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In Vivo Efficacy of a Novel, Inhaled PDGFRα/β Inhibitor, GB002, in the Rat Monocrotaline and Pneumonectomy Model of Pulmonary Arterial Hypertension

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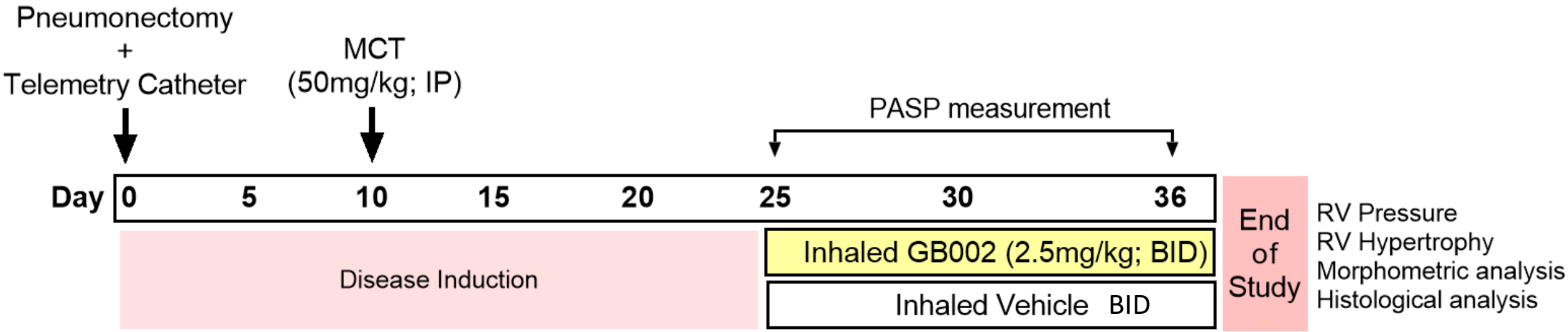
Disclosures

- The presenter, Lawrence Zisman is employed by Gossamer Bio, San Diego CA and owns stock in Gossamer Bio Inc.

Background and Hypothesis

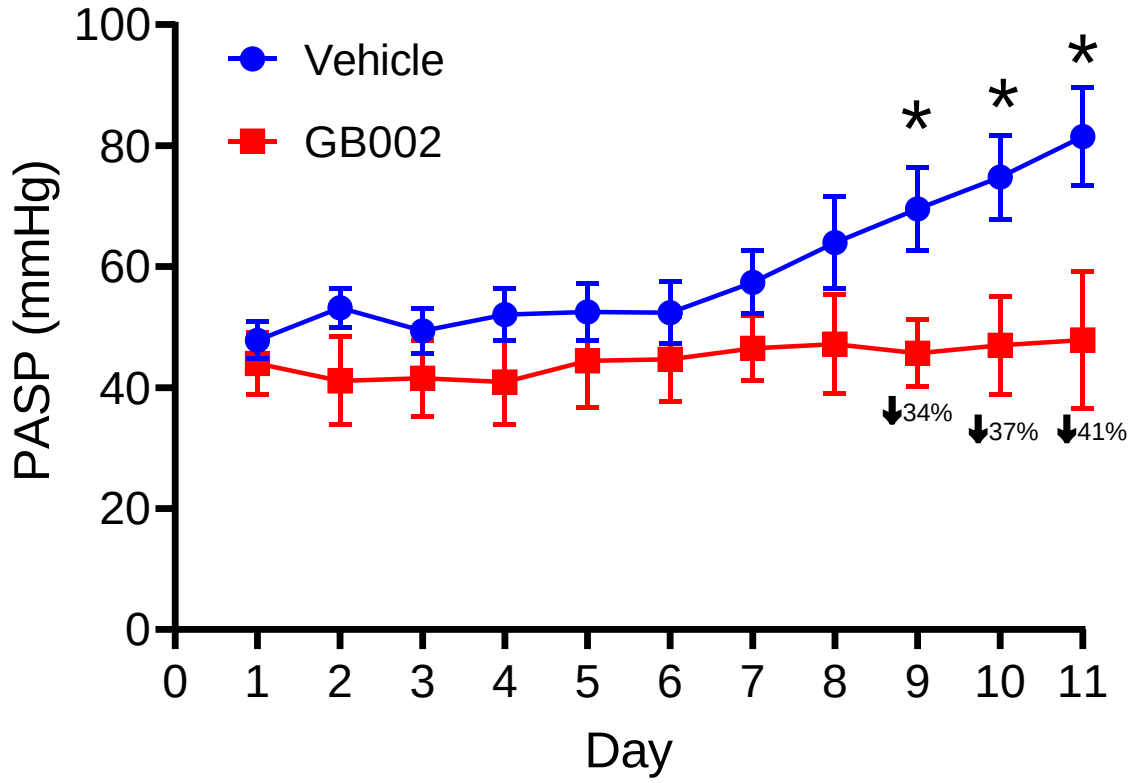
- The PDGF pathway drives adverse vascular remodeling in pulmonary arterial hypertension (PAH).
- GB002 is a novel, potent, clinical stage inhibitor of PDGFRα/β kinases.
- GB002 is formulated as a dry powder and delivered by inhalation.
- The rat Monocrotaline (MCT) Pneumonectomy (PN) model, develops a neointimal pattern of remodeling and severe right ventricle hypertrophy resembling important aspects of human PAH.
- **Hypothesis:** Inhaled GB002 would lower pulmonary artery systolic pressure (PASP) and lessen the severity of neointimal lesions in the MCT+PN model.

Study Design



GB002 and vehicle administered BID for 11 days

GB002 prevented progression of severe pulmonary hypertension in the MCT-PN model



Vehicle (n=12)
GB002 (n=7)

*p<0.05

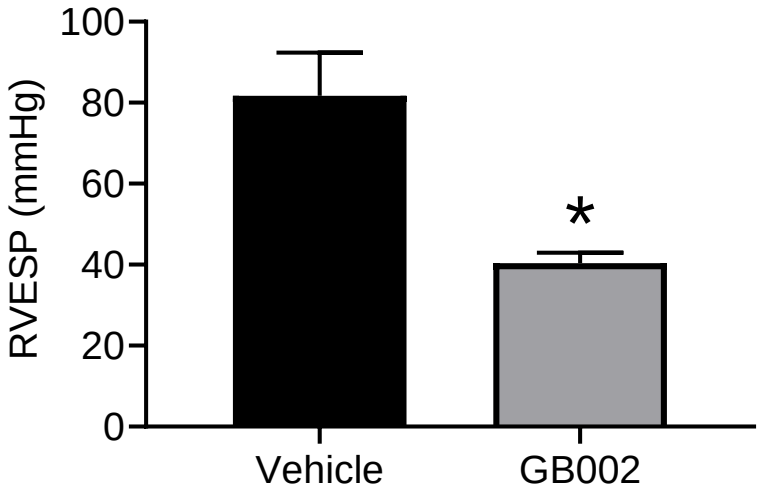
On day 9, 10, and 11, PASP was 34%, 37%, and 41% lower, respectively, in the GB002 group vs. the vehicle group.

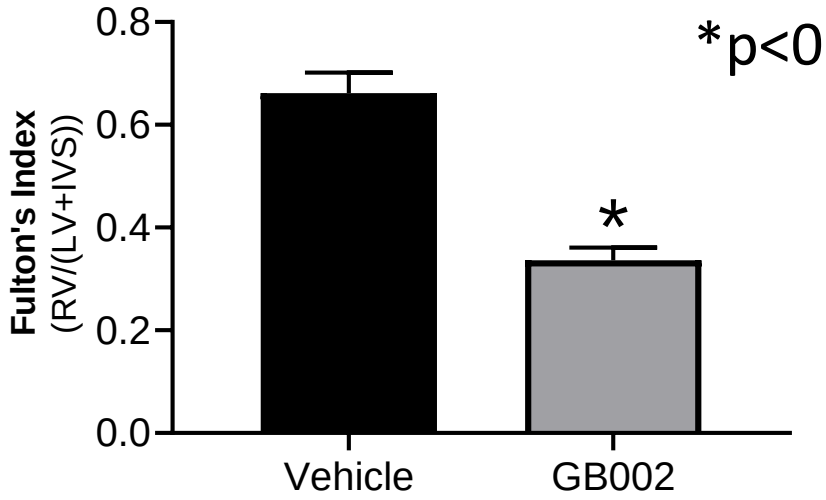
Data presented as mean ± SEM.

GB002 significantly decreased RVESP and RV hypertrophy

Vehicle (n=6)
GB002 (n=11)

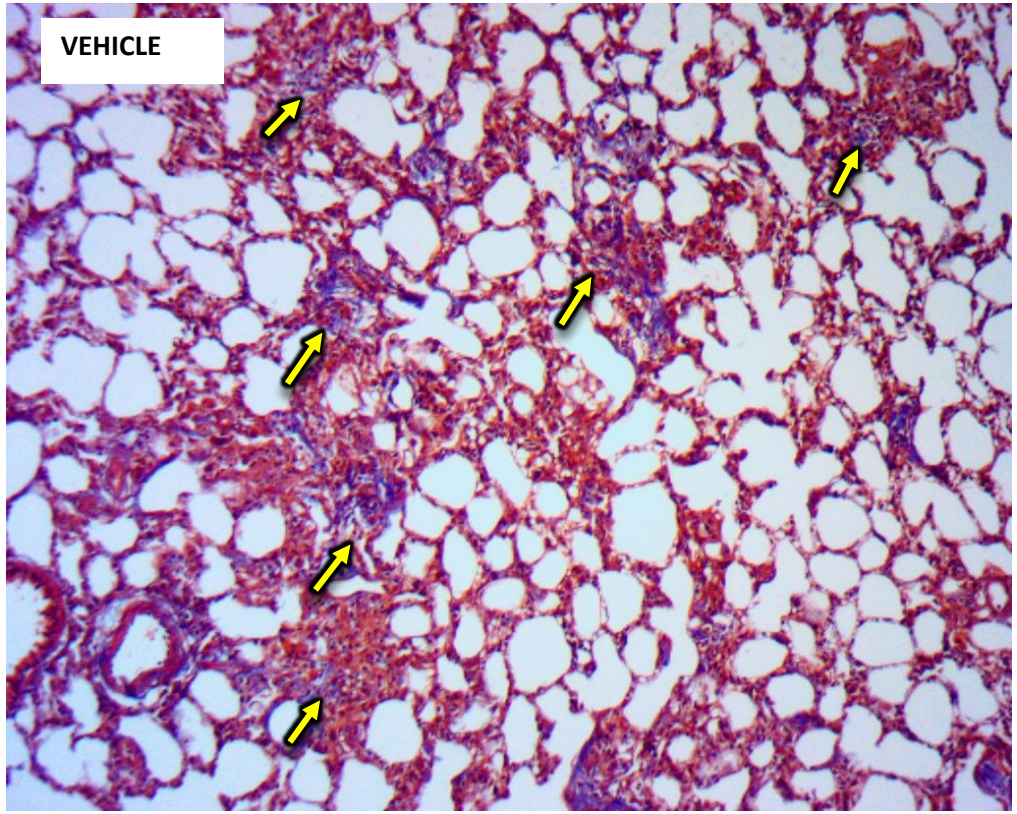
*p<0.001

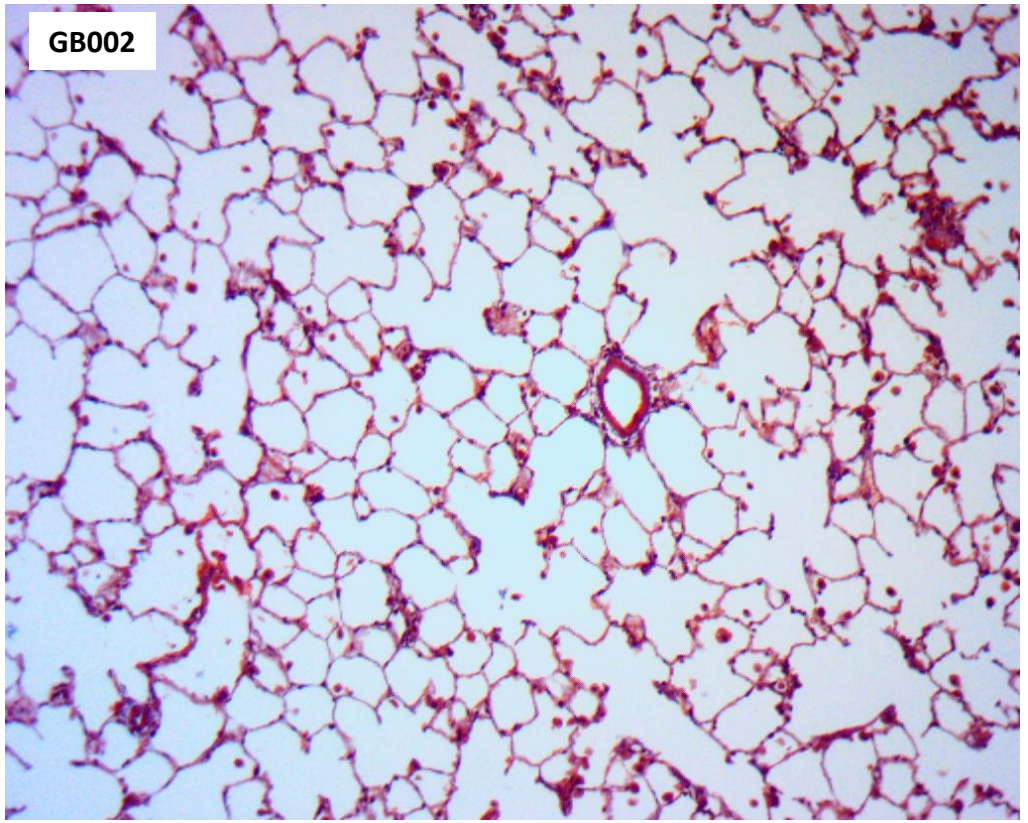




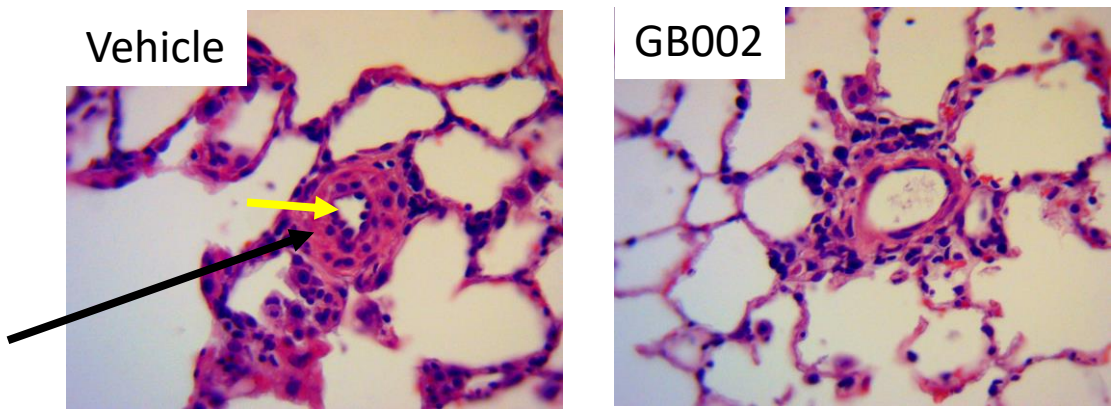
Data presented as mean ± SEM.

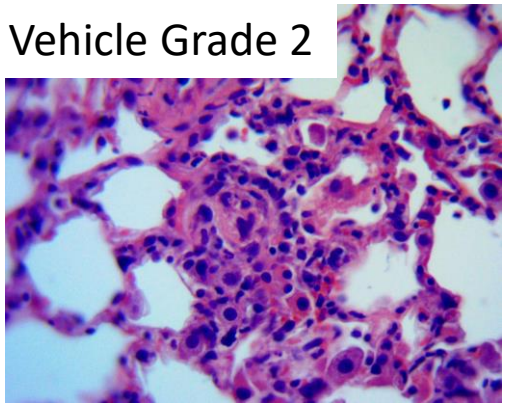
GB002 decreased neointimal lesions and fibrosis

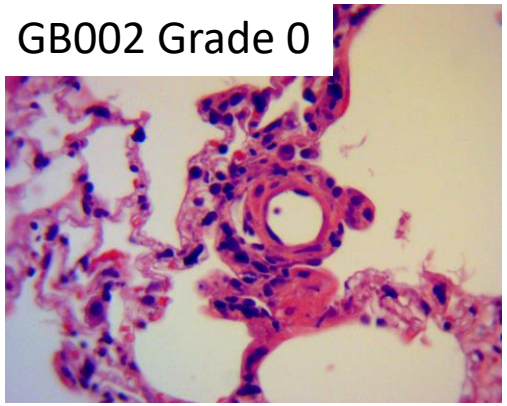


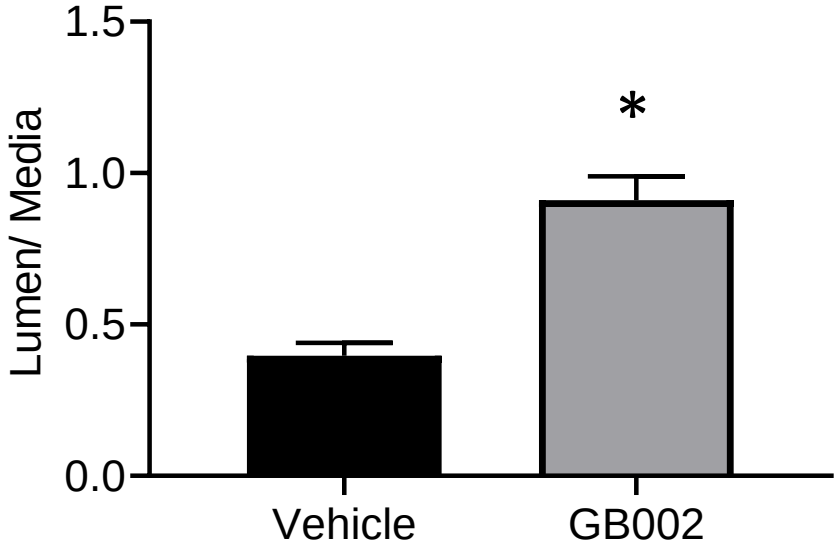


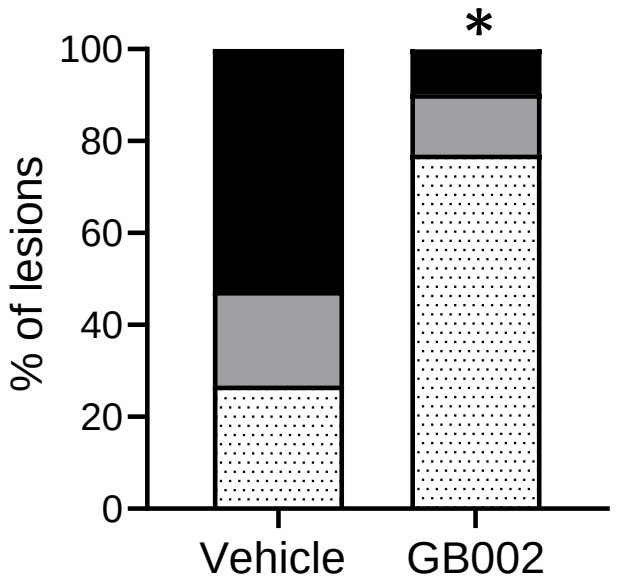
GB002 reverse remodeled pulmonary arterioles











Grade 2
Grade 1
Grade 0

Vehicle (n=6)
GB002 (n=11)

*p<0.0001

Data presented as mean ± SEM; Grading system per Toba et al. AJP 2014;306:H243.

Summary and Conclusions

- GB002 is a novel inhaled PDGFRα/β inhibitor with potentially disease-modifying characteristics
- In the rat MCT PN model, a severe model of PAH that closely replicates key features of the human disease, inhaled GB002 prevented:
  - Progression of pulmonary arterial hypertension
  - Adverse remodeling of the pulmonary vasculature
- A phase 1b clinical trial of GB002 is ongoing (NCT03926793)

Acknowledgments

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Thank you!

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