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

DATE: March 15, 2021

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 Voting Member: **Matthew Ellis, MB, PhD, FRCP**

Committee: Oncologic Drugs Advisory Committee

Meeting date: April 27, 2021

Description of the Particular Matter to Which the Waiver Applies:

Matthew Ellis, MB, PhD, 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.

On April 27th, the committee will hear updates on biologics license application (BLA) 761034/S-018, for Tecentriq (atezolizumab), submitted by Genentech, Inc., a subsidiary of Roche. Ono Pharmaceuticals and Bristol-Myers Squibb (BMS) have a global patent licensing agreement with Roche for the atezolizumab. The committee will review Tecentriq (atezolizumab) in combination with paclitaxel protein-bound for the treatment of adult patients with unresectable locally advanced or metastatic triple-negative breast cancer (TNBC) whose tumors express PD-L1 (PD-L1 stained tumor-infiltrating immune cells [IC] of any intensity covering ≥ 1% of the tumor area), as determined by an FDA-approved test. Abraxane (nab-paclitaxel) is marketed by Abraxis Bioscience, a subsidiary of Celgene; Celgene and Abraxis Bioscience are subsidiaries of BMS. This application was approved under 21 CFR 601.40 (subpart E, accelerated approval regulations) with confirmatory trial(s) that have not verified clinical benefit. The updates will provide information on: (1) the status and results of confirmatory clinical studies for a given indication; and (2) any ongoing and planned trials. Confirmatory studies are post-marketing studies to verify and describe the clinical benefit of a drug after it receives accelerated approval.

Based on the updates provided, the committee will have a general discussion focused on next steps including whether the indication should remain on the market while additional trial(s) are conducted. The topic of the meeting is a particular matter involving specific parties.

Type, Nature, and Magnitude of the Financial Interest:

Dr. Ellis reported a financial interest in (b) (6) a healthcare sector mutual fund. The value of his holdings in this fund is between $50,000 and $75,000. At the writing of this waiver, based on publicly available fund information, the sector fund contains assets in (b) (6), and potentially competing firms (b) (6), representing (b) (6) respectively, of the underlying value 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 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 currently 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 experience 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 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 a principal investigator in CPTAC3 where he

continues to translate proteogenomic findings to improve the diagnosis and treatment of breast and other cancers. He is also 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 issue depends upon an adequate number of breast cancer oncologists with vast experience with different regimens. Being able to draw upon a diverse set of competencies and knowledge is essential if the committee is to successfully address the complex issues being discussed. 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 considered sensitive.

The matter coming before the committee will garner public interest as it relates to the regulatory pathway of accelerated approval which was promulgated in 1992. This pathway has been used extensively in oncology approvals to bring new therapies to patients in an expedited fashion.

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. 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 (poly ADP ribose polymerase) inhibitors and/or immunotherapy medicine in combination with chemotherapy have been shown to have positive results for patients with metastatic disease. There is currently one other FDA-approved first-line therapy, which was also approved under the accelerated-approval process, for the treatment of unresectable locally advanced or metastatic TNBC. The product at issue for this session is Genentech's immunotherapeutic agent, Tecentriq (atezolizumab) indicated in combination with paclitaxel protein-bound for the treatment of adult patients with unresectable locally advanced or metastatic TNBC whose tumors express PD-L1 (PD-L1 stained tumor-infiltrating immune cells [IC] of any intensity covering ≥ 1% of the tumor area), as determined by an FDA-approved test. 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. According to the review division responsible for the review of the application, it would be difficult to interpret rendered advice from the committee without multiple breast cancer experts at the meeting. A strong foundation of nearly 40 years of experience as a practicing breast oncologist and recipient of numerous awards for his pioneering research in breast cancer make Dr. Ellis uniquely qualified to provide insight and feedback on supplemental biologics license application, BLA 761034/S-018 for atezolizumab.

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: 2021.04.02 08:20:38 -04'00'

April 2, 2021

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

Date