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

DATE: October 10, 2023

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

FROM: Prabhakara Atreya, Ph.D.
Director
Division of Scientific Advisors and Consultants
Center for Biologics Evaluation and Research

Name of Advisory Committee Meeting Voting member: **Wendy London, Ph.D.**

Committee: Cellular Tissue, and Gene Therapies Advisory Committee (CTGTAC)

Meeting date: October 31, 2023

Description of the Particular Matter to Which the Waiver Applies:

On October 31, 2023, the CTGTAC will meet to discuss and make recommendations on biologics license application (BLA) 125787 from Vertex Pharmaceuticals, Inc. for exagamglogene autotemcel (exa-cel). The applicant has requested an indication for the treatment of sickle cell disease in patients 12 years and older with recurrent vaso-occlusive crises

Dr. Wendy London, a Special Government Employee, has been invited to participate in the October 31, 2023, CTGTAC meeting as a voting member to provide her outstanding statistical expertise as applied to basic and clinical research on the treatment of sickle cell disease in patients 12 years and older with recurrent vaso-occlusive crises. The CTGTAC evaluates available data relating to the safety, effectiveness, and appropriate use of human cells, human tissues, gene transfer therapies and xenotransplantation products which are intended for transplantation, implantation, infusion and transfer in the prevention and treatment of a broad spectrum of human diseases and in the reconstruction, repair, or replacement of tissues for various conditions. The Committee also considers the quality and relevance of FDA's research program which provides scientific support for the regulation of these products and makes appropriate recommendations to the Commissioner of Food and Drugs.

Type, Nature, and Magnitude of the Financial Interest(s):

Dr. London disclosed that she serves as the lead biostatistician for the trial: (b) (4) .

(b) (4) provided the (b) (4) for the trial as a part of a license agreement with (b) (4) This was technology developed by (b) (4) and was included in the PCT application # PCT/ (b) (4) There was no funding by (b) (4) for the trial or the protocol. The license agreement was executed on 12/19/2014 and was terminated on 07/11/2022.

Dr. London continues to serve as the study statistician for the trial (b) (4) Her services are being funded by contracts to her institution from National Institutes of Health (NIH)/NHLBI and (b) (4)). The trial accrual is projected to end in (b) (4) , then the last patient will be followed for 2 years. Then another year will be needed for data clean-up, analysis, and manuscript generation. Assuming there is only one manuscript, Dr. London's end date related to this trial is in 2028. All funds from the NIH/NHLBI and (b) (4) go to her institution (BCH), and about (b) (6) of her salary is supported by these funds. However, Dr. London personally does not receive any funding. The amount of funding that goes to BCH depends on the number of patients that are treated at BCH. They will be publishing the results of the trial and Dr. London will be a co-author.

Therefore, Dr. Wendy London has a personal and an imputed interest with one of the affected firms, (b) (4) which is related to the topic/matter before the Committee meeting taking place on October 31, 2023.

Basis for Granting the Waiver:

Dr. London is the lead biostatistician for a phase (b) (4) trial on sickle cell disease, which is also the topic before the upcoming October 31, 2023, CTGTAC meeting. Vertex Pharmaceuticals, Inc. has requested an indication for the treatment of sickle cell disease in patients 12 years and older with recurrent vaso-occlusive crises for its exa-cel product. Dr. London is currently the lead biostatistician for (b) (4) Accordingly, the particular matter before the upcoming CTGTAC meeting on sickle cell disease will have a direct and predictable effect on Dr. London's interest.

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

Dr. London currently serves as an Associate Professor of Pediatrics, Division of Hematology/Oncology at the Boston Children's Hospital (BCH), Harvard Medical School, Harvard University, effective December 12, 2010. Prior to this appointment, Dr. London served as a Research Associate Professor/Biostatistician at the University of Florida, College of Medicine.

Dr. London received her Ph.D. in Biostatistics from Medical College of Virginia, Virginia Commonwealth University in 1997, and her Bachelor of Science degree in Atmospheric Science/Mathematics from Purdue University in 1982.

Sickle Cell Disease (SCD) is an inherited red blood cell disorder. It is marked by defective or abnormal hemoglobin. It inhibits the ability of hemoglobin in red blood cells to carry oxygen to the tissues.

In SCD, the red blood cells become hard and sticky and look like a C-shaped farm tool called a "sickle." These cells stick together and cannot easily move through the blood vessels. This can block small blood vessels and the movement of healthy, normal oxygen-carrying blood. The blockage can cause anemia, pain, acute chest syndrome, spleen problems and stroke. In the United States, the disease mainly affects communities of African ancestry or who identify themselves as African Americans.

Dr. London is uniquely qualified to serve on the Committee as a voting member because she is an accomplished medical scientist/researcher with extensive experience in biostatistics as applied to epidemiology, public health, hematology/oncology research, clinical trials, and also related to SCD.

There is limited expertise available, and it is difficult to locate similarly qualified individuals without a disqualifying financial interest.

Dr. London's strong scientific background in epidemiology, public health, hematology/oncology research and SCD will be critical for the October 31, 2023, CTGTAC discussions. The FDA Division responsible for conducting this meeting has struggled to find a qualified expert in clinical hematology/oncology and SCD, who does not have disqualifying financial interests. In order to ensure a productive committee discussion, we need experts with not only clinical experience but also extensive research experience especially in biostatistics and clinical trials designs. Several candidates have been removed from consideration due to either scheduling conflicts or disqualifying conflicts of interest. At this stage, it would be extremely difficult to find a replacement for Dr. London, given her unique qualifications in epidemiology, public health, hematology/oncology research and SCD.

The particular matter is sensitive.

The meeting topic for this session is considered sensitive and the FDA Review Division with responsibility for these products does expect that the meeting is likely to receive significant

public interest and (non-trade) press interest, as it is the first gene editing BLA and it is for SCD. However, the matter is not considered controversial.

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

As an Associate Professor in the Division of Hematology/Oncology, Dr. London subspecializes in hematology/oncology as well as sickle cell disease. She has published more than 80 articles in peer-reviewed journals and book chapters. These contributions earned her the International Society of Pediatric Oncology (STOP) Award. She has been a member of NIH study sections for more than a decade.

Dr. London is well known and has been recognized as an accomplished scientist/researcher with extensive experience in hematology/oncology as well as sickle cell disease.

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

We believe the strong need for Dr. London's demonstrated expertise and diverse perspective that she can bring to this matter before the Committee greatly outweighs any potential for a conflict of interest.

Accordingly, I recommend that you grant Dr. Wendy London, a voting member of the Cellular, Tissue, and Gene Therapies Advisory Committee (CTGTAC), a waiver from the conflict-of-interest prohibitions of 18 U.S.C. § 208 (b)(3).

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.

/S/ October 16, 2023

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

Date