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

DATE: December 23, 2020

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 Temporary Member: **Antonio C. Wolff, M.D.**

Committee: Oncologic Drugs Advisory Committee

Meeting date: February 9, 2021

Description of the Particular Matter to Which the Waiver Applies:

Antonio Wolff, M.D., is a temporary voting member of the Oncologic Drugs Advisory Committee (ODAC). The Committee's function is to review and evaluate available data concerning the safety and effectiveness of marketed and investigational human drug products for the use in the treatment of cancer and make appropriate recommendations to the Commissioner of Food and Drugs.

The committee will discuss supplemental biologic license application (sBLA) 125514/s-089, for Keytruda (pembrolizumab), submitted by Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc. The proposed indication (use) for this product is for the treatment of patients with high-risk, early-stage triple-negative breast cancer, in combination with chemotherapy as neoadjuvant treatment, then as a single agent as adjuvant treatment after surgery. The topic of this meeting is a particular matter involving specific parties.

Type, Nature, and Magnitude of the Financial Interests:

Dr. Wolff reported that he and his spouse have a financial interest in [redacted (b) (6)], a healthcare sector mutual fund. The value of the holding is between $[redacted (b) (6)]. As of the writing of this waiver, based on publicly available fund information, this sector fund contains underlying assets in [redacted (b) (6)]

(b) (6)

, respectively, of the holdings of the fund.

Under a regulatory exemption issued by the Office of Government Ethics, an employee may participate in any particular matter affecting one or more holdings in a sector mutual fund where the disqualifying financial interest in the matter arises because of ownership of an interest in the fund and the aggregate market value of interests in all funds in which there is a disqualifying financial interest and which concentrates in the same sector does not exceed $50,000. Because Dr. Wolff's financial interest in (b) (6) exceeds that amount, he has a disqualifying financial interest based on the fund holdings of the above-mentioned companies.

Basis for Granting the Waiver:

Antonio C. Wolff, M.D. has unique qualifications and specialized expertise needed for this particular matter.

Dr. Wolff is a temporary voting member of the ODAC. He is Professor of Oncology at Johns Hopkins University (JHU) and a member of the Johns Hopkins Kimmel Cancer Center. He received his medical degree at the Universidade Federal do Rio de Janeiro in Brazil and trained in medical oncology at Johns Hopkins. He is an Associate Editor of the Journal of Clinical Oncology, Chair of the Eastern Cooperative Oncology Group (ECOG) and the American College of Radiology Imaging Network (ACRIN) Breast Cancer Committee, and Chief Operating Officer for the Translational Breast Cancer Research Consortium (TBCRC). He is a Fellow of the American Society of Clinical Oncology (FASCO) and past Chair of its Clinical Practice Guidelines Committee.

Dr. Wolff's research interests include new treatment strategies, the development and implementation of prognostic and predictive biomarkers (tissue, blood, and imaging) in clinical practice, and on how to improve the survivorship experience of breast cancer patients and their caregivers. He is a Susan G. Komen Scholar, recipient of a Cancer Clinical Investigator Team Leadership Award from the National Cancer Institute at the National Institutes of Health, and has been recognized since 2017 by Clarivate Analytics (Thomson Reuters) as one of the world's most highly cited researchers (top 1% in clinical medicine). He maintains an active clinical practice dedicated to the care of patients with breast cancer and was inducted in 2018 as a member of the JHU Miller Coulson Academy of Clinical Excellence. In 2018, Dr. Wolff was recognized as one of 125 Living the Hopkins Mission Honorees, who were selected for their outstanding dedication to the institution's core values of excellence and discovery, leadership and integrity, diversity and inclusion, and respect and collegiality, as part of the 125th anniversary celebration of the JHU School of Medicine.

According to the FDA review division responsible for review of this product, a productive discussion of the meeting issue depends upon having an adequate number of breast cancer oncologists with vast experiences of different regimens. It is essential for the committee to have a diverse set of competencies and knowledge in this setting to successfully address the complex issues being discussed. Because of Dr. Wolff's background and professional experiences, his

participation in the committee's discussion will ensure the level of skillfulness and objectivity required to provide expert advice and recommendations to the Agency.

The particular matter is not sensitive.

The meeting topic is not considered to be sensitive. The FDA Division responsible for review of this product does not expect that the meeting is likely to receive significant public interest, (non-trade) press interest, nor is it considered highly controversial.

Dr. Antonio C. Wolff's expertise in this particular matter is necessary in the interest of public health.

Breast cancer is the second leading cause of cancer-related death in women in the United States each year after lung cancer and it is the most common cancer among women worldwide. Triple-negative breast cancer (TNBC) is a term that has historically been applied to cancers that lack the three most significant therapeutic markers for clinical management of breast cancer patients: estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2). TNBC accounts for 15-20% of all breast cancers but it is more aggressive and has a poorer prognosis compared to other types of breast cancers.

TNBC is more commonly diagnosed in younger, premenopausal women and among Black and Hispanic women. Presence of a BRCA-1 mutation (breast cancer susceptibility gene) is another risk factor associated with the diagnosis of TNBC. Approximately 50-70% of women with a BRCA1 mutation will develop breast cancer by 70-80 years.

Because TNBC lacks estrogen, progesterone and HER2 protein receptors, treatment options for this cancer are limited. TNBC is typically treated with a combination of surgery, radiation therapy, and chemotherapy (the main systemic option). In recent years, targeted therapies such as PARP inhibitors and/or immunotherapy medicine in combination with chemotherapy have been shown to have positive results for patients with metastatic disease. There are currently no FDA-approved targeted therapy or immunotherapy treatment options for patients with TNBC that is early stage but at high risk of relapse. The product at issue is Merck's immunotherapeutic agent, Keytruda (pembrolizumab). Its proposed indication is for the treatment of patients with high-risk, early stage triple-negative breast cancer, in combination with chemotherapy as neoadjuvant treatment, then as a single agent for adjuvant treatment after surgery. In the interest of public health, it is important that the Agency has available the unique expertise that Dr. Wolff 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. Wolff's expertise in this matter

Dr. Wolff is an internationally recognized expert in breast cancer care who oversees the design and conduct of clinical trials for breast cancer, the publication of cancer research, and the development of clinical guidelines in breast cancer. He also has several decades of experience as a practicing breast oncologist and currently maintains an active clinical practice dedicated to the care of patients with breast cancer. According to the review division responsible for the review

of the application at issue for this meeting, it would be difficult to interpret rendered advice from the committee without multiple breast cancer experts at the meeting. The clearance of multiple breast cancer experts is imperative and given Dr. Wolff's extensive experiences and background in the specific areas needed for this meeting, any potential for a conflict of interest is significantly outweighed by the need for his expertise on this panel.

Accordingly, I recommend that you grant Dr. Antonio C. Wolff, a temporary voting member of the Oncologic 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: 2021.01.15 10:32:36 -05'00'

January 15, 2021

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

Date