FOOD AND DRUG ADMINISTRATION (FDA)
Center for Drug Evaluation and Research (CDER)

Meeting of the Pediatric Subcommittee of the Oncologic Drugs Advisory Committee (pedsODAC)
FDA White Oak Campus, Building 31 Conference Center, the Great Room (Rm. 1503)
10903 New Hampshire Avenue, Silver Spring, Maryland
June 29, 2016

DRAFT QUESTIONS

Morning Session, Topic 1: LOXO-101, Loxo Oncology, Inc.

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1. **DISCUSSION:** Please consider the ongoing pediatric study and provide an opinion regarding the overall study design.

2. **DISCUSSION:** Please consider the toxicity profile of LOXO-101 in adults and discuss whether there are unique safety concerns related to potential short and long-term toxicities from the use of LOXO-101 in pediatric patients. Also, discuss potential ways to mitigate these risks.

3. **DISCUSSION:** Please consider the necessity for an international collaborative study given the very rare cancers for which LOXO-101 may prove relevant.

4. **DISCUSSION:** Please comment on the adequacy of the current pediatric formulation and any plans for evaluation of the pediatric formulation.

5. **DISCUSSION:** Please comment on the clinical availability and utility of NTRK fusion identification in current pediatric oncology practice.

DRAFT QUESTIONS (cont.)

Morning Session, Topic 2: entrectinib, Ignyta, Inc.

1. **DISCUSSION:** Please consider whether NTRK1 and 2 and ALK overexpression provides an appropriate biological rationale for the proposed target tumors. Please address the role of ROS1 inhibition in pediatric tumors.
2. **DISCUSSION:** Please comment on the clinical availability and feasibility of *NTRK1/2/3* and *ROS1* evaluation in current pediatric oncology practice.
3. **DISCUSSION:** Please consider the ongoing pediatric study and discuss the overall study design.
4. **DISCUSSION:** Please consider the toxicity profile of entrectinib in adults and discuss whether there are unique safety concerns related to potential short and long-term toxicities from the use of entrectinib in pediatric patients. Also discuss potential ways to mitigate these risks.
5. **DISCUSSION:** Please address whether evaluation of this drug in pediatrics would require international collaboration.
6. **DISCUSSION:** Please comment on the adequacy of the current pediatric formulation and any future plans for the pediatric formulation.

DRAFT QUESTIONS (cont.)

Afternoon Session: DIPG

1. **DISCUSSION:** Consider changes over time in the adverse event rate associated with surgical biopsy of the brainstem to obtain DIPG tissue for biology studies and more recently to select molecularly targeted drugs for therapy.

2. **DISCUSSION:** Consider the benefit:risk assessment of surgical biopsy of DIPG for molecular analysis of both newly diagnosed and progressive (on current therapy) tumors for the purpose of selecting an appropriate molecular phenotype-directed targeted therapeutic agent for patients with this disease.

3. **DISCUSSION:** Please discuss whether the benefit:risk assessment is favorable.