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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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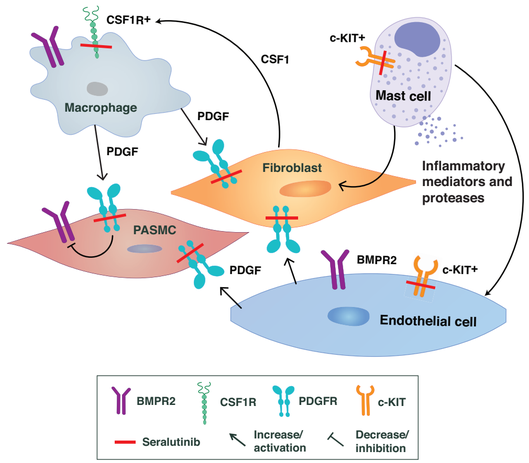
## BACKGROUND

- PDGFR, CSF1R, c-KIT and BMPR2 play a central role in cellular overgrowth in the lung vasculature and are key drivers in the development of PAH[1,2,3] (**Figure 1**)
- Seralutinib (formerly known as GB002) is a small-molecule, selective kinase inhibitor that targets these pathways and modulates BMPR2 (**Figure 1**)

Dry Powder Inhaler

- Seralutinib is delivered via inhalation by dry powder inhaler to potentially maximize the therapeutic index by directly targeting diseased pulmonary arterioles

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




- In **preclinical studies**, 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[4,5]
- **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. (see poster #1016 for more information on a Phase 1b inhaled seralutinib study in PAH patients)

POSTER 1016

## TORREY STUDY

- 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

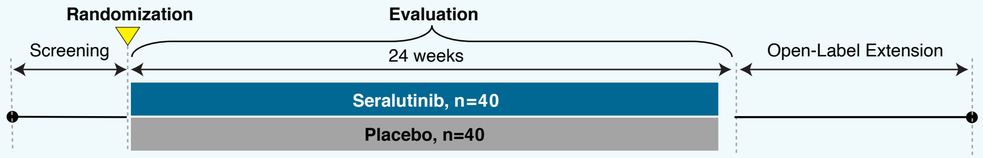
### SELECTED INCLUSION CRITERIA

- Diagnosis of symptomatic PAH
- 6MWD ≥ 150 meters and ≤ 550 meters
- WHO FC II or III
- Treatment with standard of care PAH background therapies, including PGIs
- RHC data consistent with the diagnosis of PAH and PVR ≥ 400 dyne·s/cm$^5$

### 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 at randomization

### TORREY Study Schema




**OBJECTIVES**

**PRIMARY**

Determine effect of seralutinib on pulmonary hemodynamics

**SECONDARY**

Determine effect of seralutinib on exercise capacity

**ENDPOINTS**

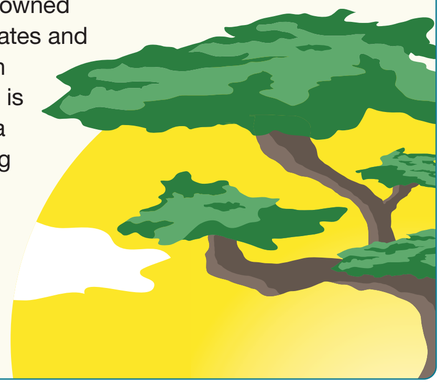
Change in pulmonary vascular resistance from Baseline to Week 24

Change in six-minute walk distance from Baseline to Week 24 (Δ6MWD)

## TORREY – SUBSTUDIES

- A Computerized Tomography Substudy will examine the effect of seralutinib on pulmonary vascular remodeling by quantifying changes in pulmonary arterial blood volume
- A separate Heart Rate Monitoring Substudy will assess the effect of seralutinib on cardiac effort during the 6-minute walk test

TORREY was named for the rare, critically endangered TORREY pine tree (*Pinus torreyana*) that is native only to San Diego County and immediate environs in California. This open-crowned pine tree creates and emits oxygen and as such, is symbolic of a life-sustaining resource.



## SUMMARY

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

## REFERENCES

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https://goss.bio/3mtRT0t