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: **Andy I. Chen, M.D., PhD.**

Committee: Oncologic Drugs Advisory Committee

Meeting date: September 23, 2022

Description of the Particular Matter to Which the Waiver Applies:

Andy Chen, M.D., PhD., 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 23, 2022, the committee will hear an update on new drug application (NDA) 211155 for Copiktra (duvelisib) capsule, submitted by Secura Bio, Inc. This product was approved under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for use in the treatment of adult patients with relapsed or refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) after at least two prior therapies. The update includes the final overall survival data from the DUO trial (IPI-145-07) submitted in response to post-marketing requirement 3494-3 detailed in the September 24, 2018 approval letter. Based on the updated overall survival along with the safety data with duvelisib, the committee will discuss a current assessment of benefit-risk. The topic of this meeting is a particular matter involving specific parties.

Type, Nature, and Magnitude of the Financial Interests:

Dr. Chen's employing institution, Oregon Health and Science University (OHSU), is participating

in the study titled *A Phase 3 Randomized Study to Assess the Efficacy and Safety of Ublituximab in Combination With TGR-1202 Compared to Obinutuzumab in Combination With Chlorambucil in Patients With Chronic Lymphocytic Leukemia (UTX-TGR-304),* NCT02612311, sponsored by TG Therapeutics, a competing firm. The study population overlaps with the indication coming before the advisory committee. The study began in March 2016 and is projected to end January of 2024. Dr. Chen is a Sub-Investigator for the study, but he did not enroll any patients and he was not involved with study conduct or design, data analysis or patient care. He further confirmed the study has closed to accrual and he will not be involved with any aspect of this study in the future.

OHSU anticipates receiving between $0 and $50,000 per year for its participation in the study. Dr. Chen does not receive any personal remuneration or salary support from this funding.

In addition, OHSU is participating in a study titled *A Phase I Study of FT819 in Subjects With B-cell Malignancies, NCT04629729,* sponsored by Fate Therapeutics, a competing firm. The study population overlaps with the indications coming before the advisory committee, specifically Chronic Lymphocytic Leukemia. The study began in 2021 and is projected to end in (b) (4). Dr. Chen is a Site Principal-Investigator for the study.

OHSU anticipates receiving between $0 and $10,000 per year for its participation in the study. Dr. Chen does not receive any personal remuneration or salary support from this funding.

Basis for Granting the Waiver:

Dr. Andy Chen has unique qualifications and specialized expertise needed for this particular matter.

Dr. Chen is Associate Professor of Hematology and Medical Oncology with the Department of Medicine at Oregon Health & Science University. His expertise is in cancer and blood disorders, with a special focus on bone marrow transplant, hematologic malignancies, and lymphoma. He is involved in research that studies new treatments for lymphoma, and he has a particular interest in chimeric antigen receptor T cell (CAR-T) therapy."

Dr. Chen received his medical degree in the Health Sciences & Technology Program from the Massachusetts Institute of Technology & Harvard Medical School and Doctor of Philosophy in Experimental Pathology from Harvard University. He subsequently completed residency in Internal Medicine, and fellowship in Hematology, Medical Oncology, and Blood & Marrow Transplant, both at Stanford University. He is the author of 39 research publications and 8 reviews and book chapters. Dr. Chen is past chair of the Patient Services Committee for the Oregon chapter of the Leukemia & Lymphoma Society and is co-chair of a national guideline committee for lymphoma.

According to the review division responsible for the review of the application, multiple hematology and oncology experts are necessary to assess the overall survival and safety concerns with this application. The regulatory history of duvelisib and the results from the DUO trial demonstrating a worse overall survival, toxicity data, and concerns with the approved dosage

requires specialized knowledge of the impact of these concerns and are necessary for the assessment of the benefit and risk in the evaluated and approved patient population. Expertise in hematology and oncology is needed to adequately contextualize the data from the randomized trial and the regulatory history of duvelisib and the PI3K inhibitor class and how it impacts the current indication. Dr. Chen's expertise in clinical trial conduct and research in patients with hematologic malignancies combined with his experiences treating these patients 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 Copiktra (duvelisib) expects the matter coming before the committee to garner public interest as it relates to postmarketing requirements under 505(o)(3) of the FDCA, safety concerns, and a potential detriment in overall survival in patients with CLL or SLL. This advisory committee meeting will discuss information regarding duvelisib and the FDA seeks input from the committee on a current assessment of benefit-risk and whether duvelisib should remain on the market given the final results from the DUO trial along with the toxicity and tolerability concerns with duvelisib and the PI3K inhibitor drug class. Discussions regarding withdrawals of indications or products from the U.S market uniformly receive significant public interest.

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

CLL and SLL are indolent cancers characterized by increased production of mature but dysfunctional B lymphocytes. The primary disease sites include peripheral blood, spleen, lymph nodes, and bone marrow. CLL and SLL are identical from a pathologic and immunophenotypic standpoint. Both CLL and SLL originate from B-cell lymphocytes but present with different manifestations depending on where the abnormal cells are found; CLL is primarily in the blood and SLL is primarily in the lymph nodes. According to the American Cancer Society, in 2022 there will be about 20,160 new cases of CLL, and about 4,410 deaths from CLL. Patients with CLL or SLL are not cured with conventional therapy, and most will relapse eventually.

There are many current first-line treatment options for CLL or SLL. Active treatment is started if the patient begins to develop disease-related symptoms or there are signs that the disease is progressing based on testing during follow-up visits. The choice of treatment depends on the stage of the disease, the patient's symptoms, the age and overall health of the patient, and the benefits versus side effects of treatment. The treatment landscape has also expanded with the development of targeted agents, in addition to the traditional chemotherapy agents. For relapsed or refractory disease, treatment may incorporate one or more of the following targeted agents, often administered as combinations: Bruton tyrosine kinase inhibitors, phosphatidylinositol-3 kinase (PI3K) inhibitors, BCL2 inhibitors and anti-CD-20 monoclonal antibodies.

In the interest of public health, it is important that the Agency has available the unique expertise that Dr. Chen will provide for the discussion of the particular matter coming before the committee.

Any potential for a conflict of interest is greatly outweighed by the strong need for Andy Chen's expertise in this matter.

Dr. Chen is uniquely qualified by having the specialized knowledge and research experiences in blood disorders, hematologic malignancies, and lymphoma. Dr. Chen's expertise in hematologic malignancies will be helpful in understanding the issues around safety with duvelisib and the PI3K inhibitor class in patients with hematologic malignancies, 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 hematologic malignancies, diseases of the blood, bone marrow, and/or immune system, which can have unique safety and efficacy considerations given the underlying disease and the treatments administered to these patients. Dr. Chen possesses the expertise to provide context to the safety and efficacy data being discussed, which will allow him to provide valuable insight and understanding to the issues brought to the committee. Duvelisib, along with other PI3K inhibitors have been approved for the treatment of patients with CLL or SLL. Hematologists, such as Dr. Chen, with knowledge of the treatment landscape and the safety and efficacy of treatments administered to these patients is needed to provide context to the data and information presented to the committee.

Accordingly, I recommend that you grant Dr. Andy Chen, 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: 2022.08.15 10:56:39 -04'00'

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

August 15, 2022
Date