1016

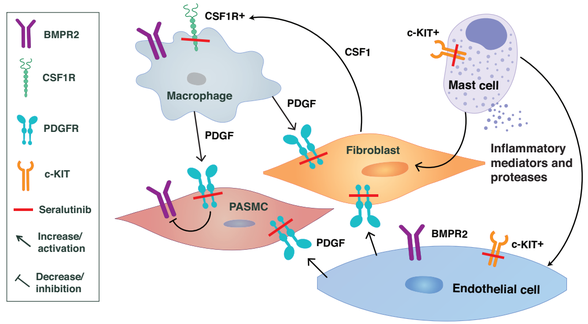
A Phase 1B, Multi-Center, Randomized, Placebo-Controlled Trial of Inhaled Seralutinib in Subjects With WHO Group 1 Pulmonary Arterial Hypertension (PAH)

Robert P. Frantz[1], Kristin B. Highland[2], John McConnell[3], Charles D. Burger[4], Robert F. Roscigno[5], Matt Cravets[5], Ramona McCaffrey[5], Lawrence S. Zisman[5], Luke S. Howard[6]

[1]Dept of Cardiovascular Diseases, Mayo Clinic, Rochester, MN, USA; [2]Respiratory Institute, Cleveland Clinic, Cleveland, OH, USA; [3]Norton Pulmonary Specialists, Louisville, KY, USA; [4]Division of Pulmonary, Allergy, and Sleep Medicine, Mayo Clinic, Jacksonville, FL, USA; [5]Gossamer Bio, Inc., San Diego, CA, USA; [6]Imperial College Healthcare NHS Trust, London, UK

BACKGROUND

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



Seralutinib is delivered using a dry powder inhaler (DPI) to directly target diseased pulmonary arterioles

OBJECTIVES

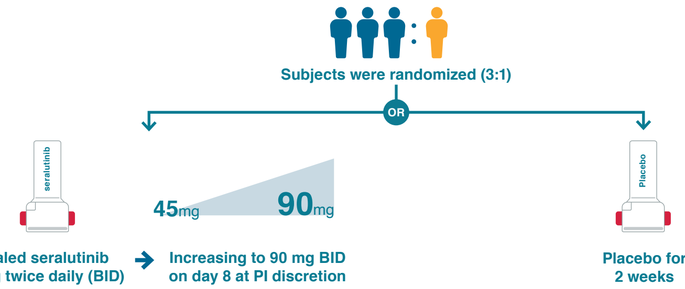
PRIMARY: Evaluate the safety and tolerability of inhaled seralutinib in subjects with WHO Group 1 PH

SECONDARY: Determine the pharmacokinetic parameters of seralutinib administered by DPI

METHODS

STUDY DESIGN Phase 1b, 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



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

NOW ENROLLING

TORREY STUDY

TORREY is a phase 2, randomized, double-blind, placebo-controlled study (**NCT04456998**) which is currently recruiting people with WHO Group 1 PH to evaluate the efficacy and safety of seralutinib **(See poster #1017 for more details)**

POSTER 1017

ACKNOWLEDGEMENTS

The authors would like to thank the study investigators, study coordinators, and especially the patients and families who participated in this study at its sites in the USA (California, Colorado, Connecticut, Florida, Kentucky, Massachusetts, Minnesota, North Carolina, Ohio, Pennsylvania, South Carolina, Texas) and the United Kingdom (Glasgow, London, Newcastle), and gratefully acknowledge the contribution of Jack Li for PK data, and Jean-Marie Bruey for target engagement data.

RESULTS

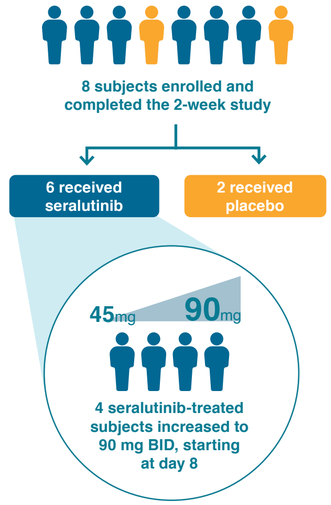


Table 1. Demographics and Baseline Characteristics (N=8)

Demographics	
Age (Range)	30 - 63 years
Female / Male, n	7 / 1
Functional Class at Baseline, n	
Class II	6
Class III	2
PAH Etiology, n	
Idiopathic	4
Heritable	2
Scleroderma/Systemic Sclerosis	2
Background PAH Medications*, n	
Double Therapy	3
Triple Therapy	5
PGI or IP Receptor Agonist**	5

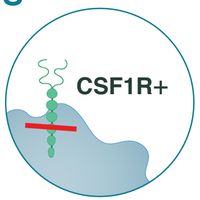
*Single or combination therapy with phosphodiesterase type 5 inhibitors, guanylate cyclase stimulators, endothelin receptor antagonists, and prostanoids (with the exception of inhaled prostanoids) was allowed
**PGI, prostaglandin; IP, prostaglandin I2 receptor

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

1. Yamamura et al. *FASEB J* 2019; 33:7363-74; **2.** Chen et al. *BMC Genomics* 2016; 17:781; **3.** Perros et al. *Am J Respir Crit Care Med* 2008; 178:81-8; **4.** Sitapara et al. *Circulation* 2019; 140:A12947; **5.** Galkin et al. *Circulation* 2019; 140:A11102; **6.** Li et al. *Am J Respir Crit Care Med* 2020; 201:A2907

https://goss.bio/2XTtSpv