U.S. FOOD & DRUG ADMINISTRATION

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: **Matthew J. Ellis, MB, PhD, FRCP**

Committee: Oncologic Drugs Advisory Committee

Meeting date: February 9, 2021

Description of the Particular Matter to Which the Waiver Applies:

Matthew Ellis, M.B, Ph.D., FRCP, 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 Interest:

Dr. Ellis reported a financial interest in [redacted (b) (6)], a healthcare sector mutual fund. The value of his holdings in this fund is between $[redacted (b) (6)]. At the writing of this waiver, based on publicly available fund information, this sector fund contains assets in [redacted (b) (6)] potentially competing/affected firms,

(b) (6) %, respectively, of the underlying value of the fund.

Under the 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 concentrate in the same sector does not exceed $50,000. Because Dr. Ellis' financial interest in the (b) (6) exceeds that amount, he has a disqualifying financial interest based on the fund's holdings of the above-listed companies.

Basis for Granting the Waiver:

Dr. Matthew J. Ellis has unique qualifications and specialized expertise needed for this particular matter.

Dr. Ellis is the Director for the Lester and Sue Smith Breast Center and Professor of Medicine and Molecular and Cellular Biology at Baylor College of Medicine. He was previously an Associate Director for Translational Research at Dan L. Duncan Comprehensive Cancer Center at Baylor College of Medicine. He received his medical degree at the University of Cambridge in the United Kingdom and doctorate degree at the University of London. He completed his residency at the Royal College of Physicians in London and a fellowship in medical oncology at Georgetown University.

Dr. Ellis has over 36 years of experiences as a clinician and researcher with a practice devoted to breast cancer. He is a recognized breast cancer specialist and clinical investigator with a strong background in molecular cell biology, molecular pharmacology, genomics and proteomics. Dr. Ellis has been an active member of the National Clinical Trials Network (NCTN; formerly Breast Cancer Intergroup of North America) since 1998 and he is a vice-chair of the Breast Committee for Alliance for Clinical Trials in Oncology. He was also co-leader for The Cancer Genome Atlas (TCGA) Breast Project where he established collaborations with several Genome Centers on massive parallel sequencing of breast cancer. He served as a co-principal investigator for the Clinical Proteomic Tumor Analysis Consortium (CPTAC2) grant. During CPTAC2, he established collaborative interactions with the Broad Institute that led to several publications on the proteogenomic analysis of breast cancer. He is also a principal investigator in CPTAC3 where he continues to translate proteogenomic findings to improve the diagnosis and treatment of breast and other cancers. Furthermore, he is a principal investigator for the Specialized Program of Research Excellence (SPORE) Program in Breast Cancer at the Baylor College of Medicine.

Dr. Ellis is a McNair Scholar and Susan G. Komen breast Cancer Scholar. He is a recipient of a Gianni Bonadonna Breast Cancer Award and Lecture for his pioneering research into the clinical relevance of activating mutations in human epidermal growth factor receptor 2 (HER2) and in the deployment of patient-derived xenografts for the pharmacological annotation of breast cancer genomes. He is also a recipient of Stand Up To Cancer's Laura Ziskin Award for breast cancer research, Joan Lunden Award from Breast Cancer Research Foundation, and IMPACT Award at

National Consortium of Breast Centers.

A productive discussion of the meeting issue depends upon having an adequate number of breast cancer oncologists with vast experience 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 at the meeting. Because of Dr. Ellis' strong foundation in breast cancer and his vast experiences as a clinical oncologist, educator and clinical researcher, his participation in the committee's discussion will ensure an expansive level of expertise and objectivity required to provide expert advice and recommendations to the Agency.

The particular matter is not sensitive.

This 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. Matthew J. Ellis' 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. The presence of a BRCA-1 mutation (breast cancer susceptibility gene) is another risk factor associated with the diagnosis of TNBC. Further, approximately 50-70% of women with a BRCA1 mutation will develop breast cancer by 70-80 years of age.

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. In the interest of public health, it is important that the Agency has available the unique expertise that Dr. Ellis 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. Ellis' expertise in this matter

Dr. Ellis is an internationally recognized clinical and translational breast cancer researcher and has several decades of experience as a practicing breast oncologist. 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. Further, triple-negative breast cancers are cancers that lack the three most significant therapeutic markers for clinical management of breast cancer patients. As recipient of a Gianni Bonadonna Breast Cancer Award and Lecture for his pioneering research into the clinical relevance of activating mutations in HER2, any potential for a conflict of interest by Dr. Ellis is significantly outweighed by the need for his unique expertise on this panel.

Accordingly, I recommend that you grant Dr. Matthew J. Ellis, 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 10:53:11 -05'00'

January 15, 2021

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

Date