

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

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

**QUESTIONS**

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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?