



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

DATE: May 22, 2019

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

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

Name of Advisory Committee Meeting Member: **Theodore Laetsch, M.D.**

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

Meeting date: June 20, 2019

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 Oncology 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 Hematology and Oncology Products 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 20, 2019, during the afternoon session of the PedsODAC meeting, information will be presented to gauge investigator interest in exploring potential pediatric development plans for ONC201, sponsored by Oncoceutics, Inc., which is in early stages of development for adult and pediatric cancer indications. In addition to the adult indications, ONC201 is currently in early phase pediatric studies for diffuse intrinsic pontine glioma (DIPG). The subcommittee will consider and discuss issues concerning potential diseases to be studied, including but not limited to DIPG, patient populations to be included, and possible study designs in the development of this product for pediatric use. The discussion will also provide information to the Agency pertinent to 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 in pediatric cancer 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, which use the industry funds to offset institutional costs for patient care and other institutional clinical research costs.

Dr. Theodore Laetsch is serving as a temporary voting member of the PedsODAC. He has been invited to participate in the afternoon session of the June 20, 2019, PedsODAC meeting. The product under consideration relevant to this waiver is ONC201, which, if approved, will be manufactured by Frontida Biopharm for Oncoceutics Inc., which will be presenting before the subcommittee. The topic of this meeting session is a particular matter involving specific parties.

Type, Nature, and Magnitude of the Financial Interests:

Dr. Laetsch is an Associate Professor, Pediatric Hematology/Oncology, and Co-Director of the Tumor Microenvironment and Immune Therapy Theme in the Experimental Therapeutics Program (ETP), University of Texas Southwestern (UTSW). He has identified a financial interest of his employer that is imputed to him under the federal conflict of interest statute, 18 U.S.C. § 208, and that can be affected by the particular matter that is the subject of the subcommittee meeting.

UTSW will participate in a clinical study titled A Phase 1 Study To Evaluate Safety and

Pharmacokinetics of Palbociclib (Ibrance) In Combination With Irinotecan And Temozolomide In Pediatric Patients With Recurrent Or Refractory Solid Tumors (NCT03709680). The focus of this study is for a range of relapsed or refractory solid tumors, including central nervous system tumors. The study does not specifically target, but could include, subjects with DIPG, which is an indication for which ONC201 is in early phase pediatric studies. UTSW is anticipated to enroll a total of two patients for this study, which is opened through the Children's Oncology Group (COG) under a contract between COG and Pfizer.

COG is a National Cancer Institute (NCI) funded clinical trials network of more than 230 pediatric institutions throughout the United States, Canada, and other foreign sites. The financial support to UTSW comes from a subcontract with COG. The total funding from the COG to UTSW is anticipated to be \$0 - \$50,000 per year. This study has not yet started but it is targeted to start in 2019; anticipated duration is 5 years dependent on patient accrual. Dr. Laetsch's employer intends to dedicate a small percentage of these funds to offset Dr. Laetsch's salary; however, his salary remains the same regardless of funds received by UTSW for his role as the study chair.

Basis for Granting the Waiver:

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

At the advisory committee (AC) meeting, information will be presented to gauge investigator interest in exploring potential pediatric development plans for ONC201 in early development for adult and pediatric cancer indications. Unlike AC meetings focused on a product and indication, this meeting will be a scientific collaboration on the current available data from the adult and pediatric DIPG studies to gain information that could inform the formulation of a written request and whether there are any other pediatric cancers in which there is an unmet clinical need that this product might fulfill.

Dr. Laetsch is a faculty member in the Department of Pediatrics at the University of Texas Southwestern Medical Center. He also leads the ETP in the Gill Center for Cancer and Blood Disorders at Children's Medical Center of Dallas. Dr. Laetsch received his undergraduate degree in Agricultural and Biosystems Engineering from the University of Arizona and his medical degree in 2005 from the University of California, San Francisco. Dr. Laetsch completed his residency at the University of Colorado/Children's Hospital Colorado, where he also served as chief resident. He completed his fellowship training and an instructorship at the Children's Hospital of Philadelphia (CHOP), where he conducted translational laboratory research focused on mechanisms to restore apoptotic signaling in neuroblastoma. In 2013, he joined the faculty at UT Southwestern.

Dr. Laetsch conducts both clinical and laboratory-based research testing potential novel therapeutics in high-risk pediatric solid tumors with a goal of "bridging the gap" between laboratory research and early phase clinical trials. In the laboratory, he has focused on signaling pathway inhibitors and novel drug delivery mechanisms in sarcomas, and the use of beta-lapachone in atypical teratoid rhabdoid tumors. As the leader of the ETP, Dr. Laetsch serves as the Principal Investigator (PI) of several phase 1 and phase 2 studies of new agents for children

with relapsed or refractory cancer and serves as the institutional Therapeutic Advances in Childhood Leukemia and Lymphoma (TACL) PI. Dr. Laetsch has a strong interest in the use of tumor molecular profiling to guide therapy. In addition to these research activities, Dr. Laetsch continues to see children with cancer in the clinic at Children's Medical Center. Brain tumors represent a major unmet clinical need in children. Therefore, his participation in the PedsODAC meeting is critical as he has significant experience in this subject matter.

*Multiple experts are needed.*

There is a need for multiple pediatric oncology subspecialties to discuss the rare cancers that this product may be a good match for. There were seven additional pediatric oncologists that were invited to this meeting but were unable to attend due to conflicts of interest and scheduling conflicts.

*The particular matter is not sensitive.*

The meeting topic is not considered sensitive and the FDA Division with responsibility for this product does not expect that the meeting is likely to receive significant public interest, (non-trade) press interest, nor is it considered highly controversial.

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

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 20, 2019, the subcommittee will meet to discuss ONC201 in early development for adult and pediatric cancer indications to assess its relevance for possible development for use in one or more pediatric cancers. One particularly critical unmet clinical need in pediatric and adolescent cancer is the optimal management of brain tumors, DIPG. Diffuse intrinsic pontine gliomas account for 10 percent of all childhood central nervous system tumors. Approximately 300 children in the U.S. are diagnosed with DIPG each year. No effective drugs have been developed for this disease. Even drugs in early development have failed to yield robust efficacy signals. In the interest of public health, it is critical that the agency have the unique expertise that Dr. Laetsch will provide for the discussion as the committee considers the potential benefit in studying this product in children.

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

The PedsODAC meeting is meant to elicit discussion of the data currently available studies, and whether there is any pediatric cancer type for which there is an unmet clinical need that this product might address. Significantly, the advisory committee members will not recommend approval or disapproval of this product. Such recommendations would be grossly premature and simply could not be made at this early stage in product development. Dr. Laetsch's participation at this advisory committee meeting session is essential as he has experience in the early clinical evaluation of molecularly targeted drugs in children which is the focus of the meeting. Furthermore, Dr. Laetsch has a leadership role in the NCI-COG Pediatric MATCH (Molecular Analysis for Therapy Choice Trial) study which focuses on targeted drugs therapies. Given his background in the specific areas needed for this meeting, any potential for a conflict of interest is significantly outweighed by the need for Dr. Laetsch's expertise on this panel.

Accordingly, I recommend that you grant Dr. Theodore Laetsch, a temporary voting member of the Pediatric Oncology Subcommittee 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 June 20, 2019, afternoon session of the subcommittee.

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.

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

May 30, 2019  
Date