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

DATE: September 21, 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: **Mary Kwok, M.D.**

Committee: Oncologic Drugs Advisory Committee

Meeting date: October 28, 2021

Description of the Particular Matter to Which the Waiver Applies:

Dr. Mary Kwok 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 new drug application (NDA) 214383, Pepaxto (melphalan flufenamide) for injection submitted by Oncopeptides AB, approved under 21 CFR 314.500 (subpart H, accelerated approval regulations), in combination with dexamethasone for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least four prior lines of therapy and whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent, and one CD38-directed monoclonal antibody.
The committee will hear an update where the confirmatory trial demonstrated a worse overall survival in the melphalan flufenamide treatment arm compared to the control arm. Confirmatory studies are post-marketing studies to verify and describe the clinical benefit of a drug after it receives accelerated approval. Based on the update provided, the committee will have a general discussion focused on next steps for the product including whether the indication should remain on the market while additional trial(s) are conducted. The topic of this meeting is a particular matter involving specific parties.

Type, Nature, and Magnitude of the Financial Interests:

Dr. Kwok is a physician at Seattle Cancer Care Alliance (SCCA) and Clinical Associate Professor, Division of Hematology, University of Washington School of Medicine (UW Medicine). The SCCA, part of UW Medicine, is a cancer treatment and research center in Seattle, Washington. Established in 1998, this nonprofit provides clinical oncology care for patients treated at its three partner organizations: Fred Hutchinson Cancer Research Center (FHCRC), Seattle Children's and UW Medicine.

Dr. Kwoks' employer, UW Medicine, is participating in a trial titled *A Phase 1/2 Open-Label, Multicenter, Dose Escalation and Dose Expansion Study of the Safety, Tolerability and Pharmacokinetics of HPN217 in Patients with Relapsed/Refractory Multiple Myeloma (NCT04184050),* sponsored by Harpoon Therapeutics which runs through UW Medicine's site of practice, the Seattle Cancer Care Alliance. The study began in July 2021 with an anticipated end date of (b) (4). Dr. Kwok is a sub-investigator for the study. Harpoon Therapeutics competes with the meeting sponsor, Oncopeptides AB.

UW Medicine anticipates receiving between $250,000 and $300,000 from Harpoon Therapeutics, if all patients are enrolled. Four patients are anticipated to be enrolled with three currently enrolled. Dr. Kwok does not receive any salary support or personal remuneration from this funding.

In addition, UW Medicine is participating in a trial titled *A phase 1/2 multicenter, open-label study to assess the safety, pharmacokinetics and efficacy of CC-92480 monotherapy and in combination with dexamethasone in subjects with relapsed and refractory multiple myeloma (NCT03374085),* sponsored by Celgene which runs through the SCCA. The study began in August 2021 and will end on (b) (4). Dr. Kwok is a sub-investigator for the study. Celgene competes with the meeting sponsor, Oncopeptides AB.

UW Medicine anticipates receiving between $200,000 and $250,000 from Celgene. Dr. Kwok does not receive any salary support or personal remuneration from this funding.

Basis for Granting the Waiver:

Dr. Mary Kwok has unique qualifications and specialized expertise needed for this particular matter.

Dr. Mary Kwok is an Associate Professor of Medicine, Uniformed Services University of Health Sciences, Clinical Associate Professor of Medicine, University of Washington School of Medicine, Physician, Multiple Myeloma Service, Seattle Cancer Care Alliance, and Inpatient attending, University of Washington Medical Center.

Dr. Kwok earned dual undergraduate degrees at the University of Washington, a BS in Biochemistry and a BA in Anthropology. She earned her medical degree from the Uniformed Services University of the Health Sciences. She completed both her Internal Medicine Residency and her Hematology-Oncology Fellowship at Walter Reed National Military Medical Center and

was a clinical fellow with Myeloma Service at the National Cancer Institute (NCI). After graduating from fellowship, she served as a staff hematologist-oncologist at Walter Reed and continued as a clinical collaborator with NCI. While at Walter Reed, she served as the Hematology-Oncology fellowship training program director at the National Capital Consortium. She served as the institutional Principal Investigator on multiple clinical trials for patients with multiple myeloma and served as the director for the FACT-accredited autologous stem cell transplant program. She is board certified in Hematology and Medical Oncology.

According to the review division responsible for the review of the application, it has been difficult to find individuals with experience in multiple myeloma medicine. Of the five experts identified, one was unable to attend, and one was disqualified due to a conflict of interest, leaving only three available to attend, including Dr. Kwok. It is important to have multiple myeloma experts on the panel to discuss the next steps for the product at issue based on the update from the confirmatory trial. Dr. Kwok's extensive experience with treating multiple myeloma and her experience in stem cell transplantation is essential to the discussion at hand.

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. Mary Kwok's expertise in this particular matter is necessary in the interest of public health.

Multiple myeloma (MM) is a systemic malignancy of plasma cells that typically involves multiple sites within the bone marrow. According to the American Cancer Society, the estimated number of new cases of MM in the United States in 2021 is 34,920 while the estimated number of deaths is 12,410. Median survival times have improved with the introduction of newer therapies. Despite the improvement, relapse of MM and disease progression is common even after the achievement of a complete remission. Relapsed/refractory MM (RRMM) is defined as a disease which becomes non-responsive or progressive on therapy or within 60 days of the last treatment in patients who had achieved a minimal response or better on prior therapy.
Despite the availability of new treatments, most patients with multiple myeloma will relapse and some patients may become refractory to the therapies that currently comprise the hematologic standard of care for the malignancy, including proteasome inhibitors, immunomodulatory agents, and monoclonal antibodies. Evidence from literature suggests that outcomes are poor for patients whose multiple myeloma has become refractory to proteasome inhibitors, immunomodulatory agents, and anti-CD38 antibodies. Three therapies are currently approved for patients who are relapsed/refractory to proteasome inhibitor, immunomodulatory agent, and anti-CD38 antibody. The product at issue for the October 28 meeting is Oncopeptides' Pepaxto (melphalan flufenamide) indicated in combination with dexamethasone for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least four prior lines of therapy and whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent, and one CD38-directed monoclonal antibody.

In the interest of public health, it is important that the Agency has available the expertise that Dr.

Kwok 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. Mary Kwok's expertise in this matter.

Multiple drugs are approved for the treatment of patients with RRMM. Although approved for specific lines, the therapies can be used in later line settings and patients can be retreated with therapies that they have failed previously. Dr. Kwok's knowledge of the treatment landscape and safety and efficacy of MM therapies in different lines is needed to provide context to the results presented at the ODAC. Additionally, her expertise in stem cell transplantation would be extremely important.

Accordingly, I recommend that you grant Dr. Mary Kwok, 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: 2021.10.08 13:50:15 -04'00'

October 8, 2021

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

Date