210

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

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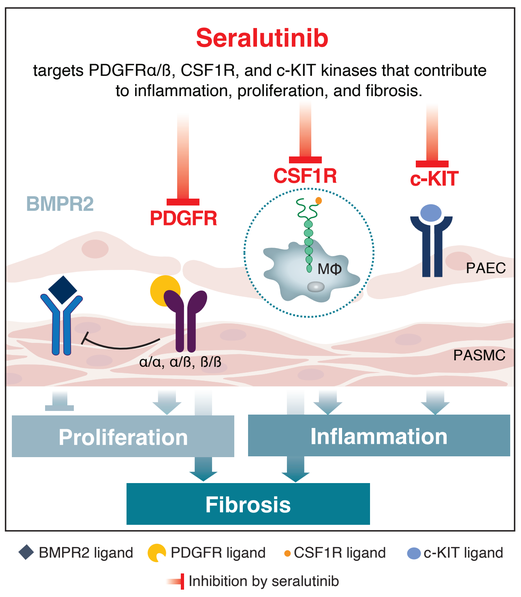
## BACKGROUND

- PDGFRα/β, CSF1R, and c-KIT kinase pathways drive inflammation, proliferation, and fibrosis that contribute to pulmonary vascular remodeling in PAH[1] (**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[2]

BMPR2, bone morphogenetic protein receptor type 2; c-KIT, mast/stem cell growth factor; CSF1R, colony stimulating factor 1 receptor; MΦ, macrophage; PAEC, pulmonary artery endothelial cell; PASMC, pulmonary artery smooth muscle cell; PDGFR, platelet-derived growth factor receptor.




### The Phase 2 TORREY Study

- Double-blind, randomized, placebo-controlled study of inhaled seralutinib in patients with WHO Group 1 Pulmonary Hypertension, PH (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[3]
- Prespecified subgroup analyses showed greater benefit in Functional Class (FC) III patients and patients with REVEAL 2.0 risk score ≥ 6
- The reduction in PVR and increase in pulmonary artery 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 ≥ 18 and ≤ 75 years old
- WHO Group 1 PH
- WHO FC II or III
- PVR ≥ 400 dyne•s/cm$^5$
- Baseline 6MWD 150 – 450 m*
- Either REVEAL Lite 2 risk score ≥ 5 or NT-proBNP ≥ 300 ng/L*
- Stable treatment with one to three standard of care PAH background therapies

*Key enrichment criteria

### Endpoints

#### Primary

- Change in 6-minute walk distance (6MWD) from baseline to Week 24

#### Key Secondary

- Time from 1$^{st}$ dose to 1$^{st}$ 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 ≥ 30% or maintenance at < 300 ng/L
  - Increase in 6MWD ≥ 10% or ≥ 30 m
- Change vs baseline in NT-proBNP at Week 24
- Proportion of patients with ≥ 1 point decrease in REVEAL Lite 2 risk score vs baseline at Week 24

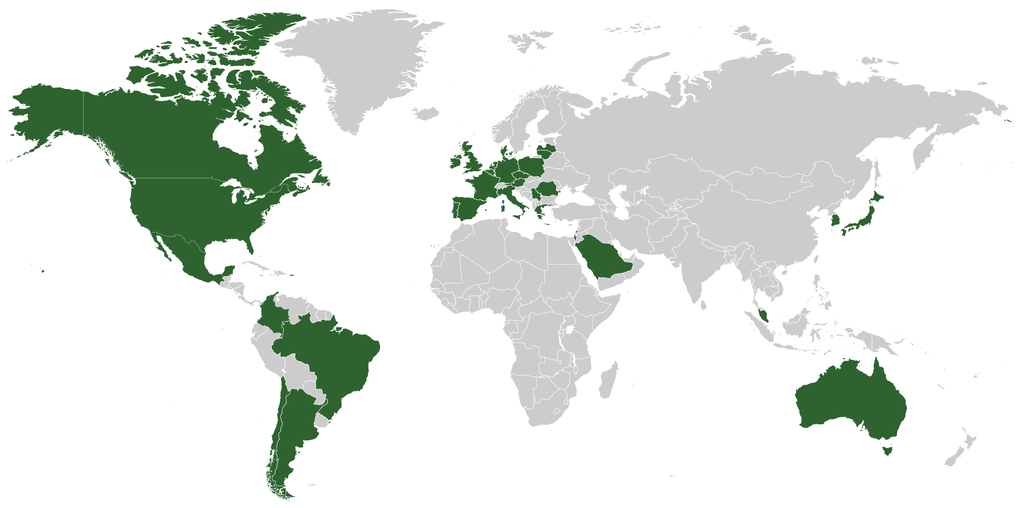
#### Safety

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

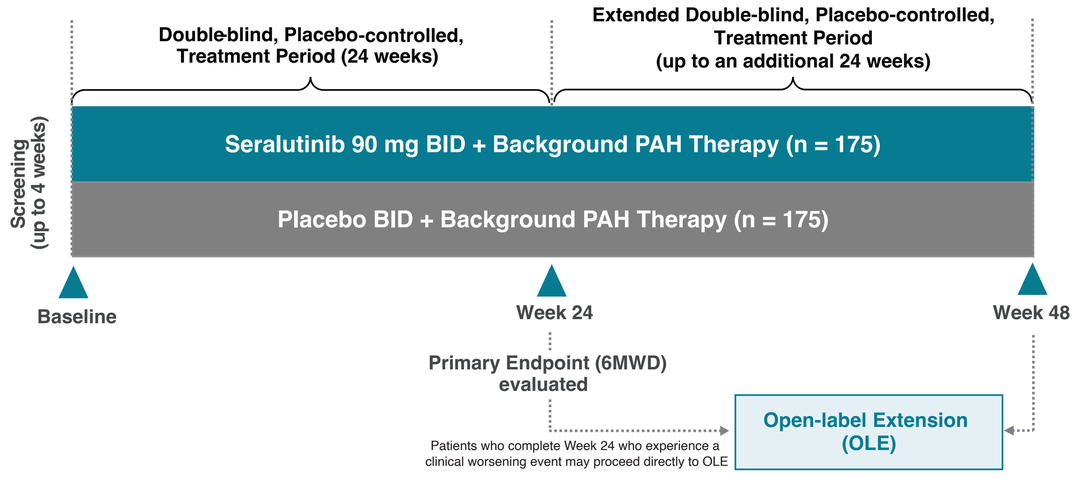
#### Exploratory

- 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 PDGFRα/β, 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. *Am J Respir Crit Care Med* 2023;207:A6726.

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