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

DATE: March 25, 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: **Harold Burstein, M.D., Ph.D.**

Committee: Oncologic Drugs Advisory Committee

Meeting date: April 27, 2021

Description of the Particular Matter to Which the Waiver Applies:
Harold Burstein, M.D., Ph.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.

On April 27th, the committee will hear updates on 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. These 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 for each product including whether the indications 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 Interests:

Dr. Burstein is a member of the Board of Directors and Executive Committee for the Alliance for Clinical Trials in Oncology (Alliance). The Alliance is part of the National Clinical Trials Network, sponsored by the National Cancer Institute (NCI), and serves as a research base for the NCI Community Research Oncology Program. The Alliance consists of about 10,000 cancer specialists at hospitals, medical centers, and community clinics across the United States and Canada. The organization develops and conducts clinical trials with promising new cancer therapies, and utilizes scientific research to develop treatment and prevention strategies for cancer, as well as researching methods to alleviate side effects of cancer and cancer treatments.

The Alliance is conducting a trial titled, *Randomized Trial Of Standard Chemotherapy Alone Or Combined With Atezolizumab As Adjuvant Therapy For Patients With Stage III Colon Cancer And Deficient DNA Mismatch Repair* (NCT02912559), sponsored by the National Cancer Institute, with financial support from Genentech. Dr. Burstein does not have any involvement in the study. The study began on September 12, 2017, and will end December 12, 2021.

The Alliance receives approximately $2.5 million and $3.5 million per year. Dr. Burstein does not receive any personal remuneration or salary support from the funds.

The Alliance is conducting another trial titled, *A Randomized Phase III Trial of Weekly Paclitaxel Compared to Weekly Nanoparticle Albumin Bound Nab-paclitaxel or Ixabepilone With or Without Bevacizumab as First-Line Therapy for Locally Recurrent or Metastatic Breast Cancer* (NCT00785291), sponsored by the National Cancer Institute, with financial support from Abraxis. Dr. Burstein does not have any involvement in the study. The study began on November 10, 2018 and will end December 31, 2021.

The Alliance receives between $950,000 and $1.5 million per year. Dr. Burstein does not receive any personal remuneration or salary support from the funds.

Basis for Granting the Waiver:

Dr. Harold Burstein has unique qualifications and specialized expertise needed for the particular matter.

Dr. Burstein is Professor of Medicine at Harvard Medical School, and a medical oncologist at Dana-Farber Cancer Institute and Brigham & Women's Hospital. Dr. Burstein attended Harvard College, and earned his Doctor of Medicine degree at Harvard Medical School where he also earned a Doctor of Philosophy degree in immunology. He trained in internal medicine at Massachusetts General Hospital and in medical oncology at Dana-Farber Cancer Institute.

His clinical research interests include therapies for early and advanced-stage breast cancer,

including neoadjuvant treatments, concurrent radiotherapy/chemotherapy and biological therapies and studies of quality of life and health behavior among women with breast cancer. Dr. Burstein has written widely on breast cancer in both traditional medical journals and on the web. Representative publications can be found in the New England Journal of Medicine, the Journal of Clinical Oncology, and other leading medical journals. He serves on international breast cancer committees including the National Comprehensive Cancer Network (NCCN), Breast Cancer Panel, The St. Gallen Breast Cancer Panel, and the Alliance Breast Cancer Committee, and chairs the ASCO guidelines on endocrine therapy for breast cancer. Dr. Burstein is an Associate Editor for Cancer Education at the Journal of Clinical Oncology.

Dr. Burstein's strong foundation in breast cancer and his experience in clinical oncology and clinical research will ensure the level of expertise and objectivity required to provide expert advice and recommendations to the Agency.

The particular matter is 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. Harold Burstein's expertise in the 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 the April 27th meeting 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

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

Dr. Burstein is an internationally recognized clinical and translational breast cancer researcher. He additionally has several decades of experience as a practicing breast oncologist and has written widely on breast cancer in both traditional medical journals and on the web. 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; the clearance of multiple breast cancer experts is imperative.

Accordingly, I recommend that you grant Dr. Harold Burstein, 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):

_____

_____

_____ Denied – The individual may not participate.

Russell Fortney -S Digitally signed by Russell Fortney -S Date: 2021.04.02 14:50:25 -04'00'

April 2, 2021

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

Date