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

DATE: August 12, 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: **Grzegorz Nowakowski, M.D.**

Committee: Oncologic Drugs Advisory Committee

Meeting date: September 22, 2022

Description of the Particular Matter to Which the Waiver Applies:

Grzegorz Nowakowski, M.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 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 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. Nowakowski's employing institution, Mayo Clinic, is participating in the study titled: *A Phase 1/2 Open-label Study Evaluating the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics, and Efficacy of AMG 701 Monotherapy, or in Combination with Pomalidomide, with and without Dexamethasone in Subjects with Relapsed or Refractory Multiple Myeloma (ParadigMM-1B) (NCT03287908),* sponsored by Amgen, a competing firm. This study population overlaps with the indication coming before the advisory committee. The study began July 30, 2018, with an anticipated end date of April 13, 2028. Dr. Nowakowski has not been involved in the study and will not be involved in the future.

Mayo Clinic receives between $250,000 and $300,000 per year from Amgen. Dr. Nowakowski does not receive any salary support or personal remuneration from this funding.

Second, Mayo Clinic is participating in the study titled: *A Phase I, Open-label, Multicenter, Study of WVT078 in Subjects With Relapsed and/or Refractory Multiple Myeloma (Protocol ID# CWVT078A12101) NCT04123418*, sponsored by Novartis, a competing firm. This study population overlaps with the indication coming before the advisory committee. The study began July 28, 2021, with an anticipated end date of January 11, 2024. Dr. Nowakowski has not been involved in the study and will not be involved in the future.

Mayo Clinic receives between $0 and $25,000 per year from Novartis. Dr. Nowakowski does not receive any salary support or personal remuneration from this funding.

Third, Mayo Clinic, is participating in the study titled: *A Phase 1/2 Multicenter, Open-label, Study to Determine the Recommended Dose and Regimen, and Evaluate the Safety and Preliminary Efficacy of CC-92480 in Combination With Standard Treatments in Subjects With Relapsed or Refractory Multiple Myeloma (RRMM) and Newly Diagnosed Multiple Myeloma (NDMM) (Protocol ID# CC-92480-MM-002),* NCT03989414, sponsored by Celgene, a competing firm. This study population overlaps with the indication coming before the advisory committee. The study began December 18, 2020, with an anticipated end date of (b) (4). Dr. Nowakowski has not been involved in the study and will not be involved in the future.

Mayo Clinic receives between $0 and $25,000 per year from Celgene. Dr. Nowakowski does not receive any salary support or personal remuneration from this funding.

Lastly, Mayo Clinic is participating in the study titled: (b) (4) sponsored by (b) (4), a competing firm. This study population overlaps with the indication coming before the advisory committee. The study has not opened at Mayo Clinic yet. Dr. Nowakowski has not been involved in the study and will not be involved in the future.

Since Dr. Nowakowski does not have direct involvement with this study, he is not aware of the funding amount being provided to Mayo Clinic from (b) (4) for its participation in this study.

Further, Dr. Nowakowski does not receive any personal remuneration or salary support from the funding.

Basis for Granting the Waiver:

Dr. Grzegorz Nowakowski has unique qualifications and specialized expertise needed for this particular matter.

Dr. Grzegorz Nowakowski serves as a Consultant and Education Chair at the Department of Internal Medicine in the Division of Hematology at Mayo Clinic, Rochester. In addition, he is the Advanced Hematology Fellowship Program Director and a Professor of Medicine and Oncology at the Mayo Clinic College of Medicine and Science. Dr. Nowakowski is also the Deputy Director of the Mayo Clinic Cancer Center for Clinical Research.

Dr. Nowakowski earned his medical degree from Medical University of Warsaw and completed a Medical Oncology/Internal Medicine Clerkship at Mississauga Hospital in Ontario, Canada. He then went on to complete a Research Fellowship in Experimental Bone Marrow Transplantation at University of Massachusetts Cancer Center followed by his internal medicine residency at Yale University Medical School, Norwalk Hospital. Following his residency, he completed a Hematology/Oncology Fellowship Program at Mayo School of Graduate Medical Education, Mayo Clinic College of Medicine. He is board certified in Internal Medicine, Medical Oncology and Hematology.

Dr. Nowakowski's research interests complement his clinical focus on hematology and hematologic cancers, including new therapies for lymphoma, chronic lymphocytic leukemia and multiple myeloma. The overarching goal of Dr. Nowakowski's research is to better understand the genetic causes of hematologic cancers, such as various types of leukemia, in order to develop personalized therapies based on the genetic profiles of individual patients. He is extensively published in hematologic cancers, including multiple myeloma. Dr. Nowakowski contributes to research in Mayo Clinic's Center for Individualized Medicine. He is also active in education and has been recognized for his leadership in Mayo's Hematology/Oncology Fellowship. Dr. Nowakowski's extensive experience in clinical trial conduct and treating patients with multiple myeloma will be invaluable to a robust and productive discussion on the issue coming before 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. Grzegorz Nowakowski'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 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 inhibitor, immunomodulatory agent, and anti-CD38 antibodies.

In the interest of public health, it is important that the Agency has available the expertise that Dr. Nowakowski 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. Grzegorz Nowakowski's *expertise in this matter.*

It is particularly important to include Dr. Nowakowski in the upcoming ODAC meeting, given his clinical experience and research in hematologic cancers. Dr. Nowakowski's experience will be helpful in understanding the issues around the safety and efficacy of 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 treatments administered to these patients. Dr. Nowakowski possesses the expertise to provide context to the safety and efficacy data being discussed, which will allow him to provide valuable insight and understanding of the issues brought to the committee. Melphalan flufenamide, along with multiple other drugs are approved for the treatment of patients with relapsed or refractory multiple myeloma. Hematologists, such as Dr. Nowakowski, 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.

According to the review division responsible for the review of the application, it is necessary to find individuals with clinical 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. Nowakowski. 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.

Finally, Dr. Nowakowski has been a previous standing member of the ODAC until 2018 and has participated in numerous ODAC meetings. His prior experience with advisory committee meetings will be invaluable for a productive discussion of the meeting topic on September 22.

Accordingly, I recommend that you grant Dr. Grzegorz Nowakowski, 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: 2022.08.30 07:24:33 -04'00'

August 30, 2022

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

Date