A Phase 1B, Multi-Center, Randomized, Placebo-Controlled Trial of Inhaled Seralutinib in Subjects With WHO Group 1 Pulmonary Arterial Hypertension (PAH)


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BACKGROUND

• PDGFR, CSF1R, c-KIT and BMPR2 play a central role in cellular overgrowth in the lung vasculature and the development of PAH1,2,3

Seralutinib (formerly known as GB002) is a small-molecule kinase inhibitor that inhibits vasculature and the development of PAH1,2,3

Inhaled seralutinib inhibition Decrease/

Seralutinib Decrease/

PDGF Frozen

CSF1

PDGFR

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METHODS

STUDY DESIGN

Phase Ib, multi-center, double-blind, randomized, placebo-controlled study (NCT03926793)

ELIGIBLE SUBJECTS

Diagnosis of WHO Group 1 PH, Functional Class II-IV, baseline 6MWT > 100 m, receiving PAH treatment

RESULTS

8 subjects enrolled and completed the 3-week study

8 received seralutinib

4 received placebo

45

90

Subjects were randomized (3:1)

Inhaled seralutinib 45 mg twice daily (BID)

Increasing to 90 mg BID on day 8 at PI discretion

Subjects who completed the 2-week treatment period were eligible to participate in a 24-week open-label extension study

CONCLUSIONS

• Seralutinib is a new inhaled therapy that targets important pathways in PAH, including inhibition of PDGFR, CSF1R, c-KIT, and modulation of BMPR2

This is the first clinical experience with seralutinib in PAH: doses up to 90 mg BID were generally well tolerated with mild headache and mild-moderate cough being the most common AEs

• The PK profile of seralutinib was consistent with low systemic exposure characteristic of an inhaled product

• A target engagement assay in whole blood showed that seralutinib blocked CSF1R activation with a time-course that was consistent with the systemic PK profile

SAFETY

• Mild headache and mild-moderate cough were the most common adverse events (AEs)

• No serious AEs were reported, and no AEs resulted in dose reduction, interruption, or discontinuation of seralutinib

PHARMACOKINETIC (PK) ASSESSMENTS

• The PK profile of inhaled seralutinib was dose-proportional and characterized by low systemic exposure and rapid clearance

• A target engagement assay in whole blood showed that seralutinib blocked CSF1R activation with a time-course consistent with the systemic PK profile

REFERENCES


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