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

DATE: May 21, 2021

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 Temporary Voting Member: **Milton Packer, M.D., M.P.H.**

Committee: Cardiovascular and Renal Drugs Advisory Committee

Meeting date: July 15, 2021

Description of the Particular Matter to Which the Waiver Applies:

Milton Packer, M.D., M.P.H., is a temporary voting member of the Cardiovascular and Renal Drugs Advisory Committee (CRDAC). 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 cardiovascular and renal disorders and make appropriate recommendations to the Commissioner of Food and Drugs.

The Committee will discuss new drug application (NDA) 213805, for the hypoxia inducible factor prolyl hydroxylase inhibitor, roxadustat tablets, submitted by FibroGen, Inc., for the treatment of anemia due to chronic kidney disease in adult patients not on dialysis and on dialysis. FibroGen and AstraZeneca are collaborating on the development and commercialization of roxadustat for the potential treatment of anemia in China, the United States, and elsewhere. The topic of this meeting is a particular matter involving specific parties.

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

Dr. Packer reported financial interests in (b) (6), and (b) (6), a competing/affected firm. The value of his holdings in (b) (6) is between $0 - $25,000 and the aggregate value of his holdings in (b) (6) and (b) (6) is between $25,000 to $50,000.

Under regulatory exemptions issued by the Office of Government Ethics, an employee may participate in any particular matter involving specific parties in which the disqualifying financial interest arises from the ownership by the employee, his spouse, or minor children of securities: (1) issued by one or more entities affected by the matter (parties to the matter) if the aggregate market value of the holdings does not exceed $15,000 (5 CFR 2640.202(a)), and, (2) issued by one or more entities that are not parties to the matter but that are affected by the matter if the aggregate market value of the holdings in the securities of all affected entities (including securities exempted under paragraph (a)) does not exceed $25,000 (5 CFR 2640.202(b)). Because Dr. Packer's financial interests exceed those amounts, he has a disqualifying financial interest based on the stock holdings in the above-listed companies.

Basis for Granting the Waiver:

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

Dr. Packer is a Distinguished Scholar in Cardiovascular Science at Baylor University Medical Center in Dallas, Texas, and Visiting Professor, Faculty of Medicine, National Heart and Lung Institute, Imperial College in London, United Kingdom. He is the former Distinguished Chair in Cardiology at University of Texas Southwestern Medical Center, the former Chief of the Division of Circulatory Physiology at the Columbia University College of Physicians and Surgeons, and the past director of the Heart Failure Center at the Columbia-Presbyterian Medical Center in New York City. Dr. Packer earned his medical degree from Jefferson Medical College in Philadelphia. He did his residency at Albert Einstein College of Medicine in New York City, and a fellowship in cardiology at Mount Sinai School of Medicine in New York.

Dr. Packer is an internationally recognized clinical investigator who has made many important contributions to the field of cardiovascular disease, both in understanding its mechanisms and defining its rational management. Dr. Packer's work has spanned nearly 40 years and has been strongly supported by numerous investigator-initiated grants from the National Institutes of Health (NIH) and from industry. His research helped establish the cornerstone of the current modern treatments for heart failure. He has been the principal investigator of more than 15 international multicenter trials.

As a leading expert in the pathophysiology and treatment of heart failure, Dr. Packer has made significant contributions to heart failure research and has been instrumental in the introduction of a number of new treatments. The author of more than 500 papers, Dr. Parker has won numerous honors for teaching and has lectured around the world on the treatment of heart failure, having been honored with a number of prestigious named lectureships. He has served or currently serves on the editorial boards of many major medical journals, including Circulation and the European Heart Journal. He has also been elected to a number of societies, including the American Society for Clinical Investigation. He is a member of the Council on Clinical Cardiology at the American Heart Association, and a fellow of the American College of Cardiology. He was a founding member and former President of Heart Failure Society of America. His research on the treatment of heart failure led to him being awarded the Lewis Katz Lifetime Achievement Award in Cardiovascular Research.

The Committee will discuss new drug application (NDA) 213805, for the hypoxia inducible factor prolyl hydroxylase inhibitor, roxadustat tablets, submitted by FibroGen, Inc., for the treatment of anemia due to chronic kidney disease (CKD) in adult patients on dialysis and not on dialysis. The principal risks of roxadustat are cardiovascular in nature, and the deliberations will focus largely on these cardiovascular risks. A productive discussion of these issues will require strong expertise in cardiovascular medicine, from many perspectives. Specifically, it will be important to include an adequate number of cardiologists at this meeting to discuss the associated cardiovascular risks at hand.

Dr. Packer has served as a highly valued member of the Cardiac and Renal Drugs Advisory Committee since 1986, and ably served as its chairman from 1997 to 2001. Through many years and over many Advisory Committee meetings, Dr. Packer has provided important, thoughtful perspectives, demonstrated an uncanny ability to unravel complex issues, and helped to bring about consensus in difficult matters. Given the complexities of the subject matter before the Committee and its cardiovascular focus, his expertise will be valuable. Because of Dr. Packer's vast knowledge, his breadth of experience as a cardiologist, educator and clinical researcher, and his wealth of experience on the CRDAC, his participation in the Committee's discussion will ensure an expansive level of expertise and objectivity required to provide expert advice and recommendations to the Agency.

The particular matter is considered sensitive.

The FDA Division responsible for review of roxadustat does expect the matter coming before the committee to garner public interest as the product at issue is the first in class for the treatment of anemia due to chronic kidney disease. It is the first oral agent for this indication, the commercial market is potentially millions of people who suffer from this disease, and the product has the potential to alter significantly the use of the currently approved products.

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

Anemia is a common complication of chronic kidney disease (CKD), and anemia often worsens as kidney disease progresses. More than 37 million American adults may have CKD, and it is estimated that more than 1 out of every 7 people with kidney disease has anemia. When the kidneys are damaged, they produce less erythropoietin (EPO), a hormone that signals the bone marrow to make red blood cells. With less EPO, the body makes fewer red blood cells, and less oxygen is delivered to organs and tissues.

Anemia related to CKD typically develops slowly and may cause few or no symptoms initially. Symptoms of advanced anemia may include fatigue or tiredness, shortness of breath, weakness, body aches, chest pain, dizziness, fainting, fast or irregular heartbeat, headaches, sleep problems, and trouble concentrating.

Many patients with CKD receive an erythropoiesis stimulating agent (ESA) for the treatment of

anemia. Although these agents have been shown to increase hemoglobin, i.e., improve anemia, they have not been shown to improve patients' symptoms. Moreover, they carry a number of important risks. When they are used in an overly aggressive way to increase hemoglobin, they can cause heart attacks, strokes, and even death. They also tend to increase blood pressure and can lead to seizures. The ESAs that are currently available must be given by injection.

Roxadustat is a new molecular entity that is intended to treat the anemia of CKD; however, its mechanism of action is somewhat different than that of the ESAs, and the drug is administered orally, which would offer a convenience advantage for some patients. Roxadustat has a number of important safety issues, and these will be discussed at the Advisory Committee meeting. The Committee will be asked to weigh the benefits and risks of roxadustat in the context of a drug that could be used in place of an ESA and would be administered orally instead of by injection.

In the interest of public health, it is important that the Agency has available the unique expertise that Dr. Packer will provide for the discussion of the particular matters before the Committee.

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

Dr. Packer is highly respected internationally for his deep insights and broad perspectives, and he has been highly valued as a member of the Cardiac and Renal Drugs Advisory Committee. Few cardiologists possess his broad perspectives, clinical acumen, public health focus, and wealth of experience in clinical trial design and analysis, and few individuals would be able to disentangle the difficult issues raised by this NDA. For these reasons, the expertise of Dr. Packer will be invaluable to a robust and productive discussion on the application coming before the Committee.

Accordingly, I recommend that you grant Dr. Milton Packer, a temporary voting member of the Cardiovascular and Renal 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: 2021.06.15 13:28:56 -04'00'

June 15, 2021

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

Date