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

DATE: August 23, 2017

TO: Rachel E. Sherman, M.D., M.P.H.
Principal Deputy Commissioner
Office of the Commissioner, Food and Drug Administration

THROUGH: Jeffrey Anderson, MS, RAC
Director (Acting), Advisory Committee Oversight and Management Staff
Office of Special Medical Programs

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

Name of Advisory Committee Member: Ronald Bukowski, M.D.

Committee: Oncologic Drugs Advisory Committee

Meeting date: September 19, 2017

Description of the Particular Matter to Which the Waiver Applies:

Dr. Bukowski is serving as 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.

The committee will discuss supplemental new drug application (sNDA) 021938/033 Sutent (sunitinib malate) oral capsules, submitted by C.P. Pharmaceuticals International C.V., represented by Pfizer, Inc. (authorized U.S. agent). The proposed indication (use) for this product is for the adjuvant treatment of adult patients at high risk of recurrent renal cell carcinoma (RCC) following nephrectomy. The topic of this meeting is a particular matter involving specific parties.

Type, Nature, and Magnitude of the Financial Interest:

Dr. Bukowski is Chair of the Data Monitoring Committee (DMC) for a Bristol Myers Squibb (BMS) sponsored study titled, A Phase 3 Randomized Study Comparing Nivolumab and Ipilimumab Combination versus Placebo in Participants with Localized Renal Cell Carcinoma Who Underwent Radical or Partial Nephrectomy and Who Are at High Risk of Relapse (NCT03138512). Dr. Bukowski has received $0 - $5,000 per year for his role. Nivolumab and ipilimumab are competing products being studied in a similar indication as the indication for the product coming before the committee.

In addition, Dr. Bukowski reported financial interests in four health sector mutual funds: Putnam Global Healthcare Fund Class A (PHSTX), Janus Henderson Global Life Sciences Fund Class A (JFNAX), Fidelity Advisor Biotechnology Fund Class A (FBTAX), and Franklin Biotechnology Discovery Fund Class A (FBDIX). The aggregate value of his holdings in these four funds is between $100,001 - $300,000. At the writing of this waiver, these funds contained assets in competing/affected firms, which represented only a small percentage of the total assets in each fund, approximately (b) (4) respectively.

Basis for Granting the Waiver:

It is important to note that the DMC for which Dr. Bukowski serves as Chair, is independent of the study itself and Dr. Bukowski does not have any other involvement with this study. The role of a DMC is to review safety and effectiveness data related to the conduct of the study. The DMC reviews the data to ensure participant safety and the integrity of the study. If concerns arise through the review of data, the DMC can issue recommendations to the sponsor.

Further, as noted above, Dr. Bukowski's healthcare sector mutual fund holdings include minimal assets, at the writing of this waiver, in potentially competing/affected firms.

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

Ronald Bukowski, M.D., is a temporary voting member of the ODAC. He received his medical degree from the Northwestern University and completed residency training at the Cleveland Clinic. He completed his fellowship in hematology and oncology at the Cleveland Clinic. He is board certified in internal medicine, medical oncology and hematology and has been in practice for over 40 years. Dr. Bukowski is currently the President of Bukowski Consulting, LLC. He is also a Consultant for CSSI Life Sciences in Baltimore and an Emeritus Professor of Medicine at Cleveland Clinic Lerner College of Medicine, Case Western Reserve University. He is a Member of the Board of Directors for the Kidney Cancer Association and the Scott Hamilton CARES Foundation. He is a lifelong researcher with interests in genitourinary (GU) oncology, biologic response modifiers, biology of renal cell carcinoma, and new drug development and investigation. He has lectured nationally and internationally on many topics related to G-U oncology and has authored more than 1,000 peer-reviewed articles.

Sunitinib (Sutent) is a targeted therapy acting as a protein-tyrosine kinase receptor inhibitor. The committee will examine the results of two clinical trials titled, *A Clinical Trial Comparing Efficacy And Safety Of Sunitinib Versus Placebo For The Treatment Of Patients At High Risk Of Recurrent Renal Cell Cancer (S-TRAC)* and *Sunitinib Malate or Sorafenib Tosylate in Treating Patients With Kidney Cancer That Was Removed By Surgery (ASSURE)*, and discuss the acceptability of the toxicity profile in the adjuvant setting. Because Dr. Bukowski is a lifelong researcher specializing in biologic response modifiers, the biology of renal cell carcinoma, new drug development and investigation, and has in-depth knowledge in cancer trials, his participation in the committee's discussions will ensure a broad diversity of expertise and objectivity required to provide adept advice and recommendations to the Agency regarding Pfizer's sunitinib oral capsule in the adjuvant setting.

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

Dr. Bukowski is one of six renal oncologists, at the writing of this waiver, scheduled to attend this advisory committee meeting. Eight other renal oncologists were invited but are unable to attend due to several reasons including, conflicts of interest, schedule conflicts, and incomplete paperwork.

Sunitinib is coming before the committee for a new treatment paradigm for renal cell cancer, i.e., adjuvant treatment of renal carcinoma. The ODAC will be asked to discuss the clinical relevance of the primary endpoint of disease free survival. Because this would potentially be the first approval for adjuvant therapy in RCC, it is imperative to render advice from several renal cancer experts. Multiple experts with diverse renal cancer backgrounds are needed in order to have a productive and collaborative scientific discussion of the current available data.

The particular matter is not sensitive.

This topic is not considered to be sensitive as the Division does not expect that the meeting is likely to receive significant public interest, (non-trade) press interest, or congressional interest nor is it considered highly controversial.

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

Renal cell carcinoma is the most common type of kidney cancer in adults. Currently, cancers of the kidney and renal pelvis are the eighth most common cancer in the US accounting for 3.8% of new cases. The American Cancer Society estimates that in 2017 there will be 63,990 cases of malignant tumors of the kidney diagnosed, with 14,400 deaths. Due to the increasing number of patients with stages I–III RCC, optimizing the management of early-stage RCC is one of the key priorities in the oncological clinical practice. Survival after relapse remains poor, and metastatic RCC continues to have the highest mortality rate of the genitourinary cancers. In addition to surgical management, relapse risk reduction through adjuvant therapy is a very important goal in patients with intermediate and high-risk early-stage RCC.

The dollar value of the potential gain or loss that may result from participation in the particular matter is small

As noted above, Dr. Bukowski receives $0 - $5,000 per year for his role as Chair of the DMC.

At the writing of this waiver, the aggregate value of the four healthcare sector fund holdings is between $100,001 - $300,000, which includes a small percentage of the total assets in potentially competing/affected firms in each fund.

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

In the interest of public health, it is critical for the Agency to review products for adjuvant treatment of adult patients at high risk of recurrent RCC following nephrectomy, including discussions of the acceptability of the toxicity profile. Dr. Bukowski's expertise in renal cell carcinoma makes him a critical participant at this meeting, and will add to the diversity of opinions needed at this meeting.

Accordingly, I recommend that you grant Dr. Ronald Bukowski, 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), to participate in the Oncologic Drugs Advisory Committee meeting on September 19, 2017.

Certification:

__X__ The individual may participate as a temporary voting member at the meeting, 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/ 9/1/2017

Rachel E. Sherman, M.D. Date
Deputy Commissioner for Medical Products and Tobacco
Office of the Commissioner, Food and Drug Administration