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

DATE: May 19, 2020

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 Member Name: **Richard Gorlick, M.D.**

Committee: Pediatric Oncology Subcommittee of the Oncologic Drugs Advisory Committee (PedsODAC)

Meeting date: June 17, 2020

Description of the Particular Matter to Which the Waiver Applies:

The Best Pharmaceuticals for Children Act of 2002 (BPCA) expressly charged that the PedsODAC, a subcommittee of the Oncologic Drugs Advisory Committee (ODAC), shall: (A) evaluate and, to the extent practicable, prioritize new and emerging therapeutic alternatives available to treat pediatric cancer; (B) provide recommendations and guidance to help ensure that children with cancer have timely access to the most promising new cancer therapies; and (C) advise on ways to improve consistency in the availability of new therapeutic agents. (Pub. Law 107-109, Section 15(a)(1)).

The role of the Pediatric Subcommittee is legislated by BPCA. Notably, the PedsODAC does not provide advice to FDA with respect to approval of any specific product for any specific pediatric cancer indication. The Office of Oncologic Diseases in the Center for Drug Evaluation and Research brings issues related to approval of any product for a cancer indication, including any pediatric cancer indication, to the ODAC, not the PedsODAC.

The cancers of adults and children are very different and although the outcome for children with cancer has improved dramatically during the past several decades, cancer remains the leading cause of death from disease in children. Those children who survive often do so at an enormous cost associated with the long term and late effects of existing therapy, which are frequently debilitating.

Thus, there is an urgent need for new drugs and biologic products for the treatment of childhood cancer.

Pediatric cancer drug development is complex and very different from drug development in other disease areas and is largely dependent upon cancer drug discovery and development in adults. Early consideration of new promising agents for study in children is critical to timely development of new treatments.

On June 17, 2020, during the PedsODAC meeting, information will be presented regarding pediatric development plans for two products that are in development for an adult oncology indication. The subcommittee will consider and discuss issues relating to the development of each product for pediatric use and provide guidance to facilitate the formulation of Written Requests for pediatric studies, if appropriate.

Because pediatric cancer care is very closely integrated with pediatric cancer clinical research and new drug development, all children with cancer are treated at academic centers, and nearly all of these centers are members of a National Cancer Institute-funded clinical trials network. As a result, the experts are invariably researchers at these institutions. The expertise that FDA seeks cannot be found outside of this context. The insights the Agency seeks can be provided only by learned researchers with extensive experience with studies of investigational agents in the pediatric age group. These investigators generally do not derive substantial personal financial benefit from industry grants and contracts to their institutions, and their institutions receive the industry funds necessary to offset institutional costs for patient care and other institutional clinical research costs.

Dr. Gorlick is serving as a temporary voting member of the PedsODAC and has been invited to participate in the June 17, 2020, PedsODAC meeting. The product under consideration, relevant to this waiver is, SP 2577, application presentation by Salarius Pharmaceuticals, Inc. There is currently one study of SP 2577 in pediatrics in Ewing sarcoma. This topic is a particular matter involving specific parties.

Type, Nature, and Magnitude of the Financial Interest:

Dr. Gorlick is Head of the Division of Pediatrics, Director of the Pediatric Sarcoma Research Laboratory Program, and Mosbacher Pediatrics Chair at the University of Texas MD Anderson Cancer Center. He has not identified any personal financial interests that are likely to be affected by the particular matter to be discussed by the subcommittee. However, he has identified a financial interest of his employer, which is imputed to him under the federal conflict of interest statute, 18 U.S.C. § 208, that can be affected by the particular matter that is the subject of the subcommittee meeting.

MD Anderson is participating in a clinical study titled: Phase 1 Trial of the LSD1 Inhibitor SP-2577 in Patients With Relapsed or Refractory Ewing Sarcoma [NCT03600649], sponsored by Salarius Pharmaceuticals. This phase 1 study is an open-label, non-randomized dose escalation study of SP-2577. The population being studied includes patients aged 12 years and older. MD Anderson is one of 8 sites participating in the study nationally. The study is funded by the

National Pediatric Cancer Foundation (NPCF), a 501(c)(3) organization, as part of the NPCF's "Sunshine Project Clinical Trials Initiative." The study drug is provided by Salarius Pharmaceuticals and there is no established dollar value for the drug.

The total funding for this study to MD Anderson is anticipated between $ (b) (4) per year. This study began in June 2018, is still recruiting patients, and is targeted to end December 2021. Dr. Gorlick does not receive any salary support or personal remuneration for his role as Site Investigator.

Basis for Granting the Waiver:

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

Unlike AC meetings focused on a product and indication, this meeting will be a scientific collaboration on the currently available data to gain information that could inform the formulation of a Written Request, if appropriate. Significantly, the advisory committee members will not recommend approval or disapproval of any particular product. Such recommendations would be grossly premature and simply could not be made at this early stage in product development. The majority of oncology products studied in the phase 1 setting in children do not proceed through development to submission and approval of a new drug application. Very few chemical entities in these early stages of evaluation and development ever proceed to a marketing application. Moreover, the role of the PedsODAC is not to provide any advice to the Agency with respect to approval of any specific product for any specific pediatric cancer indication.

Dr. Gorlick earned his medical degree from State University of New York Downstate Medical Center and completed his residency at Columbia Presbyterian Medical Center. He completed a fellowship in pediatric hematology and oncology at Memorial Sloan Kettering Cancer Center. He is board certified in Pediatrics and Pediatric Hematology-Oncology. In addition to the positions outlined above, Dr. Gorlick was previously the Division Chief of Pediatric Hematology Oncology and Vice Chairman of Pediatrics at The Children's Hospital at Montefiore, and Professor of Pediatrics and Molecular Pharmacology at The Albert Einstein College of Medicine. For more than two decades, his research and clinical efforts have focused on sarcomas, which are tumors that grow in connective tissues including the bones, muscles, tendons and cartilage. Dr. Gorlick also focuses on targeted therapies, new drugs for childhood cancers, and understanding the mechanisms behind the development and progression of osteosarcoma, the most common form of childhood bone cancer.

Dr. Gorlick is extensively published in leading medical journals with the vast majority of these manuscripts focused on sarcomas. He has served as an active member, advisor, and leader in a number of organizations, including the National Cancer Institute's Pediatric Preclinical Testing Consortium, the Sarcoma Alliance for Research through Collaboration Consortium and the Children's Oncology Group (COG). With COG, Dr. Gorlick has held a number of roles, including his current position as Chairman of the Bone Tumor Disease

Committee. His early involvement in COG led to his laboratory establishing a bone-tumor bank, which is now a national resource and home to the world's largest osteosarcoma tissue bank. Dr. Gorlick is an internationally recognized expert in pediatric bone sarcomas and directs one of the largest childhood bone tumor programs in the country. His experience and expertise are essential to the discussion of these meetings.

The particular matter is not sensitive.

The meeting topic is not considered to be sensitive and the FDA 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. Moreover, the discussion at the meeting will be only one source of information for the Agency's plans related to the submission of a Written Request for evaluating these drugs in children.

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

On June 17, 2020, the subcommittee will meet to discuss SP 2577, which is in early stage development for treatment of Ewing sarcoma. Ewing sarcoma is a rare bone tumor that occurs most often in adolescents; it is a very rare cancer in adults. The National Institutes of Health reports that Ewing sarcoma accounts for about 1.5 percent of all childhood cancers, and it is the second most common type of bone tumor in children. The median age of patients with Ewing sarcoma is 15 years, and more than 50% of patients are adolescents. Approximately 200-250 children and adolescents in the United States are diagnosed with a tumor in the Ewing family of tumors each year. Treatment options for Ewing sarcoma include chemotherapy, surgery, radiation therapy and high-dose chemotherapy and stem cell transplant. Patients experience side effects of treatment for Ewing sarcoma including severe delayed late effects from radiation therapy, such as bone growth retardation and secondary cancers. The five-year survival rate is 76% for children younger than 15 and 60% for adolescents aged 15 to 19. About 30% of patients have a recurrence within the first five years. The same chemotherapy drugs that were used during initial treatment cannot be used again due to toxicity concerns. As a result, physicians must seek alternatives to treatment. The potential use of this product in Ewing sarcoma is in the context of recurrent/relapsed disease, for which no curative therapies currently exist, therefore, the need for new therapies represents a particularly dire, unmet clinical need. In the interest of public health, it is critical that FDA have available the unique expertise that Dr. Gorlick will provide the committee.

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

The PedsODAC meeting is meant to elicit discussion of the data currently available. The advisory committee members will not recommend approval or disapproval of the

products under discussion. To meet statutory responsibilities to evaluate and prioritize new and emerging therapeutic alternatives to treat pediatric cancer and to provide recommendations and guidance to help ensure that children with cancer have timely access to the most promising new cancer therapies, this meeting of the PedsODAC requires the participation of experts with a wide and deep knowledge of pediatric oncology and product development. Such experts typically develop their knowledge through their work at centers of excellence for the treatment of pediatric cancers, the very sites where investigational drugs are studied. This is particularly true for experts in rare pediatric cancers; patients frequently must travel to be treated by a physician with experience in a particular rare cancer.

As multiple possible childhood tumor indications are being considered in the discussions of SP-2577, the perspective of multiple pediatric oncologists with specific sub-specialty expertise is required. Dr. Gorlick is an internationally recognized expert in pediatric bone sarcomas and directs one of the largest childhood bone tumor programs in the country. His experience and expertise are essential to the discussion of these meetings. Dr. Gorlick has the unique combination of expertise in the clinical management of bone tumors and new cancer drug discovery and development. His input is essential for any Agency decision-making related to the evaluation of this product in children. Given his extensive experience and background in the specific areas needed for this meeting, any potential for a conflict of interest is significantly outweighed by the need for Dr. Gorlick's expertise on this panel.

Accordingly, I recommend that you grant Dr. Richard Gorlick, a temporary voting member of the Pediatric Oncology Subcommittee of the Oncology 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):

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_____ Denied – The individual may not participate.

Russell Fortney -S Digitally signed by Russell Fortney -S
Date: 2020.06.01 16:43:07 -04'00'

June 1, 2020

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

Date