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

Pediatric Subcommittee of the Oncologic Drugs Advisory Committee (pedsODAC) Meeting
FDA White Oak Campus, Building 31 Conference Center, the Great Room (Rm. 1503)
10903 New Hampshire Avenue, Silver Spring, Maryland
June 21 - 22, 2017

DRAFT QUESTIONS

Day 1, Topic 1: APX005M, Apexigen, Inc.

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1. **DISCUSSION:** Please comment on the unique safety concerns that arise from the use of immune activator agents, in particular with CD40 agonistic antibodies in pediatric patients, and on methods to mitigate these safety issues in clinical trials.

2. **DISCUSSION:** Please consider the way in which CD40-agonistic antibodies can be used synergistically with current pediatric cancer treatment modalities, including cancer vaccines, given their immunomodulatory effects.

3. **DISCUSSION:** Please consider the importance of evaluating the correlation of tumor cell CD40 expression and antigen burden in various pediatric solid tumors with the activity of CD40-agonistic antibodies, and whether the combined use of CD40-agonistic antibodies with immune checkpoint inhibitors may prove to be useful in tumors with lower CD40 expression and/or antigen burden.

DRAFT QUESTIONS (cont.)

Day 1, Topic 2: PM01183 (Lurbinectedin), Pharma Mar USA, Inc.

1. **DISCUSSION:** Please discuss the preliminary pediatric development plan, including the tumor types proposed for further study. In addition, please include considerations regarding a targeted approach based on bio- or other markers versus one that is broader in scope.

2. **DISCUSSION**: Given the mechanism of action of lurbinectedin, please consider other pediatric tumor types for which there is a biologic rationale for evaluation of its activity. Address any differences in biology between adult and pediatric hematologic malignancies that might support its evaluation in pediatric diseases for which its activity in adults has been limited.

3. **DISCUSSION:** Please discuss the impact of low CNS and testicular penetration of lurbinectedin in tissue distribution studies on potential areas of study in the pediatric population.

4. **DISCUSSION:** Please address any potential safety concerns unique to the pediatric population, including consideration as to whether any pediatric age groups should be excluded from study.

DRAFT QUESTIONS (cont.)

Day 1, Topic 3: ASP2215 (Gilteritinib), Astellas Pharma Global Development

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1. **DISCUSSION:** Please discuss the preliminary pediatric development plan, including the indications proposed for further study and, in particular, the proposal to study gilteritinib only in children with Acute Myeloid Leukemia and FLT3 Internal Tandem Duplication.

2. **DISCUSSION:** Please discuss any potential safety concerns unique to the pediatric population, including toxicities that may be seen when gilteritinib is added to multi-agent chemotherapy. Consider whether any pediatric age groups should be excluded from study and mechanisms to minimize risk on the proposed clinical trials.

3. **DISCUSSION:** Please comment on the sponsor's proposal to include one year of maintenance therapy with gilteritinib monotherapy after Intensification II or hematopoietic stem cell transplantation in Study 0604.