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

Pediatric Oncology Subcommittee of the Oncologic Drugs Advisory Committee (pedsODAC) Meeting
June 17-18, 2020

DRAFT QUESTIONS

Day 1, Topic 1: SP-2577, Salarius Pharmaceuticals, Inc.

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1. **DISCUSSION:** Given that SP-2577 targets LSD1 and studies have demonstrated increased expression of LSD1 in other tumor types in addition to Ewing sarcoma, address other pediatric solid tumors and hematologic malignancies in which there is a biologic rationale for evaluation of its activity.

2. **DISCUSSION:** Given the non-clinical results of synergistic effect and increased antitumor activity of SP-2577 in combination with chemotherapeutic and epigenetic agents, and immune checkpoint inhibitors, consider its use as a combination treatment in pediatric tumors.

3. **DISCUSSION:** Please discuss the use of SP-2577 in patients <12 years of age given the range of tumor types that appear to be susceptible to the anti-tumor effects of SP-2577 based on non-clinical data.

DRAFT QUESTIONS (cont.)

Day 1, Topic 2: Marizomib (MRZ), Celgene International II Sàrl

1. **DISCUSSION:** Please discuss thoughts on trial design and rational combination partners for MRZ investigation in pediatric patients with high grade glioma.

2. **DISCUSSION:** Considering the CNS toxicity profile associated with MRZ in the adult clinical experience to date, discuss possible risk mitigation provisions that could be included in pediatric clinical trials. Comment on any developmental or age-related assessments and management guidelines that could potentially mitigate risk in younger children who may experience CNS adverse reactions that have been common and occasionally dose-limiting in the adult MRZ clinical experience.

3. **DISCUSSION:** Are there non-CNS pediatric cancers that should be considered for evaluation in the MRZ development program?

DRAFT QUESTIONS (cont.)

Day 2, Topic 1: CD30.CAR-T, Tessa Therapeutics

1. **DISCUSSION:** Pediatric age groups include:

   a. Neonates (birth to age less than one month)
   b. Infants (ages one month to less than two years)
   c. Children (ages two years to less than 12 years)
   d. Adolescents (ages 12 years to less than 17 years)

   Please discuss which pediatric age groups are candidates for study with CD30.CAR-T and which can reasonably be excluded.

2. **DISCUSSION:** Please discuss the variability of the preparatory lymphodepletion therapies and their potential applicability to the pediatric population. Please discuss CD30-positive malignancies other than classical Hodgkin lymphoma which could be studied in pediatric patients.

3. **DISCUSSION:** Please comment on manufacturing issues related to autologous CAR T cell products in pediatric populations, including collection of leukapheresis material and pediatric sites' ability to contribute to or complete the manufacturing process.

DRAFT QUESTIONS (cont.)

Day 2, Topic 2: SNDX-5613, Syndax Pharmaceuticals, Inc.

1. **DISCUSSION:** Please consider the adequacy of evidence of activity and lack of serious acute toxicity, given the timeline of the development of SNDX-5613 in adults to date, to support development of this product in children.

2. **DISCUSSION:** Please consider the adequacy of the currently available PK data in children from the compassionate use experience in attempts to model exposure:response after the adult RP2D has been defined and demonstrated to be active. Discuss alternative strategies for efficient RP2D definition in children. Discuss the effect of CYP-3A inhibition on possible activity.

3. **DISCUSSION:** Given the adult experience to date and the requirement for extended continuous dosing to achieve a response, consider how the activity of SNDX-5613 might be assessed in a single agent setting in a disease characterized by an aggressive clinical course at relapse. Given the adult experience with added cytoreductive therapy consider a possible development strategy using a relapse therapy backbone that would allow isolation of the effect of SNDX-5613 in MLLr ALL, AML, and AMPL.

Key: Mixed lineage leukemia (MLL), acute lymphobastic leukemia (ALL), acute myeloid leukemia (AML), and acute mixed phenotype leukemia (AMPL)