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

DATE: December 28, 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 Member: **Philip C. Hoffman, MD**

Committee: Oncologic Drugs Advisory Committee

Meeting date: February 9, 2021

Description of the Particular Matter to Which the Waiver Applies:

Philip C. Hoffman, M.D., is a standing, voting member, and Chairperson 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. Hoffman's employing institution, the University of Chicago, is participating in the study titled *A Phase III, Randomized, Double-blind Study to Evaluate Pembrolizumab Plus Chemotherapy vs Placebo Plus Chemotherapy as Neoadjuvant Therapy and Pembrolizumab vs Placebo as Adjuvant Therapy for Triple Negative Breast Cancer (KEYNOTE 522),* sponsored by Merck and Co. Data from the KEYNOTE 522 study supports the sBLA for Keytruda and is a pivotal study that will be discussed at the meeting. The study accrual period was between September 29, 2017 and August

21, 2018, during which two patients were enrolled and Dr. Hoffman's colleague at the University of Chicago was the institutional principal investigator. One patient at this site has finished treatment and is being followed for long-term survival. Dr. Hoffman advised that he does not have any direct experience with the trial.

The University of Chicago receives between $0 and $50,000 per year, from Merck and Co. for this study.

Basis for Granting the Waiver:

Dr. Philip C. Hoffman has unique qualifications and specialized expertise needed for this particular matter.

Philip C. Hoffman, MD, received his medical degree from Thomas Jefferson University and completed a fellowship in Hematology/Oncology at the University of Chicago. He is currently a Professor of Medicine, Section of Hematology/Oncology at the University Chicago.

Dr. Hoffman is an expert in cancers of the lung, breast and esophagus. His academic interests lie mainly with malignancies of the chest. He has participated in clinical trials in lung and esophageal cancer, with particular emphasis on patients with advanced disease. He has conducted a series of studies of combined chemotherapy plus radiation therapy for locally advanced lung cancer, as well as chemotherapy drug trials for patients with lung cancer that has spread to other body sites. For many years, he has also had an active interest in management of breast cancer, both early stage and later stage, and has participated in a number of clinical trials. As the author of more than 80 medical journal articles, Dr. Hoffman's research interests include small cell and non-small cell lung cancer and breast cancer. He is also the author of book chapters ranging from cancer emergencies to breast cancer. In addition to serving on several University and national committees, Dr. Hoffman is a reviewer for several medical journals, including the Journal of Clinical Oncology, the Lancet and JAMA.

It is particularly important to include Dr. Hoffman in the upcoming ODAC meeting, given his experience in early and late stage breast cancer treatment and research. His background in clinical trials research and breast cancer research will be valuable to the discussion at this meeting.

The particular matter is not sensitive.

The meeting topic coming before the committee is not considered to be sensitive. The FDA review division responsible for the review of the application at issue for this meeting does not expect that the meeting is likely to receive significant public interest, non-trade press interest, nor is it considered highly controversial.

Dr. Philip C. Hoffman'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. 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. Hoffman 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. Hoffman's expertise in this matter

Multiple breast cancer experts were invited to attend this meeting to allow for a diverse panel of experts and provide a balanced assessment of the acceptability of the known and anticipated risks associated with the proposed treatment setting. 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. Dr. Hoffman is a seasoned oncologist with extensive experiences in early stage and late stage breast cancer research. Further, he has been a standing member of the Committee since 2017 and Chairperson since 2019. Dr. Hoffman's professional experiences combined with his diverse collection of previous experiences with advisory meetings and as a standing member and Chairperson of the ODAC will be invaluable to a robust and productive discussion of the meeting topic.

Accordingly, I recommend that you grant Dr. Philip C. Hoffman, the Chair and a 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: 2021.01.15 10:46:50 -05'00'

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

January 15, 2021
Date