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

DATE: February 26, 2024

TO: Rachel Bressler
Acting 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 Temporary Voting Member: **Mary Kwok, MD**

Committee: Oncologic Drugs Advisory Committee

Meeting date: March 15, 2024

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 data concerning the safety and effectiveness of marketed and investigational human drug products for use in the treatment of cancer and makes appropriate recommendations to the Commissioner of Food and Drugs.

On March 15, 2024, during the morning session, the committee will discuss supplemental biologics license application (sBLA) 125746.74 for Carvykti (ciltacabtagene autoleucel), suspension for intravenous infusion, submitted by Janssen Biotech, Inc. The proposed indication for this product is for the treatment of adult patients with relapsed or refractory multiple myeloma, who have received at least one prior line of therapy, including a proteasome inhibitor, and an immunomodulatory agent, and are refractory to lenalidomide. The Committee will have a general discussion focused on the overall survival data in the Study MMY3002 (CARTITUDE–4) and the risk and benefit of ciltacabtagene autoleucel in the intended population.

During the afternoon session, the Committee will discuss sBLA 125736.218 for Abecma (idecabtagene vicleucel), suspension for intravenous infusion, submitted by Celgene Corp., a Bristol-Myers Squibb Co. The proposed indication is for the treatment of adult patients with relapsed or refractory multiple myeloma who have received an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody. The Committee will have a general discussion focused on the overall survival data in the Study MM–003 (KarMMa–3) and the risk

and benefit of idecabtagene vicleucel in the intended population. The topics of the meeting are particular matters involving specific parties.

Type, Nature, and Magnitude of the Financial Interests:

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 (UW Medicine), Physician, Multiple Myeloma Service, Fred Hutchinson Cancer Center (FHCC), and Inpatient Attending, University of Washington Medical Center.

Dr. Kwok's institution is participating in the following studies that potentially can be affected by the particular matters coming before the advisory committee. Dr. Kwok serves as a sub-investigator on the following studies, and she receives no salary support or personal remuneration for her role. The estimated per year funding to her institution varies dependent on patient accrual and projected study completion date.

- *A Phase 2, Multicohort Open-Label Study of JNJ-68284528, a Chimeric Antigen Receptor T Cell (CAR-T) Therapy Directed Against BCMA in Subjects With Multiple Myeloma (CARTITUDE-2)* NCT04133636, sponsored by Janssen, a party to the matter for the Carvykti session and competing firm for the Abecma session. The study began on January 11, 2011, with an anticipated end date of (b) (4). The FHCC receives between $0 and $50,000 per year. (b) (4) patients have been enrolled to date.
- *FH10062, A Phase I Study of SEA-BCMA in Patients with Relapsed or Refractory Multiple Myeloma (RRMM)* NCT03582033, sponsored by Seagen, a competing firm for the Carvykti and Abecma sessions. The study began on January 10, 2016, and ended October 2023. Dr. Kwok's institution has received between $0 and $50,000 per year.
- (b) (4), sponsored by (b) (4), a competing firm for both the Carvykti and Abecma sessions. The study population overlaps with the indications coming before the advisory committee. The study began (b) (4). The study closed to accrual in (b) (4) and as of January 2024 the study has ceased enrolling patients. The FHCC receives between $0 and $50,000 per year for the study.
- *RG1121006, 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. The study population overlaps with the indications coming before the advisory committee. The study began in July 2021 with an estimated study completion date of (b) (4). (b) (4) patients are anticipated to enroll; (b) (4) patients have enrolled thus far. The estimated funding is between $300,000 and $500,000 per year for the study.
- *RG1121238, 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 for the Carvykti session and party to the matter for the Abecma session. The study began in August 2021 with an

estimated study completion date of (b) (4). The estimated funding is between $0 and $50,000 per year for the study.

- *Protocol RG1121388: A Multi-arm Phase 1b Study of Teclistamab With Other Anticancer Therapies in Participants With Multiple Myeloma* NCT04722146, sponsored by Janssen, a party to the matter for the Carvykti session and competing firm for the Abecma session. The study began on September 24, 2021, with an estimated study completion date of (b) (4). Dr. Kwok's institution receives between $100,000 and $300,000 per year.
- *Isatuximab, Carfilzomib, Pomalidomide, and Dexamethasone for the Treatment of Relapsed or Refractory Multiple Myeloma* NCT04883242, sponsored by Sanofi, a competing firm for both the Carvykti and Abecma sessions. The study population overlaps with the patient population being discussed at the advisory committee meeting. The study began on July 16, 2021, with an estimated study completion date of December 31, 2029. Dr. Kwok's institution receives between $100,000 and 300,000 per year.
- *A Study Comparing Talquetamab in Combination With Daratumumab or in Combination With Daratumumab and Pomalidomide Versus Daratumumab in Combination With Pomalidomide and Dexamethasone in Participants With Multiple Myeloma That Returns After Treatment or is Resistant to Treatment (MonumenTAL-3)* NCT05455320, sponsored by Janssen Research & Development, a party to the matter for the Carvykti session and competing firm for the Abecma session. The study population overlaps with the patient population being discussed at the advisory committee meeting. The study opened to accrual on April 12, 2023, with an estimated study completion date of April 6, 2029. Dr. Kwok's institution receives between $100,000 and $300,000 for the (b) (4) enrolled.
- *A Study to Assess Adverse Events and Change in Disease Activity of Intravenously (IV) Infused ABBV-383 in Combination With Anti-Cancer Regimens for the Treatment of Adult Participants With Relapsed/Refractory Multiple Myeloma* NCT05259839, sponsored by TeneoOne and AbbVie, competing firms for both the Carvykti and Abecma sessions. The study population overlaps with the patient population being discussed at the advisory committee meeting. The study opened to accrual on May 4, 2023, with an estimated study completion date of November 29, 2028. Dr. Kwok's institution receives between $100,000 to $300,000 for the (b) (4) patients enrolled.
- *A Study to Learn How Linvoseltamab (REGN5458) Will Work Compared to the Elotuzumab, Pomalidomide and Dexamethasone (EPd) Combination, in Participants With Relapsed/Refractory Multiple Myeloma (LINKER-MM3)* NCT05730036, sponsored by Regeneron Pharmaceuticals, a competing firm for both the Carvykti and Abecma sessions. The study population overlaps with the patient population being discussed at the advisory committee meeting. The study opened to accrual on January 30, 2024, with an estimated completion of December 26, 2032. The estimated funding is between $50,000 and $100,000 per patient enrolled. (b) (4) patients have been enrolled to date.

In addition, Dr. Kwok is in negotiation to consult with (b) (4), a competing entity for the Carvykti session and (b) (4) the matter for the Abecma session. Dr. Kwok will be participating in the Scientific Review Committee for the competing product, (b) (4) At the writing of the waiver, the estimated consulting period is from (b) (4); and the compensation to be received from the firm is still under negotiation.

Basis for Granting the Waiver:

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

Dr. Kwok 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. Dr. Kwok's research interest focuses on multiple myeloma, both newly diagnoses and relapsed/refractory. Her interests include global hematology. She is board certified in Hematology and Medical Oncology.

It is important to have multiple myeloma experts on the panel to discuss the next steps for the applications being presented at the ODAC. There is limited expertise available, and it is difficult to locate similarly qualified individuals without a disqualifying financial interest. Dr. Kwok's extensive experience with treating hematologic malignancies, specifically the treatment landscape of multiple myeloma, will be helpful in clarifying the issues around the benefit-risk profile of ciltcabtagene-autoleucel for the proposed patient population considering the results of MMY3002 (CARTITUDE-4), and benefit-risk profile of idecabtagene vicleucel for the intended population in the study MM-003 (KarMMa-3). Furthermore, Dr. Kwok's professional proficiency in multiple myeloma, combined with her extensive experience in treating these patients, will be invaluable to a robust and productive discussion of the issues coming before the committee.

The particular matter is sensitive.

The FDA Division responsible for the review of Carvykti (ciltacabtagene autoleucel) and Abecma (idecabtagene vicleucel) expects the matters coming before the committee to garner significant public interest.

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. Multiple myeloma constitutes 1.8% of all new cancer cases and 2.1% of all cancer deaths yearly in the United States, with an incidence of 4.5 to 6 per 100,000 annually. According to the American Cancer Society, the estimated number of new cases of MM in the United States in 2024 is 35,780 while the estimated number of deaths is 12,540. 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. 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:

___X___ 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.

Rachel S. Bressler -S Digitally signed by Rachel S. Bressler -S
Date: 2024.02.28 09:20:46 -05'00'

_____ _____

Rachel Bressler Date
Acting Director
Advisory Committee Oversight and Management Staff
Office of the Chief Scientist