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

Cardiovascular and Renal Drugs Advisory Committee (CRDAC) Meeting
July 15, 2020

DRAFT QUESTIONS

---

1. **DISCUSSION**: Although FDA prospectively agreed to "HRS reversal" as the primary endpoint in CONFIRM, FDA also noted that the primary endpoint captured treatment effects on a laboratory parameter (serum creatinine) and, as such, FDA considered the endpoint to be a surrogate endpoint (as opposed to a clinical outcome). Acknowledging the challenges of designing a trial to assess effects on clinically significant outcomes in hepatorenal syndrome Type 1 (HRS-1), FDA expressed the view that, along with success on the primary endpoint, FDA expected to observe favorable trends in clinical outcomes thought to be important in the treatment of HRS-1.

   Discuss whether the trial findings provide reassurance that terlipressin's effect on verified HRS reversal is accompanied by treatment effects on clinical outcomes thought to be important in HRS-1, such as renal replacement therapy-free survival, post-transplant outcomes, and length of intensive care unit stay.

2. **DISCUSSION**: Discuss the safety findings in CONFIRM, including the serious adverse events of respiratory failure and sepsis.

   a) What are the serious risks of terlipressin?

   b) Do the available data indicate that the serious risks of terlipressin can be adequately mitigated, and, if so, how (e.g., by appropriate patient selection, monitoring)?

3. **VOTE**: Do you recommend approval of terlipressin for the treatment of HRS-1?

DRAFT