated with Alzheimer's disease in particular is directly related to the application

under review. 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 joint meeting of the Psychopharmacologic Drugs Advisory Committee and 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):

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_____

_____ Denied – The individual may not participate.

Russell Fortney -S Digitally signed by Russell Fortney -S Date: 2023.03.22 10:57:58 -04'00'

March 22, 2023

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

Date