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

DATE: March 22, 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 Meeting Temporary Voting Member: **Colin Weekes, M.D., Ph.D.**

Committee: Oncologic Drugs Advisory Committee

Meeting date: April 29, 2021

Description of the Particular Matter to Which the Waiver Applies:

Colin Weekes, M.D., Ph.D., is a temporary voting member of the Oncologic Drugs Advisory Committee (ODAC). ODAC's function is to review and evaluate available data concerning the safety and effectiveness of marketed and investigational human drug products for the use in the treatment of cancer and make appropriate recommendations to the Commissioner of Food and Drugs.

On April 29th, the committee will hear updates on (1) BLA 125514/S-024, trade name Keytruda (pembrolizumab), submitted by Merck Sharp & Dohme Corp. and indicated for the treatment of patients with recurrent locally advanced or metastatic gastric or gastroesophageal junction adenocarcinoma whose tumors express PD-L1 [Combined Positive Score (CPS) ≥1] as determined by an FDA-approved test, with disease progression on or after two or more prior lines of therapy including fluoropyrimidine and platinum-containing chemotherapy and if appropriate, HER2/neu-targeted therapy; (2) BLA 125514/S-042, trade name Keytruda (pembrolizumab), submitted by Merck Sharp & Dohme Corp. and indicated for the treatment of patients with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib; and (3) BLA 125554/S-041, trade name Opdivo (nivolumab), submitted by Bristol Myers Squibb Company and indicated as a single agent for the treatment of patients with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib.

These applications were approved under 21 CFR 601.40 (subpart E, accelerated approval regulations) with confirmatory trial(s) that have not verified clinical benefit. These updates will provide information on: (1) the status and results of confirmatory clinical studies for a given indication; and (2) any ongoing and planned trials. Confirmatory studies are post-marketing studies to verify and describe the clinical benefit of a drug after it receives accelerated approval. Based on the updates provided, the committee will have a general discussion focused on next steps for each product including whether the indications should remain on the market while additional trial(s) are conducted. These topics are particular matters involving specific parties.

Type, Nature, and Magnitude of the Financial Interests:

Dr. Weekes' employing institution, Massachusetts General Hospital, is participating in a study titled *A Phase 2 Study of Cabiralizumab Administered In Combination With Nivolumab With and Without Chemotherapy In Patients With Advanced Pancreatic Cancer (NCT03336216)*, sponsored by Bristol Myers Squibb. The study aims to provide clinical efficacy data on dual CSF1R and PD1 targeted therapy in patients with advanced metastatic pancreas adenocarcinoma. Dr. Weekes is the site Principal Investigator (PI) for this large phase II/III trial that began on December 1, 2017, with an anticipated end date in 2023. Massachusetts General Hospital is the Harvard Cancer Center primary site for the study. The study is no longer enrolling patients and is in the surveillance stage to meet survival endpoints. Dr. Weekes advised that he is not actively managing any patients at this time.

Massachusetts General Hospital anticipates receiving between $50,000 and $100,000 per year, for this study. Dr. Weekes does not receive salary support or personal remuneration from these funds.

In addition, Massachusetts General Hospital is in negotiations with (b) (4) for a study titled (b) (4) This study will be funded by (b) (4) and it is anticipated that (b) (4) will provide drug support. This program project (P01) grant is comprised of (b) (4) projects based on clinical trials, and one project uses (b) (4) as one of the study drugs for treatment of (b) (4). This is a multi-institution P01 to be conducted at Massachusetts General Hospital and (b) (4). Dr. Weekes is co-PI of the overall program project grant and is co-leader of a project within the grant and co-leader of a program core. The negotiated period of the program project is from (b) (4)

Massachusetts General Hospital anticipates receiving between (b) (4) per year from (b) (4) for this study. The study drug, (b) (4), is anticipated to be provided by (b) (4) Dr. Weekes anticipates receiving between $ (b) (4) per year in salary support from this funding.

Basis for Granting the Waiver:

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

Dr. Weekes is an Associate Professor of Medicine in Hematology/Oncology at Harvard Medical School and an Associate Physician in the Department of Medicine, Division of Hematology/Oncology at Massachusetts General Hospital. In addition, he is the Director of Medical Oncology Research for Pancreatic Cancer and the Director of Cancer Center Grand Rounds at Massachusetts General Hospital. His clinical interests include pancreatic cancer, hepatocellular carcinoma, colon and rectal cancer, cholangiocarcinoma, clinical trials of new agents, and clinical trials in the development of novel drug combinations.

Dr. Weekes earned his Doctor of Medicine degree and Doctor of Philosophy degree in Cell Biology at the University of Nebraska Medical Center. He then completed a residency in Internal Medicine at The University of Alabama at Birmingham, followed by a fellowship in Oncology at Johns Hopkins Hospital. He is an ad hoc reviewer of 20 publications, most of which are related to Oncology and Research. He also has 18 published articles in various oncology-related journals.

It is critically important to include Dr. Weekes in the upcoming ODAC meeting, given his experience in medical oncology and in particular, gastrointestinal cancers including hepatocellular carcinoma and gastric or gastroesophageal adenocarcinoma. His background in clinical trials research will be valuable to the discussion of the gastric or gastroesophageal adenocarcinoma and hepatocellular carcinoma topics.

The particular matter is sensitive.

The matter coming before the committee will 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.

Dr. Colin Weekes' expertise in this particular matter is necessary in the interest of public health.

Cancers that start in glandular cells are called adenocarcinomas. According to the American Cancer Society, about 90% to 95% of the stomach cancers are adenocarcinomas. A gastroesophageal junction adenocarcinoma is a cancer that begins in glandular cells located near the gastroesophageal junction. This cancer has also been referred to as esophagogastric junction adenocarcinoma. According to NCI, there were about 27,600 new cases of stomach cancer and about 18,440 new cases of esophageal cancer in the U.S. in 2020. The estimated number of deaths in 2020 were 11,010 for stomach cancer and 16,170 for esophageal cancer.

Treatment of gastric or gastroesophageal junction adenocarcinoma depends on the stage and may include surgery, chemotherapy, targeted drug therapy, immunotherapy, and radiation therapy. These treatment options depend on the extent of the cancer. Tipiridine/trifluracil combination product and pembrolizumab are FDA-approved treatments for disease progression on or after

two or more prior lines of therapy including fluoropyrimidine and platinum-containing chemotherapy and if appropriate, HER2/neu-targeted therapy.

Hepatocellular carcinoma or HCC starts in the liver and is one of the most prevalent cancers in the world. HCC accounts for about 85%-90% of all primary liver cancers. The number of people who develop HCC in the U.S. has risen in the last four decades. There are approximately six new cases of HCC per every 100,000 people in the general population of the U.S. Most patients with HCC have an underlying liver disease such as infection with hepatitis B or C virus, or non-alcoholic fatty liver disease.

Treatment for HCC is either surgical (liver resection or transplantation), nonsurgical (ablation or embolization), or systemic treatments. Systemic treatment includes molecularly targeted therapy and immunotherapy with immune checkpoint inhibitors. Atezolizumab in combination with bevacizumab, sorafenib, or lenvatinib are FDA-approved for first-line therapy for HCC. Regorafenib, ramucirumab, nivolumab, (ipilimumab in combination with nivolumab), cabozantinib and pembrolizumab are approved second-line treatments for HCC.

In the interest of public health, it is important that the Agency has available the unique expertise that Dr. Weekes 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. Colin Weekes' expertise in this matter.

Dr. Weekes is an expert in gastrointestinal cancers and these applications will need multiple discussants with expertise in these cancers. As an example, the treatment of HCC is complex, and involves a careful assessment of both the cancer and the underlying liver function and related abnormalities such as varices or ascites. Both gastric and hepatocellular carcinoma are also undergoing rapid changes with respect to standard of care and gastrointestinal oncology expertise will be necessary to put these applications in perspective. There may be different perspectives with respect to treatment of these tumors and the discussion should not be directed by a single individual.

Accordingly, I recommend that you grant Dr. Colin Weekes, 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):_____

_____ Denied – The individual may not participate.

Russell Fortney -S Digitally signed by Russell Fortney -S
Date: 2021.04.02 08:33:09 -04'00'

April, 2, 2021

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

Date