



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

DATE: March 22, 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: April 22, 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 April 22, 2022, the committee will discuss supplemental new drug application (sNDA) 213176/S-002, for Ukoniq (umbralisib) tablets, and biologics license application (BLA) 761207, for ublituximab injection, both submitted by TG Therapeutics, Inc. The proposed indication (use) for these two products is in combination for the treatment of adult patients with chronic lymphocytic leukemia or small lymphocytic lymphoma. In addition, the committee will also discuss the existing umbralisib indications in patients with relapsed or refractory follicular lymphoma and marginal zone lymphoma under 21 CFR 314.500 (subpart H, accelerated approval regulations). The matters under review by the advisory committee are particular matters 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*

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*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 party to the matter. 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 the study titled *A Multi-Center, Open-Label, Study to Evaluate the Safety and Efficacy of Ublituximab (TG-1101) in Combination With TGR-1202 for Patients Previously Enrolled in Protocol UTX-TGR-304 (UTX-TGR-204)*, NCT02656303, sponsored by TG Therapeutics, a party to the matter. The study began in June 2016 and is projected to end March 2025. Dr. Chen is a Sub-Investigator for the study, but he did not enroll any patients and he was not involved with study. He further confirmed the study 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.

OHSU is also participating in the study titled *A Phase II, Single Arm, Multicenter Open Label Trial to Determine the Efficacy and Safety of Tisagenlecleucel (CTL019) in Adult Patients With Refractory or Relapsed Follicular Lymphoma*, NCT03568461, sponsored by Novartis. The study began in April 2019 and is projected to end November 2022. Dr. Chen is a Site Principal-Investigator for the study.

OHSU anticipates receiving between \$50,000 and \$100,000 per year for its participation in the study. Dr. Chen does not receive any personal remuneration or salary support from this funding.

OHSU is participating in a study titled *A Phase I Study of FT819 in Subjects With B-cell Malignancies*, NCT04629729, sponsored by Fate Therapeutics. The study began in 2021 and is projected to end in 2025. Dr. Chen is a Site Principal-Investigator for the study.

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.

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."

He 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 is the author of 36 research publications and 8 reviews and book chapters.

The committee will discuss umbralisib (Ukoniq) and ublituximab in combination for the treatment of adult patients with CLL or SLL. In addition, the committee will discuss the existing umbralisib indications for relapsed or refractory follicular lymphoma and marginal zone lymphoma. Multiple hematologist/oncologists are needed at the meeting to assess the overall survival and safety concerns along with concerns for support for the selected doses of the combination, which require expertise to contextualize the dosing considerations.

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. Hematologists with knowledge of the treatment landscape and the safety and efficacy of treatments administered to these patients are needed to provide context to the data and information presented at the ODAC. Multiple hematologist/oncologists were invited but either declined due to schedule conflicts or had financial interests creating more significant conflicts. Dr. Chen is uniquely qualified by having the specialized knowledge in clinical trial conduct and research experiences in blood disorders, hematologic malignancies, and lymphoma.

*The particular matter is sensitive.*

The FDA Division responsible for review of umbralisib and ublituximab does expect 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. The Division seeks ODAC's input on the risk-benefit of the combination in the proposed indication and how the current information impacts the existing indications under accelerated approval.

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

Non-Hodgkin lymphoma (NHL) is one of the most common cancers in the United States, accounting for about 4% of all cancers. The American Cancer Society's estimates for Non-Hodgkin Lymphoma in 2022 are about 80,470 people (both adults and children) will be diagnosed with NHL and about 20,250 people will die from this cancer. There are an estimated 672,980 people living with or in remission from non-Hodgkin lymphoma. Indolent lymphomas are slow-moving and tend to grow more slowly and have fewer signs and symptoms when first diagnosed. Slow-growing or indolent subtypes represent about 40 percent of all NHL cases. Indolent NHL subtypes include but are not limited to Follicular lymphoma (FL), which is the most common subtype of indolent NHL, followed by Marginal Zone Lymphoma (MZL) and

## Chronic Lymphocytic Leukemia or Small-Cell Lymphocytic Lymphoma (CLL/SLL).

Chronic lymphocytic leukemia or small lymphocytic lymphoma is an indolent malignancy characterized by increased production of mature but dysfunctional B lymphocytes. CLL comprises 25% to 30% of total leukemias in the United States. According to the American Cancer Society, in 2021 there were an estimated 21,250 new CLL cases and about 4,320 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, phosphoinositide 3'-kinase (PI3K) inhibitors, BCL2 inhibitors and anti-CD-20 monoclonal antibodies.

For lymphoma, about 1 out of 5 lymphomas in the United States is a follicular lymphoma. FL is the second common form of NHL in the U.S with an estimated incidence of 6 new cases/100,000 persons/year. The vast majority of patients treated for FL will have an initial response to therapy with 40% to 80% demonstrating a complete response, depending on the initial regimen used. However, conventional therapy for FL is not curative and most of these patients will ultimately develop progressive disease. In addition, less than 10% of patients treated with initial chemoimmunotherapy will not respond to treatment (i.e., refractory disease). Marginal zone lymphomas account for about 5% to 10% of lymphomas. MZL is the second most common indolent non-Hodgkin's lymphoma which accounts for approximately 8% of all NHL cases. Although conventional first-line treatment options are proved beneficial, many of the patients become resistant to or experience a relapse following treatment.

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 Dr. 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. His expertise in clinical trial conduct and research in patients with hematologic malignancies is essential for the umbralisib and ublituximab ODAC session. His professional experiences combined with experiences with treating these patients will be invaluable to a robust and productive discussion on the issues coming before the committee.

Accordingly, I recommend that you grant Dr. Andy Chen, M.D., Ph.D., 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.

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

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April 5, 2022  
Date