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

DATE: July 15, 2019

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

FROM: Jayne E. Peterson, B.S.Pharm., J.D.
Director, Division of Advisory Committee and Consultant Management
Office of Executive Programs
Center for Drug Evaluation and Research

Name of Advisory Committee Member: **Barbara Gripshover, M.D.**

Committee: Antimicrobial Drugs Advisory Committee (AMDAC)

Meeting date: August 7, 2019

Description of the Particular Matter to Which the Waiver Applies:

Dr. Gripshover is a standing voting member of the Antimicrobial Drugs Advisory Committee. 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 infectious diseases and disorders and make appropriate recommendations to the Commissioner of Food and Drugs.

On August 7, 2019, the committee will discuss supplemental new drug application (sNDA) 208215, supplement 12, DESCOVY (emtricitabine (FTC) 200 mg and tenofovir alafenamide (TAF) 25 mg tablets), submitted by Gilead Sciences, Inc., proposed for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired human immunodeficiency virus (HIV)-1 infection among individuals who are HIV-negative and at risk for HIV. The topic of this meeting is a particular matter involving specific parties.

Type, Nature, and Magnitude of the Financial Interest:

Dr. Gripshover is employed by Case Western University/University Hospitals of Cleveland, which has a local AIDS Clinical Trials Unit/ Case Clinical Research Site (ACTU/Case CRS). Dr. Gripshover is listed as an investigator on several studies related to HIV Vaccines at the ACTU/Case CRS. Dr. Gripshover has no involvement in the studies including seeing patients, contributing data or involvement in study design. She has the potential to be called if an emergency occurs and the

usual ACTU medical leadership are not available. The studies are funded by the HIV Prevention Trials Network (HPTN) and the HIV Vaccine Treatment Network (HVTN). Overall support for the HIV Prevention Trials Network (HPTN) is provided by the National Institute of Allergy and Infectious Diseases (NIAID) of the National Institutes of Health (NIH). The HVTN is also a publicly-funded network, with their main funding coming from the NIAID/NIH. Another significant funding source of the HVTN is the Bill & Melinda Gates Foundation. The Network's clinical research sites are located in over 30 cities on five continents.

- Dr. Gripshover is listed as co-investigator on "A Phase 2b Study to Evaluate the Safety and Efficacy of VRC01 Broadly Neutralizing Monoclonal Antibody in Reducing Acquisition of HIV-1 Infection Among Men and Transgender Persons Who Have Sex with Men" (NCT02716675) (HVTN 704/HPTN 085). The study began in May 2016 with an estimated end date of October 2020. Case CRS receives between $300,000 and $400,000 annually from the federally funded networks for this study. Dr. Gripshover does not receive any salary support or personal remuneration for this study.

- Dr. Gripshover is listed as sub-investigator on the following three Phase I studies:
  - "A Phase 1 Clinical Trial to Evaluate the Safety and Immunogenicity of pDNA Vaccines Expressing HIV M Group p24^Gag Conserved Elements and/or p55^Gag, Administered With IL-12 pDNA by Intramuscular Electroporation, in Healthy, HIV-Uninfected Adult Participants" (NCT03181789) (HVTN 119). This study began October 2017 and is estimated to end April 2020. ACTU/Case CRS receives between $50,001 and $100,000 per year. Dr. Gripshover does not receive any salary support or personal remuneration for this study.
  - "A Phase 1/2a Clinical Trial to Evaluate the Safety and Immunogenicity of ALVAC-HIV (vCP2438) and of MF59®- or AS01B-adjuvanted Clade C Env Protein, in Healthy, HIV-uninfected Adult Participants" (NCT03122223) (HVTN 120). This study began January 2018 and is estimated to end September 2019. ACTU/Case CRS receives between $0 and $50,000 per year. Dr. Gripshover does not receive any salary support or personal remuneration for this study.
  - "A Phase 1 Clinical Trial to Evaluate the Safety and Immunogenicity of Polyvalent Env (A,B,C,A/E) / Gag (C) DNA and gp120 (A,B,C,A/E) Protein/GLA-SE HIV-1 Vaccines (PDPHV-201401) as a Prime-boost Regimen or Co-administered in Repeated Doses, in Healthy, HIV-1-Uninfected Adult Participants" (NCT03409276)(HVTN 124). This study began March 2018 and is estimated to end August 2020. ACTU/Case CRS receives between $50,001 and $100,000 per year. Dr. Gripshover does not receive any salary support or personal remuneration for this study.

Basis for Granting the Waiver:

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

Dr. Barbara Gripshover, M.D., received her medical degree from Vanderbilt University Medical School followed by an Internal Medicine Residency at the University Hospitals of Cleveland.

She completed a fellowship in Infectious Diseases with the University Hospitals of Cleveland.

She is currently Medical Director of the John T. Carey Special Immunology Unit at the University Hospitals of Cleveland and Attending Physician of Infectious Diseases and Internal Medicine at University Hospitals of Cleveland. Previously she was Medical Director of the HIV Inpatient Care unit at University Hospitals of Cleveland. She is also Associate Professor of Medicine in the Division of Infectious Diseases and HIV Medicine at Case Western Reserve University School of Medicine. She is Board certified in Internal Medicine and Infectious Diseases.

Her research interests are in antiretroviral therapy including salvage therapy and the complications of antiretroviral therapy. She has over 20 years of experience in caring for the disenfranchised population with chronic illness through her position at University Hospitals of Cleveland and engaging them to participate in research. She is extensively published in the field of antiretroviral therapy and HIV.

She has been a standing, voting member of the Antimicrobial Advisory Committee since 2016 and has attended numerous Advisory Committee (AC) meetings. Dr. Gripshover's combined research background, clinical experience with HIV and experience with complex AC meetings will be invaluable to the discussion regarding the clinical trial data submitted for Descovy for HIV PrEP indication.

A key topic of discussion at this advisory committee meeting will be the applicant's strategy to support approval of the PrEP indication for Descovy specifically in women and adolescent girls. In this supplement, the applicant proposes a PrEP indication for Descovy (FTC/TAF) to be consistent with that approved for Truvada (emtricitabine (FTC)/tenofovir disoproxil fumarate (TDF)); i.e., to reduce the risk of HIV infection in at-risk adults and adolescents. To support the indication, a single, randomized, double-blind, active-controlled, non-inferiority trial (DISCOVER) was conducted in adult men having sex with men (MSM) and trans-gender women comparing the safety and efficacy of Descovy to approved Truvada; this trial demonstrated noninferiority of Descovy to Truvada in reducing the risk of HIV-1 acquisition in a population of high-risk MSM.

The effectiveness of Descovy as PrEP, however, has not been clinically evaluated in women or adolescents. While extrapolation of efficacy from the DISCOVER trial can support a PrEP indication in adolescent MSM, the applicant proposes to rely on a bridging strategy to support the indication in women and adolescent girls. Dr. Gripshover's extensive background in clinical trials and her expertise in infectious diseases, with a focus on HIV, are essential for this meeting.

The particular matter is not sensitive.

This topic is not considered to be sensitive as the FDA Division with responsibility 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 given that the newsworthy and controversial issues of PrEP were fully addressed 7 years ago at the time of the initial approval of Truvada and PrEP has now been widely embraced as part of a public health strategy to reduce

new HIV infections. In addition, Descovy is already approved for the indication of HIV treatment.

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

HIV/Acquired Immunodeficiency Syndrome (AIDS) is a global pandemic. As of 2017, approximately 36.9 million people were infected with HIV globally. More than 1.1 million Americans are currently living with HIV. An estimated 40,000 Americans are being newly diagnosed each year. The U.S. government spends $20 billion in annual direct health expenditures for HIV prevention and care. There is currently no effective cure that exists for HIV but strict adherence to anti-retroviral therapy can dramatically slow the disease's progress and prevent secondary infections and complications, prolonging life.

In February 2019, the U.S. Department of Health and Human Services (HHS) proposed a new initiative to address the nation's HIV epidemic (Ending the HIV Epidemic: A Plan for America) with the goals of reducing the number of incident HIV infections in the U.S. by 75% within 5 years, and by 90% within 10 years. A key component of this strategic initiative is to prevent at-risk individuals from acquiring HIV infection, including the use of PrEP. HHS estimates that increasing PrEP use among high-risk groups could prevent almost 50,000 HIV infections by 2020. If approved for a PrEP indication, Descovy will likely play a direct role in this HHS initiative as the second potential product for this indication. In the interest of public health, it is important that the agency have available the unique expertise that Dr. Gripshover 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. Gripshover's expertise in this matter.

Dr. Gripshover's expertise in the area of HIV treatment and prevention and specific expertise in the care of HIV-infected disenfranchised populations including women of color make her essential for the success of the upcoming meeting. Women of color in the U.S. are at a higher risk of HIV-infection. One of the key voting issues is whether data in men can be extrapolated to women using drug exposure bridging data from a bioavailability study. If not, the committee will need to discuss what kind of trial in women could be conducted as a post-marketing commitment. In addition, Dr. Gripshover is the only female physician on the committee currently providing direct patient care to HIV-infected patients. For this meeting, the determination of the efficacy of Descovy in women is one of the critical issues for discussion and the primary reason for presenting this application to an advisory committee. It is imperative that there is adequate representation of women on this committee, with HIV expertise, to make important decisions about HIV prevention in this population.

Accordingly, I recommend that you grant a waiver for Dr. Barbara Gripshover, a standing voting member of the Antimicrobial Drugs Advisory Committee, 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: 2019.07.22 08:15:30 -04'00'

July 22, 2019

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

Date