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

DATE: July 29, 2022

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 Meeting Temporary Voting Member: **Mary Kwok, M.D.**

Committee: Oncologic Drugs Advisory Committee

Meeting date: September 22, 2022

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 use in the treatment of cancer and make appropriate recommendations to the Commissioner of Food and Drugs.

On September 22, 2022, the committee will hear an update on new drug application (NDA) 214383, for Pepaxto (melphalan flufenamide) for injection, submitted by Oncopeptides A.B. This product was approved under 21 CFR 314.500-560 (subpart H, accelerated approval regulations) for use in combination with dexamethasone for the treatment of adult patients with relapsed or refractory multiple myeloma (MM) 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 confirmatory trial demonstrated a worse overall survival and failed to verify clinical benefit. 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 the product. 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 employed by the University of Washington School of Medicine (UW Medicine) and Clinical Associate Professor, Division of Hematology, UW Medicine. As part of her employment at UW Medicine, she also serves on the Multiple Myeloma Service of the Fred Hutchinson Cancer Center, a cancer treatment and research center in Seattle, Washington.

Dr. Kwok's 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, a competing firm, which runs through UW Medicine's site of practice, the Fred Hutchinson Cancer Center. The study population overlaps with the indication coming before the advisory committee. The study began in July 2021 with an anticipated end date of January 2, 2024. Dr. Kwok is a sub-investigator for the study.

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.

Second, 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, a competing firm, which runs through the Fred Hutchinson Cancer Center. The study population overlaps with the indication coming before the advisory committee. The study began in August 2021 and will end on (b) (4). Dr. Kwok is a sub-investigator for the study.

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.

Third, UW Medicine is participating in a trial titled *A phase 1, open-label, multi-center, dose escalation and dose expansion study of NKTR-255 as a single agent in relapsed or refractory hematological malignancies and in combination with daratumumab as a salvage regimen for multiple myeloma (NCT 04136756)*, sponsored by Nektar Therapeutics, a competing firm. The study population overlaps with the indication coming before the advisory committee. The study began on January 31, 2020, and will end on (b) (4). Dr. Kwok is an associate investigator for the study.

UW Medicine anticipates receiving between $300,000 and $350,000 from Nektar Therapeutics. Dr. Kwok does not receive any salary support or personal remuneration from this funding.

Lastly, UW Medicine is participating in a trial titled *A Multi-arm Phase 1b Study of Teclistamab With Other Anticancer Therapies in Participants With Multiple Myeloma (NCT04722146)*, sponsored by Janssen, a competing firm. The study population overlaps with the indication

coming before the advisory committee. The study began on September 24, 2021, and will end on (b) (4). Dr. Kwok is an associate investigator for the study.

UW Medicine anticipates receiving between $250,000 to $300,000 from Janssen. Dr. Kwok does not receive any salary support or personal renumeration 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 a Clinical Associate Professor of Medicine at the University of Washington School of Medicine; Physician, Multiple Myeloma Service at Fred Hutchinson Cancer Center; and inpatient attending at the 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. Dr. Kwok 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 the NCI. While at Walter Reed, Dr. Kwok 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. Dr. Kwok is board certified in Hematology and Medical Oncology.

Dr. Kwok is uniquely qualified by having specialized knowledge in hematologic malignancies with a focus in multiple myeloma. Dr. Kwok's experience in multiple myeloma will be helpful in understanding the issues around the safety and efficacy with melphalan flufenamide, the assessment of benefit and risk, and the overall clinical trial design concepts being discussed in order to provide informative insight. Further, the information being discussed relates to safety and efficacy outcomes in patients with multiple myeloma, a disease of the bone marrow and blood, which has unique safety and efficacy considerations given the underlying disease and the treatment administered to these patients. Dr. Kwok possesses the expertise to provide context to the safety and efficacy data being discussed, which will allow her to provide valuable insight and understanding of the issues brought to the committee.

The particular matter is sensitive.

The FDA Division responsible for review of Pepaxto (melphalan flufenamide) expects the matter coming before the committee to 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 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 2022 is 34,470 while the estimated number of deaths is 12,640. Median survival times have improved with the introduction of newer therapies. 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 or refractory to proteasome inhibitors, immunomodulatory agents, and anti-CD38 antibodies.

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.

Melphalan flufenamide and multiple other drugs are approved for the treatment of patients with relapsed or refractory MM. Hematologists, such as Dr. Kwok, with knowledge of the treatment landscape and the safety and efficacy of treatments administered to these patients is needed to provide context to the results presented at the ODAC. Dr. Kwok's extensive experience in clinical trial conduct and treating patients with multiple myeloma will be invaluable to a robust and productive discussion on the issues coming before the committee.

According to the review division responsible for the review of the application, it is necessary to find individuals with experience in multiple myeloma. Of the four experts identified, two were disqualified due to conflicts of interest, leaving only two 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.

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):

_____

_____

_____ Denied – The individual may not participate.

Russell Fortney -S Digitally signed by Russell Fortney -S Date: 2022.08.15 10:50:55 -04'00'

August 15, 2022

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

Date