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# Phase 2 Clinical Study to Evaluate the Efficacy and Safety of Inhaled Seralutinib for the Treatment of World Health Organization Group 1 Pulmonary Arterial Hypertension



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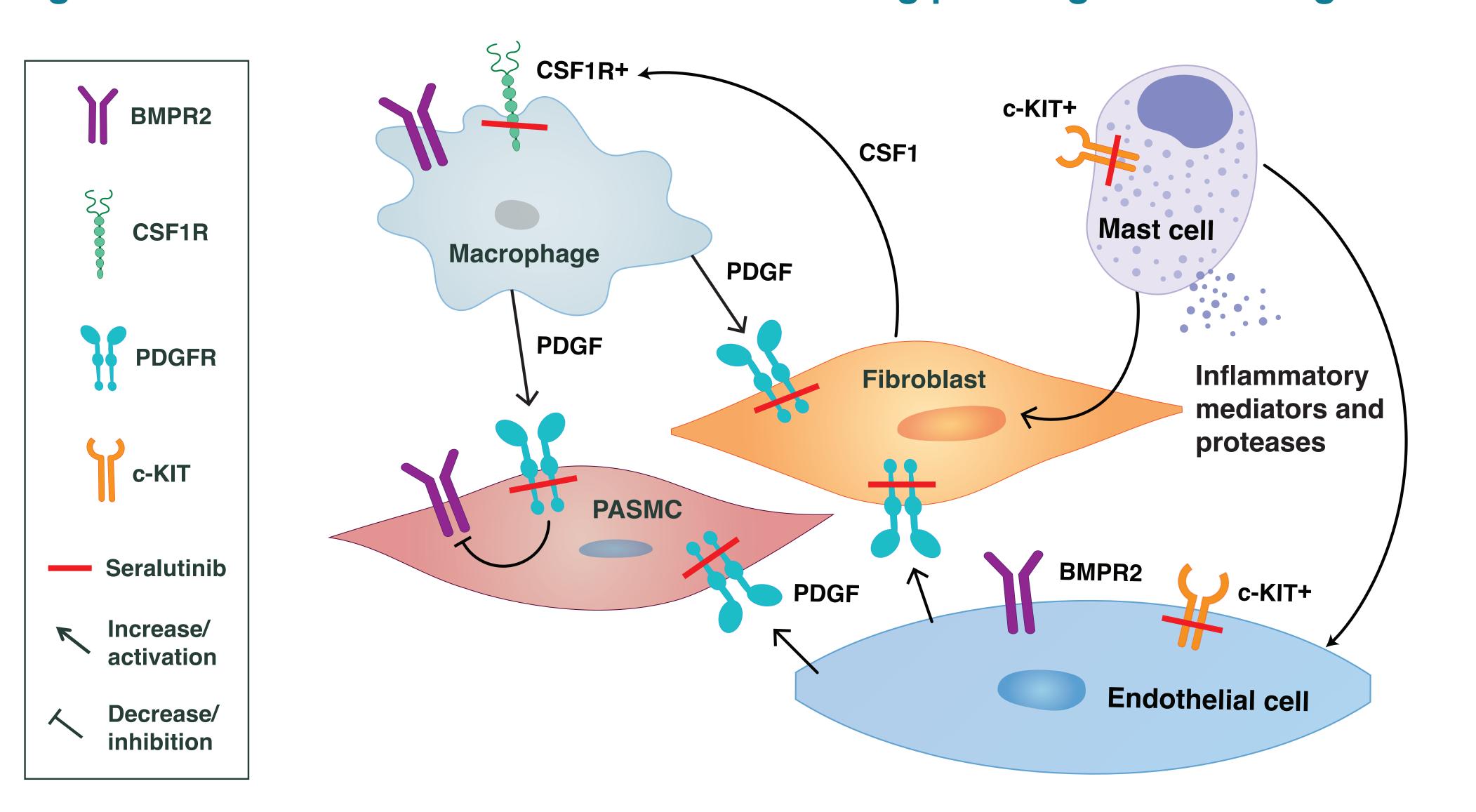
## BACKGROUND

- Abnormal signaling of PDGFRα/β, CSF1R, and c-KIT, and BMPR2 deficiency, drive cellular overgrowth in the lung vasculature and play key roles in PAH progression<sup>1,2,3</sup> (Figure 1)
- Seralutinib is a small-molecule kinase inhibitor that targets these pathways and modulates BMPR2 (Figure 1)
- Seralutinib is administered by dry power inhalation and maximizes the therapeutic index by directly targeting diseased pulmonary arterioles, minimizing systemic exposure, and decreasing the potential off-target adverse effects



**Dry Powder Inhaler** 

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



- Seralutinib was evaluated in two preclinical animal models, monocrotaline/ pneumonectomy<sup>4</sup> and sugen 5416/hypoxia<sup>5</sup>
- these models replicate key features of human PAH, including the development of neointimal proliferative lesions in the pulmonary arterioles and severe pulmonary hypertension
- seralutinib reversed pulmonary vascular remodeling, improved hemodynamic parameters, reduced N-terminal pro-B-type natriuretic peptide (NT-proBNP), and increased lung BMPR2 expression vs controls<sup>5</sup>
- Phase 1 studies in healthy and PAH participants showed that seralutinib at doses up to 90 mg twice daily was well tolerated and achieved higher concentrations in lung tissue vs plasma<sup>6</sup>



• The TORREY study is a randomized, double-blind, placebo-controlled trial (NCT04456998) designed to examine the efficacy and safety of inhaled seralutinib in subjects with PAH over a 24-week course of treatment

### SELECTED INCLUSION CRITERIA

### Diagnosis of symptomatic PAH

- 6MWD ≥ 150 meters and ≤ 550 meters
- WHO FC II or III

**OBJECTIVES** 

**ENDPOINTS** 

 Treatment with standard of care PAH background therapies, including PGIs

**PRIMARY** 

RHC data consistent with the diagnosis of PAH and PVR ≥ 400 dyne·s/cm5

Determine effect of seralutinib on

Change in pulmonary vascular

resistance from Baseline to Week 24

### SELECTED EXCLUSION CRITERIA

- Evidence of chronic thromboembolic disease or acute pulmonary embolism
- WHO Pulmonary Hypertension Group 2-5
- HIV-associated PAH
- History of left-sided heart disease and/or clinically significant cardiac disease
- Inhaled prostanoids
- Use of anticoagulants

**SECONDARY** 

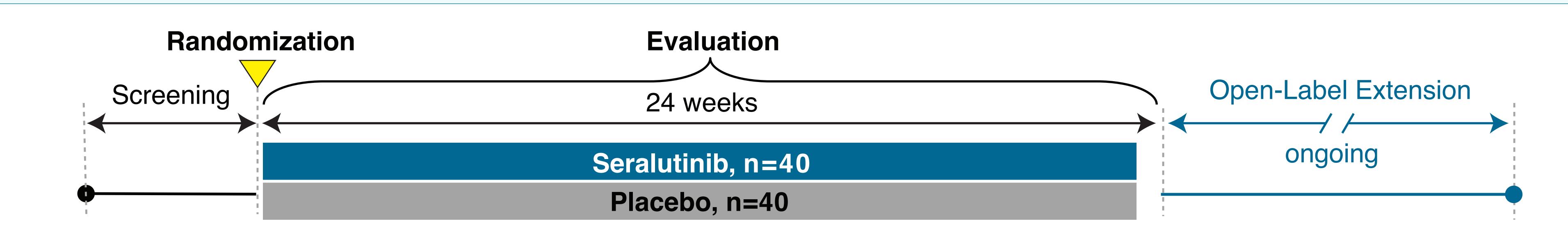
exercise capacity

- Determine effect of seralutinib on
- Change in six-minute walk distance from Baseline to Week 24 (Δ6MWD)



### Study Schema: TORREY and Open-Label Extension Study

pulmonary hemodynamics



## **Open-Label Extension (OLE) Study of Seralutinib**

- Subjects may be eligible to participate in an OLE study (NCT04816604) provided they have completed study treatment and all associated assessments of TORREY or another seralutinib study
- Objectives are to evaluate the long-term safety, tolerability, and efficacy of inhaled seralutinib in subjects with PAH
- Subjects will receive seralutinib for up to 18 months
- Safety data will be collected periodically through week 72; right heart catheterization will be performed at week 48 to evaluate ongoing efficacy on pulmonary vascular resistance

# SUMMARY

blood volume

TORREY SUBSTUDIES

Heart Rate Expenditure Substudy

effort during the 6-minute walk test

Functional Respiratory Imaging Substudy

pathophysiology of PAH

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

Two substudies will explore novel endpoints relevant to the underlying

This substudy will examine the effect of seralutinib on pulmonary

vascular remodeling by quantifying changes in pulmonary arterial

This separate substudy will assess the effect of seralutinib on cardiac

- The inhaled route of administration for seralutinib targets the diseased pulmonary arterioles at doses predicted to be locally effective while limiting systemic exposure which may reduce the risk of adverse events
- A phase 2 trial (TORREY; NCT04456998) in subjects with WHO Group 1 PAH is ongoing
- Eligible subjects may participate in a 72-week open-label extension study

### REFERENCES

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