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

DATE: August 25, 2023

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 Standing Voting Member: **Alberto Pappo, M.D.**

Committee: Oncologic Drugs Advisory Committee

Meeting dates: October 4, 2023

Description of the Particular Matter to Which the Waiver Applies:

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

On October 4, 2023, the committee will discuss new drug application (NDA) 215500, for eflornithine tablets, submitted by USWM, LLC (doing business as U.S. WorldMeds). The proposed indication (use) for this product is to reduce the risk of relapse in pediatric patients with high-risk neuroblastoma who have completed multiagent, multimodality therapy. The topic is a particular matter involving specific parties.

Type, Nature, and Magnitude of the Financial Interests:

Dr. Pappo holds the Alvin Mauer Endowed Chair at St. Jude Children's Research Hospital. The St. Jude Children's Research Hospital (SJCRH) is participating in the study titled *A Phase 2 Randomized Study of Irinotecan/Temozolomide/Dinutuximab With or Without Eflornithine (DFMO) in Children With Relapsed, Refractory or Progressive Neuroblastoma (ANBL1821, NCT03794349)*, sponsored by Children's Oncology Group. The study began on May 8, 2019, and the estimated study completion date is in (b) (4). Dr. Pappo serves as the Children's Oncology Group Principal

Investigator (COG PI) for SJCRH. As the COG PI, Dr. Pappo supervises the administrative issues and all clinical trials offered by the COG at SJCRH. Dr. Pappo was not and is not involved in the design of this clinical trial. He has no direct involvement in the clinical trial and will not be reviewing any of the data from the study.

St. Jude Children's Research Hospital receives between $0 and $1,000 per year from Children's Oncology Group for this study. The study drug is provided by Cancer Prevention Pharmaceuticals. Dr. Pappo does not receive any salary support or personal remuneration from the study funding.

Basis for Granting the Waiver:

Dr. Alberto Pappo has unique qualifications and specialized expertise needed for this particular matter.

Dr. Pappo received his medical degree from Medical School Universidad Anahuac, Mexico City. After medical school, Dr. Pappo enrolled in a pediatric residency at the University of Texas Health Science Center in San Antonio, Texas. He pursued a pediatric hematology-oncology fellowship at both Children's Medical Center of Dallas and the University of Texas Southwestern Medical Center at Dallas.

Dr. Pappo is Director of the Solid Tumor Division, Co-Leader of Developmental Biology and Solid Tumor Program, and holds the Alvin Mauer Endowed Chair at St. Jude Children's Research Hospital. He is a Professor of Pediatrics at the University of Tennessee Health Science Center. Since completing fellowship, but prior to his current Director role at SJCRH, Dr. Pappo has held various roles related to oncology and pediatrics. Dr. Pappo was both an Assistant Professor and Assistant Member in the Department of Pediatrics and Department of Hematology-Oncology at the University of Tennessee, College of Medicine, and St. Jude Children's Research Hospital, respectively. Dr. Pappo was an Associate Member in the Department of Hematology-Oncology at St. Jude Children's Research Hospital. He concurrently held positions as Professor of Pediatrics and Head Solid Tumor Section at The Hospital for Sick Children. Dr. Pappo was a Professor of Pediatrics at Baylor College of Medicine's Head-Division of Solid Tumors at the Texas Children's Cancer Center. Dr Pappo's professional expertise is in pediatric oncology, with a focus on melanoma, soft tissue sarcoma, and gastrointestinal stromal tumors. He has active grants for various ongoing studies in his field of specialty.

It is particularly important to include Dr. Pappo in the upcoming ODAC meeting, given his vast experience and research in pediatric oncology. Dr. Pappo has been a standing member of the ODAC since 2015. He has also served as a chairperson for various pediatric oncology subcommittees of the ODAC.

The matter is not sensitive.

This meeting topic is not considered to be sensitive as the FDA Division responsible for review of this product does not expect that the meeting is likely to receive significant public interest, (non-trade) press interest, nor is it considered highly controversial.

Dr. Alberto Pappo's expertise in this particular matter is necessary in the interest of public health.

Neuroblastoma is a term commonly used when describing a spectrum of neuroblastic tumors that arise from primitive sympathetic ganglion cells. They account for 97% of all neuroblastic tumors and widely vary in the clinical presentation, location, histology, and biologic characteristics. They exhibit a broad spectrum of clinical behavior, which ranges from maturation into benign masses, to terminal metastases.

Neuroblastoma is the most common cause of cancer in infants younger than 1 year of age and the most common extra-cranial solid tumor in children. Annually, there are approximately 700 to 800 new cases of neuroblastoma in the United States, a number that has held steady for many years. Although many children are cured, current data suggests that the 5-year survival rate, depending on risk classification, can range from 50% (high risk) to 95% (low risk). The variables associated with risk classification for patients with neuroblastoma that determine treatment include the stage of the disease, patient age, resection findings, tumor genotype and other genetic findings, and the histologic appearance of the tumor. As it relates to patients with high-risk neuroblastoma (HRNB), 20% of patients will have no/mixed response or progressive disease at the end of induction with chemotherapy, and at least 40% will experience disease recurrence after completing multimodal therapy.

The current standard of therapy for HRNB is multimodal treatment that includes an induction, consolidation, and maintenance period. The induction phase includes chemotherapy and surgical resection. The consolidation phase of treatment includes tandem cycles of myeloblative therapy, stem cell transplantation and radiation therapy. The maintenance phase (also known as post-consolidation) includes treatment with dinutuximab with granulocyte macrophage colony-stimulating factor and isotretinoin therapy. Despite improvements in patient outcomes with intensive multimodal therapy, recurrence and death are still common in high-risk patients, and improvement in survival rates in this subgroup is needed.

In the interest of public health, it is important that the Agency has available the unique expertise that Dr. Pappo 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. Alberto Pappo's expertise in these matters.

It is particularly important to include Dr. Pappo in the upcoming ODAC meeting, given his vast experiences and research in pediatric hematology-oncology. Dr. Pappo has been a standing member of the ODAC since 2015 and chairperson for various pediatric oncology subcommittees of the ODAC. His robust professional and research experience in pediatric oncology, combined with extensive previous experience with advisory committee meetings at the FDA, which is unique among pediatric oncologists, will be invaluable to a robust and productive discussion on the issue coming before the committee.

Accordingly, I recommend that you grant Dr. Alberto Pappo, the Chairperson 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: 2023.09.15 11:34:11 -04'00'

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

September 15, 2023
Date