

# TRIAL IN PROGRESS: PROSERA, A PHASE 3 STUDY OF THE EFFICACY AND SAFETY OF SERALUTINIB IN ADULTS WITH PULMONARY ARTERIAL HYPERTENSION (PAH)



V Simposio Latinoamericano Hipertensión Pulmonar en Niños y Adolescentes  
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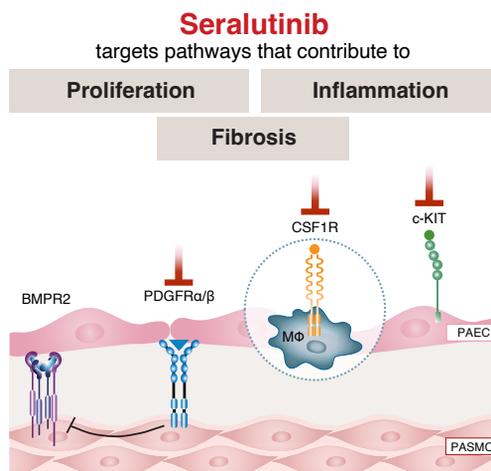
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## BACKGROUND

- PDGFR $\alpha/\beta$ , CSF1R, and c-KIT kinase pathways drive inflammation, proliferation, and fibrosis that contribute to pulmonary vascular remodeling in PAH<sup>1</sup> (Figure)
- Seralutinib is a potent tyrosine kinase inhibitor (TKI) targeting these pathways
- Seralutinib is the only inhaled TKI intentionally developed as a treatment for PAH and specifically formulated as a dry powder to reach the site of the disease and limit systemic exposure<sup>2</sup>



## The Phase 2 TORREY Study

- Double-blind, randomized, placebo-controlled study of inhaled seralutinib in patients with WHO Group 1 pulmonary hypertension (PAH; NCT04456998)
- TORREY met its primary endpoint, demonstrating a significant reduction in pulmonary vascular resistance (PVR) from baseline to Week 24 (-14.3%;  $p = 0.0310$ ), with favorable tolerability<sup>3</sup>
- Prespecified subgroup analyses showed greater benefit in Functional Class (FC) III patients and patients with REVEAL 2.0 risk score  $\geq 6$
- The reduction in PVR and increase in pulmonary arterial compliance in conjunction with a reduction of NT-proBNP indicates that seralutinib is reducing right ventricular afterload and having a beneficial effect on the right heart

## PROSERA, A PHASE 3 STUDY OF SERALUTINIB IN PAH

- PROSERA is a phase 3, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of inhaled seralutinib in adults (ages 18–75 y) with WHO Group 1 PH (NCT05934526)
- 350 patients are to be enrolled at ~160 investigational sites globally throughout North America, Europe, Latin America, and Asia Pacific (Figure 1)
- Eligible patients will be randomized 1:1 to receive seralutinib 90 mg or placebo twice daily (BID) by dry powder inhalation, in addition to background PAH therapy (Figure 2)

### Key Inclusion Criteria

- Adults  $\geq 18$  and  $\leq 75$  years old
- WHO Group 1 PH
- WHO FC II or III
- PVR  $\geq 400$  dyne $\cdot$ s/cm<sup>5</sup>
- Baseline 6-minute walk distance (6MWD) 150–475 m
- Either REVEAL Lite 2 risk score  $\geq 5$  or NT-proBNP  $\geq 300$  ng/L or PVR  $\geq 800$  dyne $\cdot$ s/cm<sup>5</sup>
- Stable treatment with at least one stable PAH background therapy

### Endpoints

#### Primary

- Change in 6MWD from baseline to Week 24

#### Key Secondary

- Time from 1<sup>st</sup> dose to 1<sup>st</sup> event of clinical worsening
- Proportion of patients who achieve all components of a composite endpoint of clinical improvement at Week 24 in the absence of clinical worsening:
  - Decrease in WHO FC or maintenance of WHO FC II
  - Decrease in NT-proBNP  $\geq 30\%$  or maintenance at  $< 300$  ng/L
  - Increase in 6MWD  $\geq 10\%$  or  $\geq 30$  m
- Change vs baseline in NT-proBNP at Week 24
- Proportion of patients with  $\geq 1$  point decrease in REVEAL Lite 2 risk score vs baseline at Week 24

#### Safety

- Incidence of treatment-emergent adverse events (TEAEs), serious TEAEs, and TEAEs of special interest

#### Exploratory

- Seralutinib plasma concentrations and pharmacodynamic biomarkers measured in blood and plasma samples

Figure 1. Countries with PROSERA study sites.

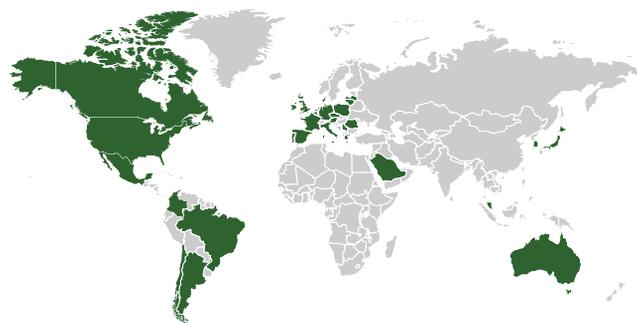
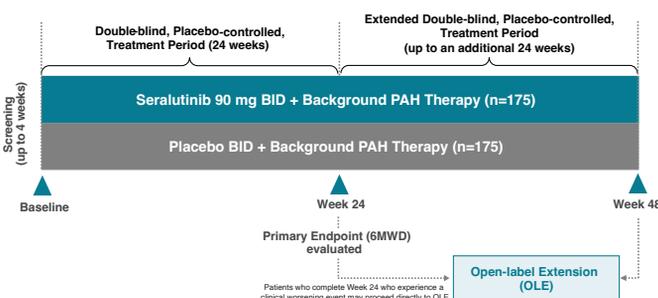


Figure 2. PROSERA study schema.



### Functional Respiratory Imaging (FRI) Substudy

#### Objective:

- To evaluate the effect of seralutinib vs placebo on changes in the pulmonary vasculature as assessed by high-resolution chest computed tomography

#### Endpoints include changes in:

- Pulmonary vasculature blood volume
- Pulmonary blood volume as % total lung volume
- Fibrosis score
- Image-based ventilation-to-perfusion score from baseline to Week 24

## SUMMARY

- Seralutinib is a potent small-molecule TKI that targets PDGFR $\alpha/\beta$ , CSF1R, and c-KIT, and was specifically designed for inhalation to maximize the therapeutic index and limit systemic exposure
- In the phase 2 TORREY study in patients with PAH, seralutinib demonstrated significant reduction in PVR compared to placebo, and significant improvements in NT-proBNP and right heart function, with favorable tolerability
- The phase 3 PROSERA study in patients with WHO Group 1 PH, FC II/III, is now enrolling (NCT05934526)

References: 1 Pullamsetti SS et al. *Int J Mol Sci* 2023;24(16):12653. 2 Galkin A et al. *Eur Respir J* 2022;60(6):2102356. 3 Frantz RP et al. *Lancet Respir Med*. 2024;12(7):523-534.

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