

# ALG-801 demonstrates superior therapeutic efficacy in sugen-hypoxia model of pulmonary hypertension



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## Introduction

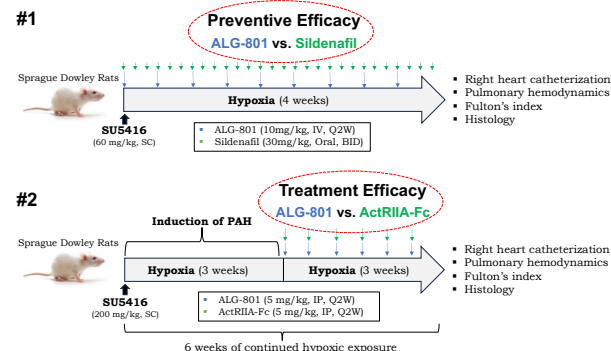
Pulmonary arterial hypertension (PAH) is a progressive disease characterized by increased pulmonary vascular resistance, leading to chronic elevation in pulmonary arterial pressure, right-sided heart failure, and premature death. Despite many available therapies over the last two decades, survival has remained poor with a median transplant-free survival of approximately six years.

Smad2/3 signaling ligands including activins, GDF8 and GDF11 play a critical role in vascular remodeling and pathogenesis of PAH.

ALG-801, a novel selective ligand trap, potently inhibits activins, GDF8 and GDF11 and completely spares BMP9, a key Smad1/5/8-signaling ligand whose function is essential for vascular homeostasis and integrity. ALG-801 has been shown to be safe and well-tolerated while eliciting strong pharmacodynamic and biomarker responses in Phase 1 clinical studies.

To evaluate ALG-801's potential for treating PAH, here we examined the efficacy of ALG-801 in head-to-head comparison with Sildenafil and Sotatercept (ActRIIA-Fc), both approved for use in patients with PAH, in sugen-hypoxia (SuHx) rats, a well-characterized and widely used animal model for pulmonary hypertension.

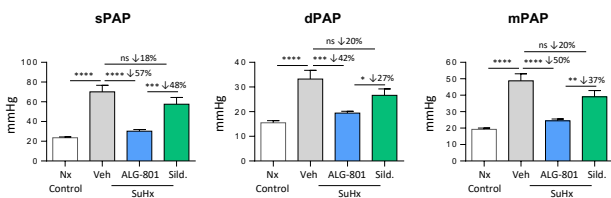
## Experimental Design



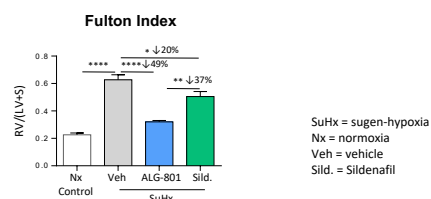
## Results

### Head-to-head comparison: ALG-801 vs. Sildenafil

ALG-801 prevents pulmonary arterial hypertension more effectively than Sildenafil

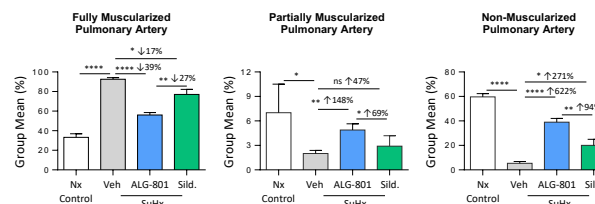


ALG-801 prevents right ventricular hypertrophy more effectively than Sildenafil



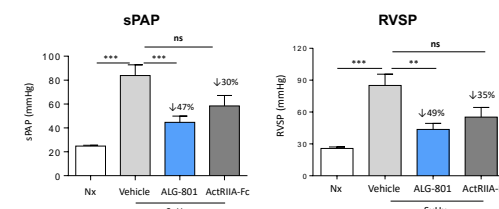
SuHx = sugen-hypoxia  
Nx = normoxia  
Veh = vehicle  
Sild. = Sildenafil

ALG-801 prevents muscularization of pulmonary arteries more effectively than Sildenafil

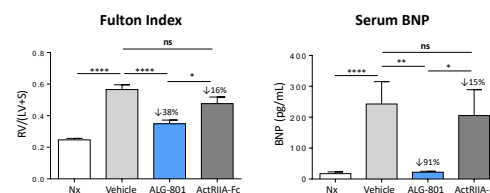


### Head-to-head comparison: ALG-801 vs. ActRIIA-Fc

ALG-801 treatment alleviates pulmonary arterial hypertension more effectively than ActRIIA-Fc

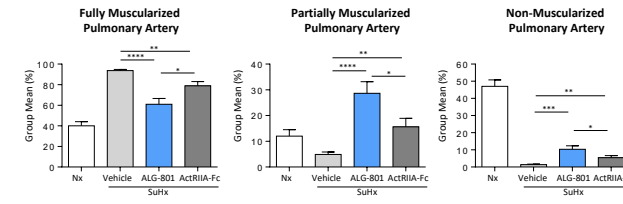


ALG-801 reduces right ventricular hypertrophy and serum BNP more effectively than ActRIIA-Fc

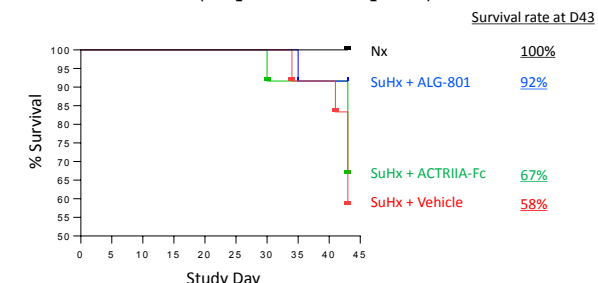


ns: not significant; \*: p < 0.05; \*\*: p < 0.01; \*\*\*: p < 0.001; \*\*\*\*: p < 0.0001

ALG-801 treatment reverses pulmonary artery muscularization more effectively than ActRIIA-Fc



ALG-801 treatment leads to prolonged survival (Kaplan-Meier plots)



## Conclusion

- ALG-801 demonstrates a significantly superior efficacy compared with either Sildenafil or Sotatercept (ActRIIA-Fc) in SuHx rats, a disease model of pulmonary hypertension
- ALG-801 holds a promising therapeutic potential for treating pulmonary hypertension

## Reference

- Johnson et al., Pulmonary Hypertension: A Contemporary Review. Am J Respir Crit Care Med. 2023 Sep 1;208(5):528-548
- Yung et al., ACTRIIA-Fc rebalances activin/GDF versus BMP signaling in pulmonary hypertension. Sci Transl Med. 2020 May 13;12(543)