

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

*Pediatric Oncology Subcommittee of the Oncologic Drugs Advisory Committee (pedsODAC) Meeting*  
FDA White Oak Campus, Building 31, The Great Room (Rm. 1503)  
White Oak Conference Center, Silver Spring, Maryland  
December 4, 2012

**QUESTIONS**

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**Session 1: TRAMETINIB**  
**Applicant: GLAXOSMITHKLINE, LLC**

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1. **DISCUSSION:** Please provide an opinion regarding the following aspects of the Proposed Pediatric Study Request (PPSR):
  - a. the adequacy of existing preclinical data to support studies in pediatric patients
  - b. the proposed patient subpopulations to be studied
  - c. safety monitoring that should be incorporated in the proposed studies, in light of the ophthalmologic and cardiac toxicities observed in adults receiving trametinib.
2. **DISCUSSION:** Is there a need for additional studies not included in the PPSR to elucidate the role of trametinib in the treatment of pediatric cancers (e.g. studies in combination in a front line setting)?
3. **DISCUSSION:** Does the panel agree that pediatric melanoma is sufficiently similar to melanoma occurring in adults to use adult data to extrapolate the efficacy of trametinib in pediatric patients with V600-mutant metastatic melanoma?

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**Session 2: TH-302**

**Applicant: THRESHOLD PHARMACEUTICALS, INC.**

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1. **DISCUSSION:** Does the panel consider TH-302 a viable drug candidate for further study in pediatric patients?
  - a. Please comment on specific diseases where TH-302 would be of interest to the investigator community.
  
2. **DISCUSSION:** Does the panel consider TH-302 a viable drug candidate for further study in pediatric and young adult patients with sarcomas?
  - a. Please comment on potential study designs.
  - b. Please comment on potential combination regimens with other agents.

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**Session 3: VOLASERTIB (BI 6727)**

**Applicant: BOEHRINGER INGELHEIM PHARMACEUTICALS, INC.**

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1. **DISCUSSION:** Please comment on whether the strength of the company's efficacy data in the subset of adult patients who are not considered appropriate candidates for intensive acute myeloid leukemia induction therapy warrant evaluation of volasertib in the pediatric population. If so, please comment on the proposed plan to evaluate toxicity and single agent efficacy in the relapsed/refractory setting.
2. **DISCUSSION:** Please comment as to whether any specific pediatric age group (including neonates) should be excluded from any possible pediatric development plan.

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**Session 4: BLINATUMOMAB (MT 103)**  
**Applicant: AMGEN INC.**

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1. **DISCUSSION:** Given the observed activity in adult patients and the association between the incidence of toxicities and degree of tumor burden, what phase of therapy for childhood acute lymphoblastic leukemia (ALL) (given current multi-agent treatment strategies), i.e. Induction or Consolidation or Delayed Intensification, would be most appropriate for the evaluation of blinatumomab in either the relapsed/refractory or front-line setting?
2. **DISCUSSION:** What special considerations related to potential central nervous system (CNS) toxicities are required given the CNS-directed treatment component of standard regimens for childhood ALL?
3. **DISCUSSION:** Given the re-induction treatment objective in relapsed/refractory ALL to achieve a complete response in order to proceed with allogeneic hematopoietic cell transplantation and the prognostic importance of post-induction/pre-transplant minimal residual disease, what endpoint(s) might be considered in designing a trial to evaluate the isolated effect of blinatumomab in the relapsed/refractory ALL setting?
4. **DISCUSISON:** A recurring challenge in the evaluation of new drugs for children with cancer with respect to requirements for regulatory approval is determining the isolated contribution to clinical benefit of a drug under investigation. Can the Subcommittee provide some scenarios as to how a study(ies) might be designed to achieve this objective in both newly diagnosed and relapsed ALL?