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

Endocrinologic and Metabolic Drugs Advisory Committee (EMDAC) Meeting
FDA White Oak Campus, Building 31 Conference Center, the Great Room (Rm. 1503)
10903 New Hampshire Avenue, Silver Spring, Maryland
January 17, 2019

QUESTIONS

1. **DISCUSSION**: Discuss the benefits claimed by the applicant, e.g. glycemic control, effects on body weight and risk for hypoglycemia, for patients with type 1 diabetes. Comment on the strength of the statistical evidence and clinical meaningfulness of each of these claimed benefits.

2. **DISCUSSION:** Discuss your level of concern about the observed risk of diabetic ketoacidosis (DKA) in adult patients in the sotagliflozin clinical studies and DKA risk associated with sotagliflozin use in a real-world setting.

3. **DISCUSSION**: Comment on any relevant differences in efficacy and/or safety observed between the two proposed doses of sotagliflozin (200 mg and 400 mg). In your discussion please consider the clinical pharmacology data as well as clinical trial data, i.e. improvement in glycemic control and risk for DKA.

4. **DISCUSSION**: Discuss the overall benefit risk profile of sotagliflozin for patients with type 1 diabetes. What specific benefits and risks did you consider; what was your approach and rationale for how they were weighed against each other? Specifically comment on the composite endpoint used by the applicant (HbA1c<7% with no episodes of severe hypoglycemia or diabetic ketoacidosis) to represent net benefit. If you would recommend an alternative strategy, please explain your rationale.

5. **VOTE:** Do the available data suggest that the benefits outweigh the risks and support approval of sotagliflozin, administered orally once daily, as an adjunct to insulin to improve glycemic control in adults with type 1 diabetes mellitus?

    a. If yes, comment on whether you recommend any labeling restrictions, whether any additional studies should be required after approval, and comment on whether your vote indicates support for both proposed doses of sotagliflozin (200 mg and 400 mg).

    b. If no, please describe your rationale and what further studies you believe the applicant should conduct to establish a favorable benefit risk profile to support approval.