Figure 1. Mode of action of seralutinib in reversing pathologic remodeling

Figure 2. Impact of inhaled seralutinib on hemodynamic parameters and disease biomarkers in the S54168a rat model

Figure 3. Effect of seralutinib on pulmonary hemodynamic parameters in response to 6MWT

Figure 4. Primary and secondary efficacy end points for Phase 2 study of Seralutinib in PAH

Figure 5. Preclinical studies of Seralutinib

Phase 1 Studies

- Phase 1a – Randomized, placebo-controlled, double-blind, two-part single ascending dose study (18 mg to 75 mg) and multiple ascending dose study (18 mg to 90 mg, BID, 7 doses) in healthy volunteers (N=69)

- Summary of results:
  - Seralutinib was rapidly absorbed into and cleared from systemic circulation
  - Exposure increased in a dose-proportional manner; minimal accumulation in plasma was observed
  - Seralutinib was well tolerated at doses up to 90 mg BID

- Phase 1b – A study of seralutinib administered for 14 days in PAH subjects who have been completed, inclusive of target engagement and biomarker assessments; an OLE study is ongoing

Preclinical Studies

- Seralutinib inhibited proliferation of human pulmonary arterial smooth muscle cells (HPASMCs) in vitro with an IC_{50} approximately 10-fold lower than imatinib (data shown as mean ± SEM)

- Seralutinib treatment led to significant reduction in right ventricular systolic pressure, data shown as mean ± SEM (n=4–8), reduction in pulmonary arterial blood volume based on image reconstruction from high resolution CT scans

- Seralutinib was rapidly absorbed into and cleared from systemic circulation

- Exposure increased in a dose-proportional manner; minimal accumulation in plasma was observed

- Seralutinib was well tolerated at doses up to 90 mg BID

- Phase 1b – A study of seralutinib administered for 14 days in PAH subjects who have been completed, inclusive of target engagement and biomarker assessments; an OLE study is ongoing

Summary

- Seralutinib is a unique, inhaled, small-molecule kinase inhibitor that targets PDGFR α/β, CSF1R, and c-KIT, and modulates BMPR2

- The inhaled route of administration for seralutinib targets the disease pulmonary arteries at doses predicted to be locally effective while limiting systemic exposure which may reduce the risk of adverse events

- A Phase 2 trial (TREORRY; NCT04456998) in subjects with WHO Group 1 PAH is currently recruiting

References

1. Yamashita et al. PASSE, 2018; 137:362-76
2. Chen et al. BMC Genomics, 2016; 17:761

Acknowledgements

The authors gratefully acknowledge the contribution of Mike Kennedy for ADME data, and Bryan Clemons and Eduardo Garcia for PD data.

Presented at the ISHLT Virtual Meeting, April 24, 2021