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
November 14, 2019

DRAFT QUESTIONS

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1. **DISCUSSION:** Please discuss your interpretation of the efficacy results from the REDUCE-IT Trial, including the following:

    a. Overall strengths and limitations of the data, including the use of a single trial to support a first-in-class cardiovascular outcomes indication and robustness of the results
    b. Confidence in the trial outcomes when considering the mineral oil placebo
    c. Magnitude/clinical relevance of the observed treatment effect
    d. Components of the primary composite endpoint or secondary endpoints, including the robustness of the data to support an indication for CV death

2. **DISCUSSION:** Please discuss your level of concern about the new safety findings (increased risk of atrial fibrillation/atrial flutter and bleedings events) from the REDUCE-IT trial and whether labeling can reasonably manage these risks.

3. **DISCUSSION:** The applicant has proposed an indication for cardiovascular risk reduction in adult patients with triglyceride levels greater than 135 mg/dL and additional risk factors for cardiovascular disease (CVD), without regard for age, diabetes status, or adequacy of low-density lipoprotein (LDL-C) control. Please discuss the population – beyond the subset of patients with established CVD – for whom you believe the data from REDUCE-IT provide evidence of cardiovascular risk benefit, addressing the following factors:
    - Age
    - Diagnosis of diabetes
    - Additional risk factors for CVD
    - Plasma LDL-C concentration
    - Plasma triglyceride concentration
    - Intensity of statin therapy
    - Any other factor you believe is important

4. **VOTE**: Has the applicant provided sufficient evidence of efficacy and safety to support the approval of Vascepa for an indication to reduce the risk of cardiovascular events?

    a. If yes, provide your recommendations regarding the indicated population and components of the primary endpoint to include in labeling.

    b. If no, provide your rationale and comment on what additional data would be needed to support approval.