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Gossamer Bio: PAH Investor Day

December 15, 2020

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Forward Looking Statements

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Presenters on Today's Call

Faheem Hasnain

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Co-Founder, Chairman and Chief Executive Officer

Lewis J. Rubin, MD

UCSD School of Medicine

Professor of Medicine, Emeritus
Former Dir., Division of Pulmonary and Critical Care Medicine

Vallerie McLaughlin, MD

University of Michigan

Kim A. Eagle, MD, Endowed Professor of Cardiovascular Medicine
Dir., Pulmonary Hypertension Program

Larry Zisman, MD

Gossamer Bio

Senior Director, Clinical Development

Robert Roscigno, PhD

Gossamer Bio

Vice President, Clinical Development

Mario Orlando

Gossamer Bio

Vice President, Commercial, New Product Planning

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Agenda

Topic	Presenter
Introductions and Agenda Overview	Faheem Hasnain
PAH Overview	Lewis J. Rubin, MD
Targeting New Pathways in PAH	Vallerie McLaughlin, MD
Seralutinib for the Treatment of PAH	
▪ **Preclinical and Early Development**	Larry Zisman, MD
▪ **Clinical Development Program**	Robert Roscigno, PhD
▪ **Commercial Opportunity**	Mario Orlando
Q&A	*All presenters moderated by Robert Roscigno, PhD*
Closing Remarks	Faheem Hasnain

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is now known as

Seralutinib

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Pulmonary Arterial Hypertension (PAH) Overview

Lewis J. Rubin, MD

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Clinical Classification of Pulmonary Hypertension

1. Pulmonary Arterial Hypertension

- **1.1** Idiopathic PAH
- **1.2** Heritable PAH
- **1.3** Drugs and toxins induced
- **1.4** Associated with:
  - **1.4.1** Connective tissue disease
  - **1.4.2** HIV infection
  - **1.4.3** Portal hypertension
  - **1.4.4** Congenital heart disease
  - **1.4.5** Schistosomiasis
- **1.5** PAH long-term responders to calcium channel blockers
- **1.6 PAH with overt signs of venous/capillaries (PVOD/PCH) involvement**
- **1.7** Persistent PH of the Newborn syndrome

2. PH due to left heart disease

- **2.1** PH due to heart failure with preserved E.F
- **2.2** PH due to heart failure with reduced E.F
- **2.3** Valvular heart disease
- **2.4** Congenital post-capillary obstructive lesions

3. PH due to lung diseases and/or hypoxia

- **3.1** Obstructive lung disease
- **3.2** Restrictive lung disease
- **3.3** Other lung disease with mixed restrictive/ obstructive pattern
- **3.4** Hypoxia without lung disease
- **3.5** Developmental lung disorders

4. PH due to pulmonary artery obstruction

- **4.1** Chronic thromboembolic PH
- **4.2** Other pulmonary artery obstructions

5. PH with unclear mechanisms

- **5.1** Hematologic disorders
- **5.2** Systemic disorders
- **5.3** Others
- **5.4** Complex congenital heart disease

Source: Simonneau, et al, *Eur Resp J 2019* 53: 1801913

Pulmonary Hypertension WHO Group 1: PAH Overview

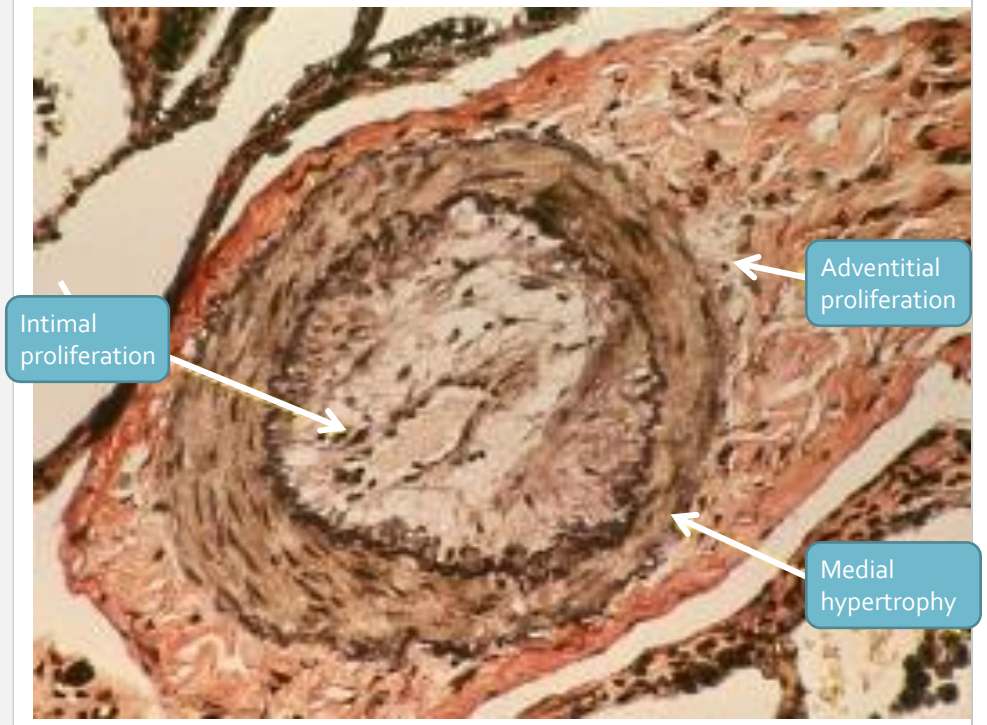
Pulmonary Arterial Hypertension (PAH)

- Rare, orphan disease
- Characterized by high blood pressure in the blood vessels carrying deoxygenated blood from the right side of the heart to the lungs
- Caused when the arteries in the lungs become narrowed, thickened and / or stiff as a result of pathological remodeling and vasoconstriction
- Heart works harder to pump blood to the lungs, potentially leading to right heart failure
- Progressive disease and often fatal

Symptoms

- **Dyspnea**
- **Fatigue**
- **Dizziness**
- **Chest pressure / pain**
- **Edema in ankles, legs, abdomen**
- **Cyanosis**
- **Heart palpitations**

PAH is Characterized by Vascular Remodeling



Muscular pulmonary artery from iPAH patient[1]

Source: [1]Gaine S and Rubin L: Lancet 1998; 352: 719-725

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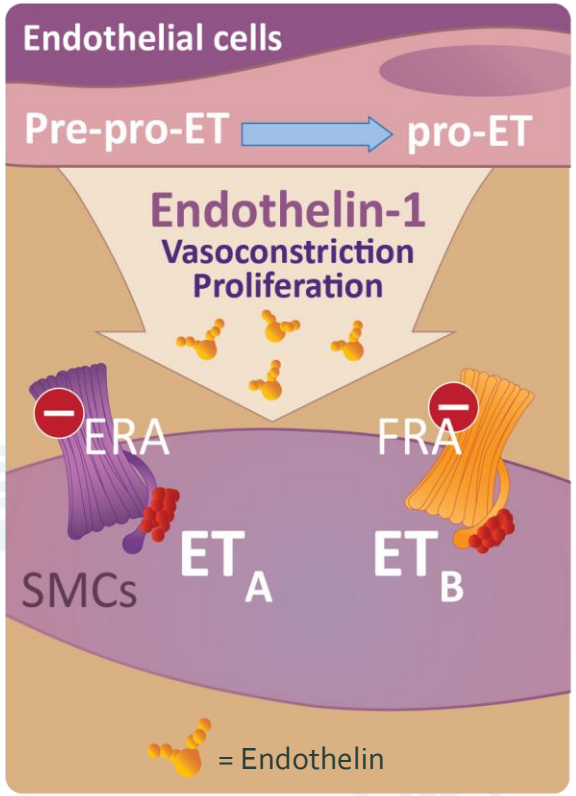
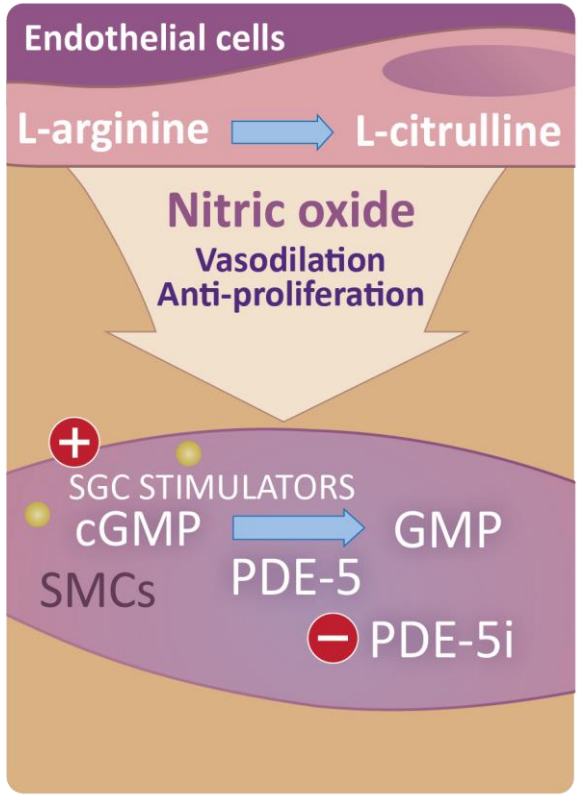
Currently Approved PAH Therapies Address One of Three Pathways in PAH

Endothelin Pathway



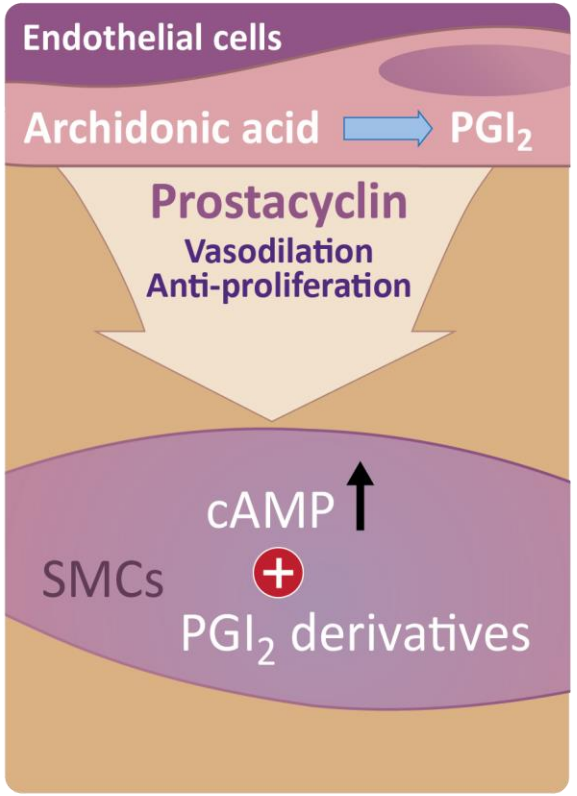
ERAs

Nitric Oxide Activators



PDE-5i/ sGC Stim

Prostacyclin Pathway



PGI_2 derivatives

cAMP: cyclic adenosine monophosphate; cGMP: cyclic guanosine monophosphate; ERA: endothelin receptor agonist; ET: endothelin; PDE5: phosphodiesterase-5; PDE-5i: phosphodiesterase-5 inhibitor; PGI_2: prostacyclin; sGC stim: soluble guanylate cyclase stimulators

Source: Adapted from Humbert, et al., *N Engl J Med* 2004, 351:1425

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Simplified Risk Stratification in PAH

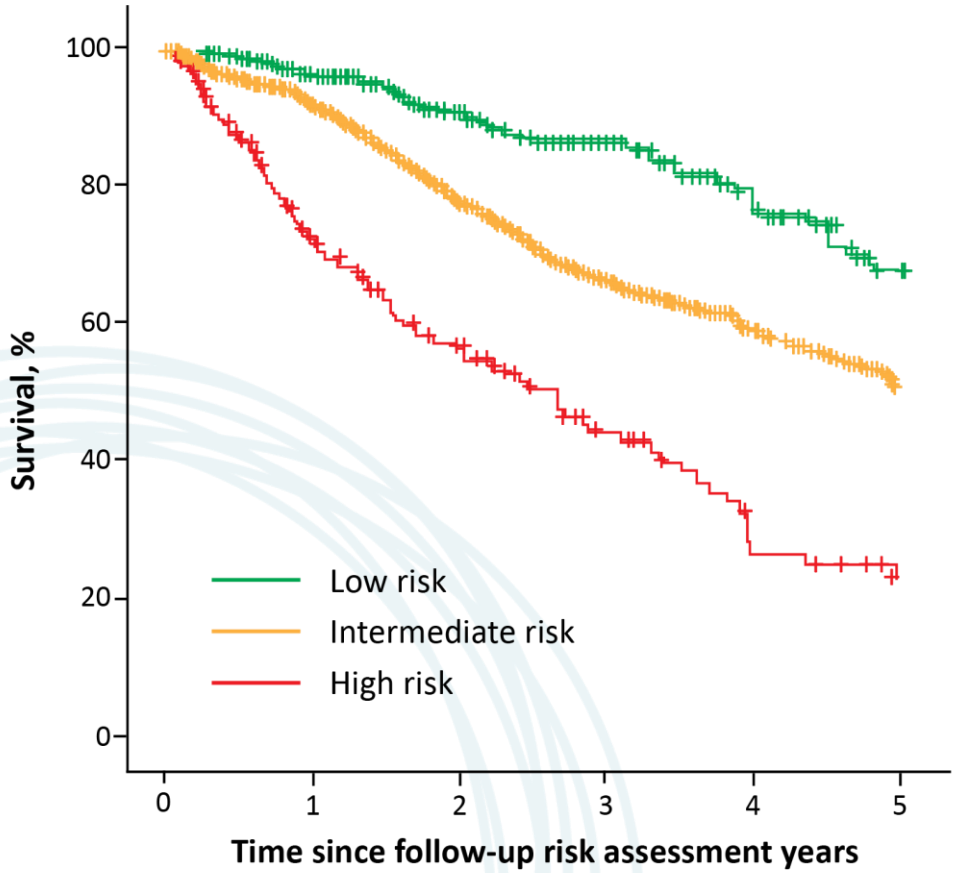
Prognostic Criteria		Low Risk Variables	Intermediate Risk Variables	High Risk Variables
1	**WHO functional class**	I, II	III	IV
2	**6MWD**	>440 m	165-440 m	<165 m
3	**NT-proBNP plasma levels**	BNP <50 ng/l NT-proBNP <300 ng/l	BNP 50-300 ng/l NT-proBNP 300-1400 ng/l	BNP >300 ng/l NT-proBNP >1400 ng/l
		Or	*Or*	*Or*
	RAP	RAP < 8 mmHg	RAP 8-14 mmHg	RAP >14 mmHg
4	**CI**	CI ≥2.5 l/min/m²	CI 2.0-2.4 l/min/m²	CI <2.0 l/min/m²
		Or	*Or*	*Or*
	SvO_2	SvO_2 >65%	SvO_2 60-65%	SvO_2 <60%

WHO: World Health Organization; 6MWD: six-minute walk distance; NT-proBNP: N-terminal-pro hormone B-type natriuretic peptide; RAP: right atrial pressure; CI: cardiac index; SvO_2: mixed venous oxygen saturation

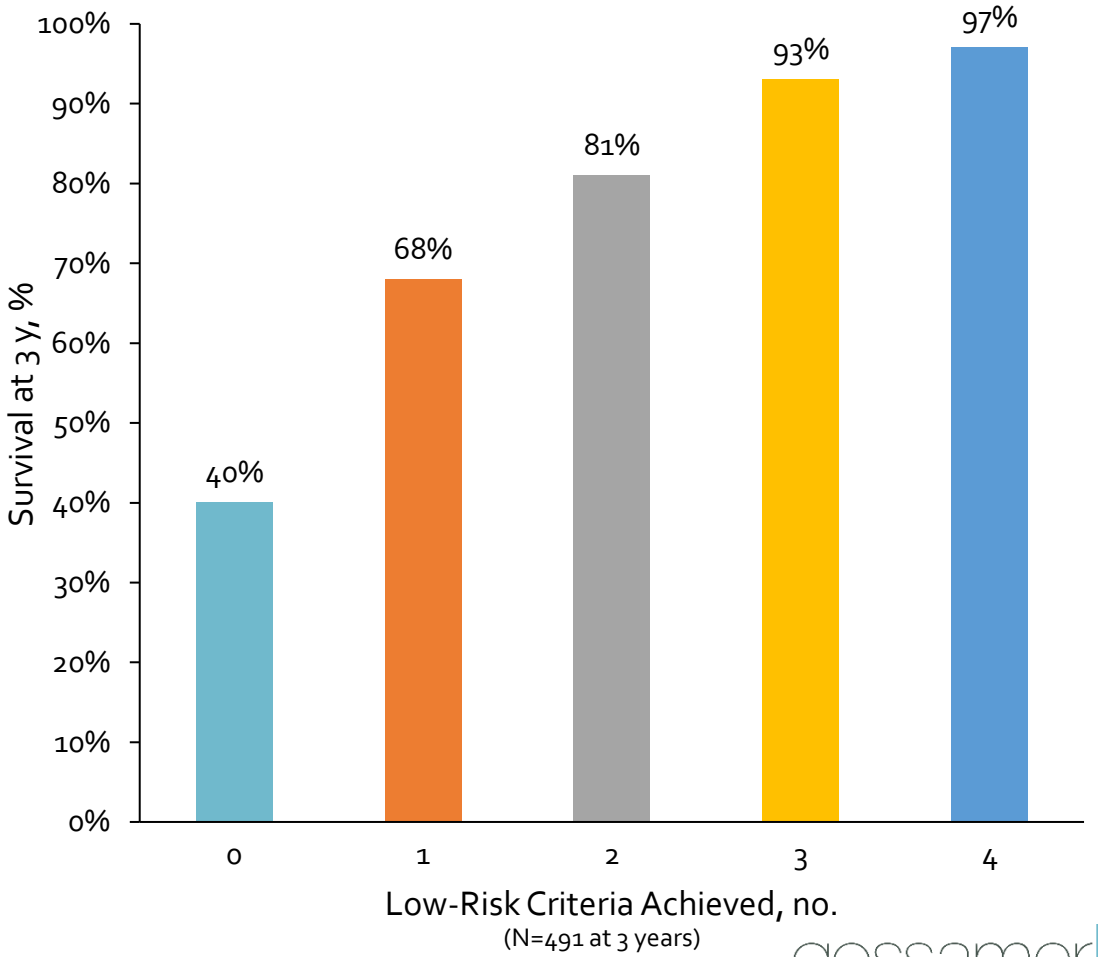
Source: Galie, et al., 2015 ESC/ERS Guidelines, *Eur Heart J* 2016; depicted variables studied mostly in IPAH; GlobalData

Despite Availability of Currently Approved Therapies, the Morbidity and Mortality of PAH Remain High

COMPERA Registry: Survival Based on Risk Assessment Achieved at First Evaluation[1]



French Registry: Survival Based on Number of Low-Risk Criteria Achieved at First Evaluation[2]



Source: [1]Hoeper, et al, *Eur Respir J* 2017 50: 1700740; [2]Boucly, et al, *Eur Respir J* 2017 50: 1700889

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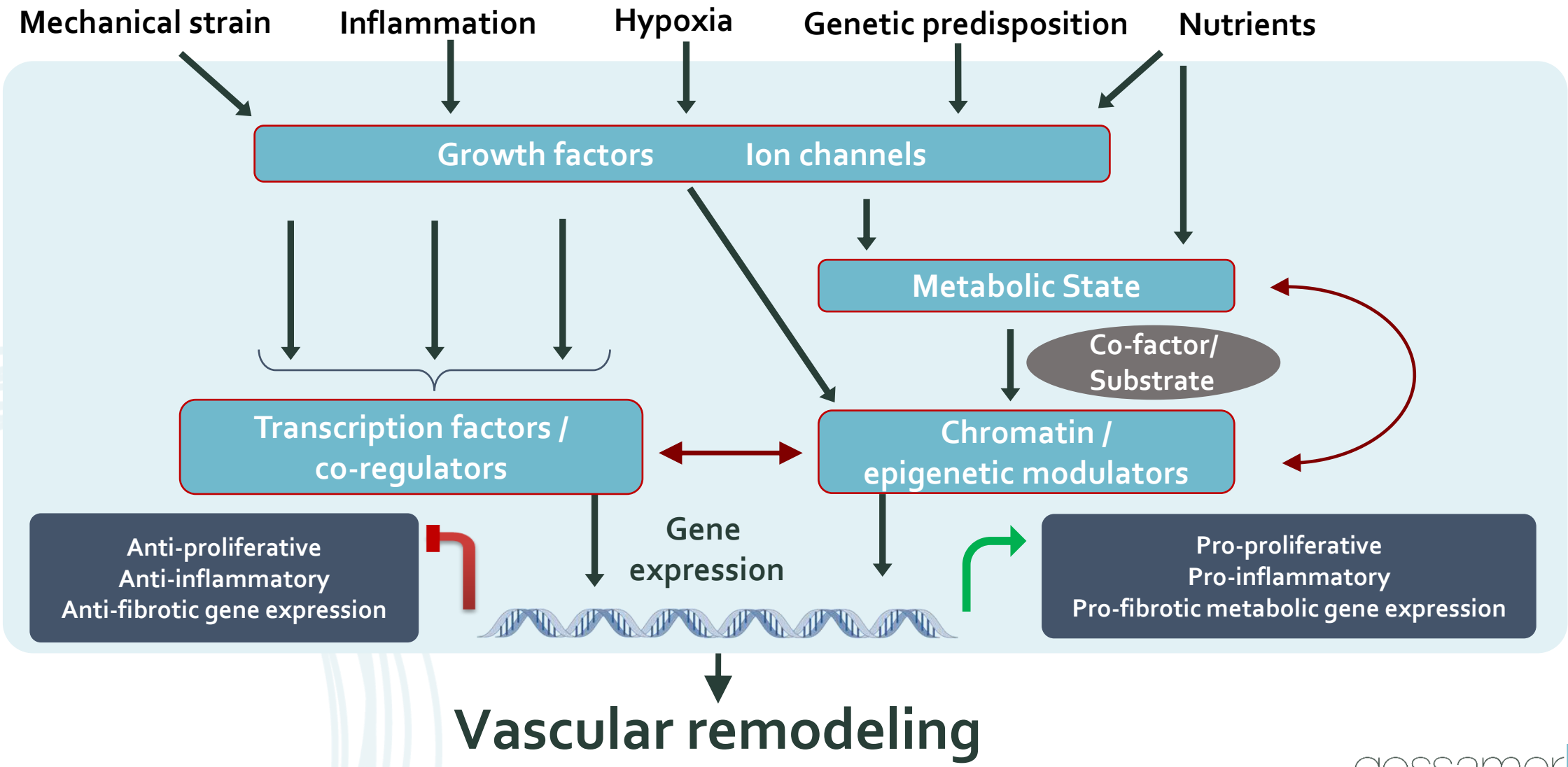
Currently Approved Therapies Do Not Adequately Address the Pathways Responsible for Pathologic Vascular Remodeling in PAH



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Targeting New Pathways in PAH

Vallerie McLaughlin, MD

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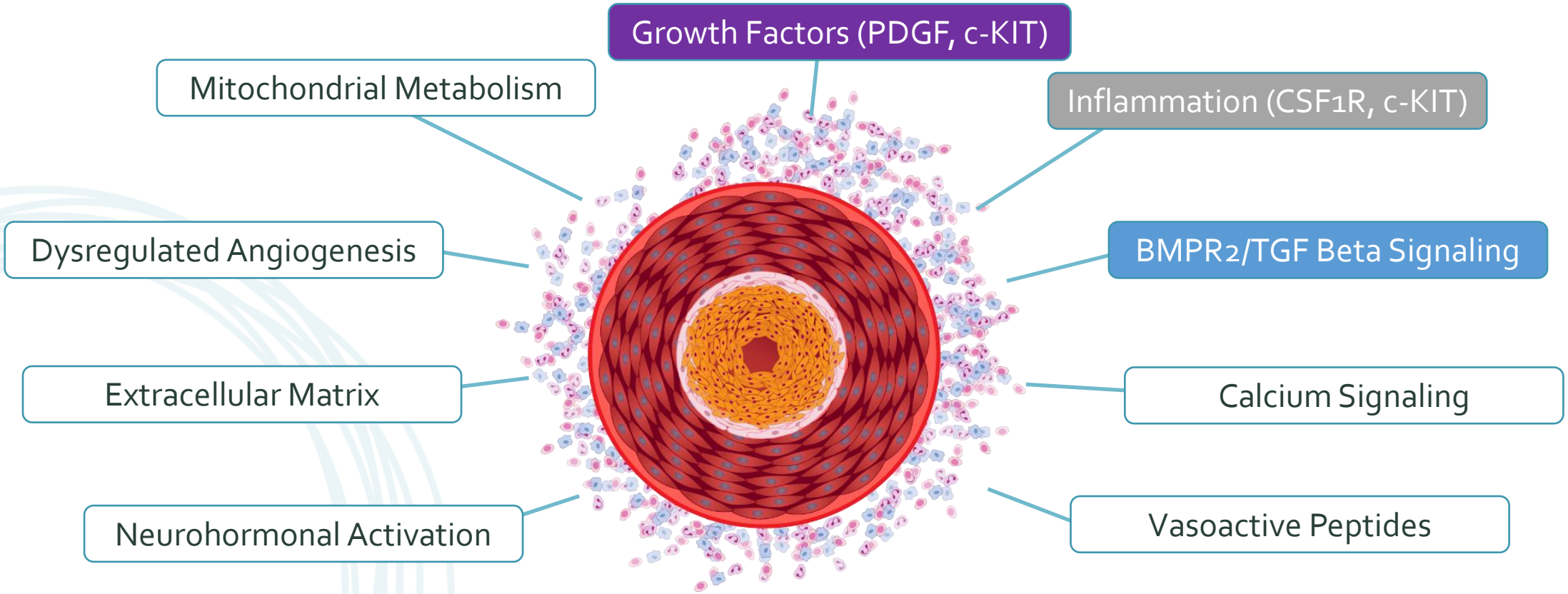
Novel Treatment Approaches in PAH

- All approved drugs in PAH target 3 pathways primarily focused on vasodilation
- Exciting era in PAH clinical research with multiple approaches in the clinic attempting to address the underlying disease pathogenesis



BMPR2: bone morphogenetic protein receptor type 2; TGF Beta: transforming growth factor beta
Source: Adapted from Humbert, et al. *Circulation* 2014

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PDGF Has Been a Known Contributor to PAH for Over 20 Years

Growth Factors

EUROPEAN RESPIRATORY journal
OFFICIAL SCIENTIFIC JOURNAL OF THE ERS

Eur. Resp. Journ. 1998 11: 554-559

Platelet-derived growth factor expression in primary pulmonary hypertension: comparison of HIV seropositive and HIV seronegative patients

M Humbert, G Monti, M Fartoukh, A Magnan, F Brenot, B Rain, F Capron, P Galanaud, P Duroux, G Simonneau, D Emilie

JCI

J Clin Invest. 2005 Oct;115(10):2811-21

Reversal of experimental pulmonary hypertension by PDGF inhibition

R Schermuly, E Dony, H Ghofrani, S Pullamsetti, R Savai, M Roth, A Sydykov, Y Lai, N Weissmann, W Seeger, F Grimminger

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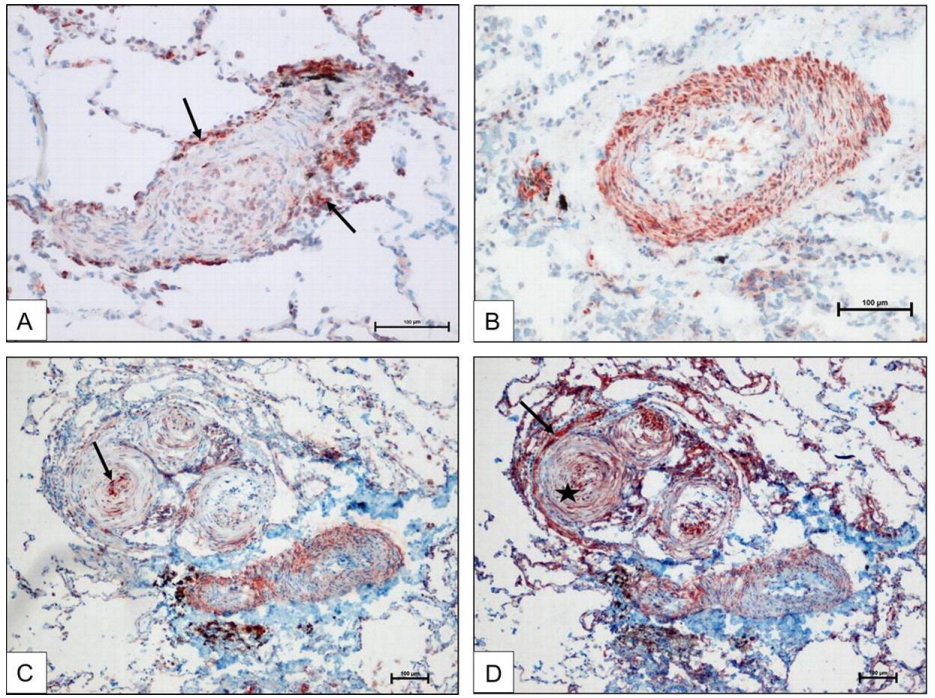
Targeting of the PDGF Pathway in PAH Supported by Strong Scientific and Clinical Rationale

Growth Factors

Evidence Supporting Role of PDGF Pathway in PAH

- ✓ PDGF pathway upregulated in PAH; PDGFB most upregulated gene in PH*
- ✓ Ablation of PDGFRβ signaling prevented hypoxia induced PAH
- ✓ PDGFR inhibition effective in animal models of PAH
- ✓ Phase 3 IMPRES study with Imatinib in PAH demonstrated efficacy



Photomicrograph from Perros, et al 2008 shows (A) PDGFA, (B) PDGFRα, (C) PDGFB, and (D) PDGFRβ in PAH lesions

* In gene ontology blood vessel development and cardiovascular pathways

Source: Perros, et al, *Am J Respir Crit Care Med* 2008, 178:81; Saygin, et al, *Pulm Circ* 2020, 10(1):1; Ten Freyhaus, et al, *Arterioscler Thromb Vasc Biol* 2015, 35(5):1236; Barst, et al, *J Clin Invest* 2005, 115(10):2691; Hoeper, et al, *Circ* 2013;127(10):1128.

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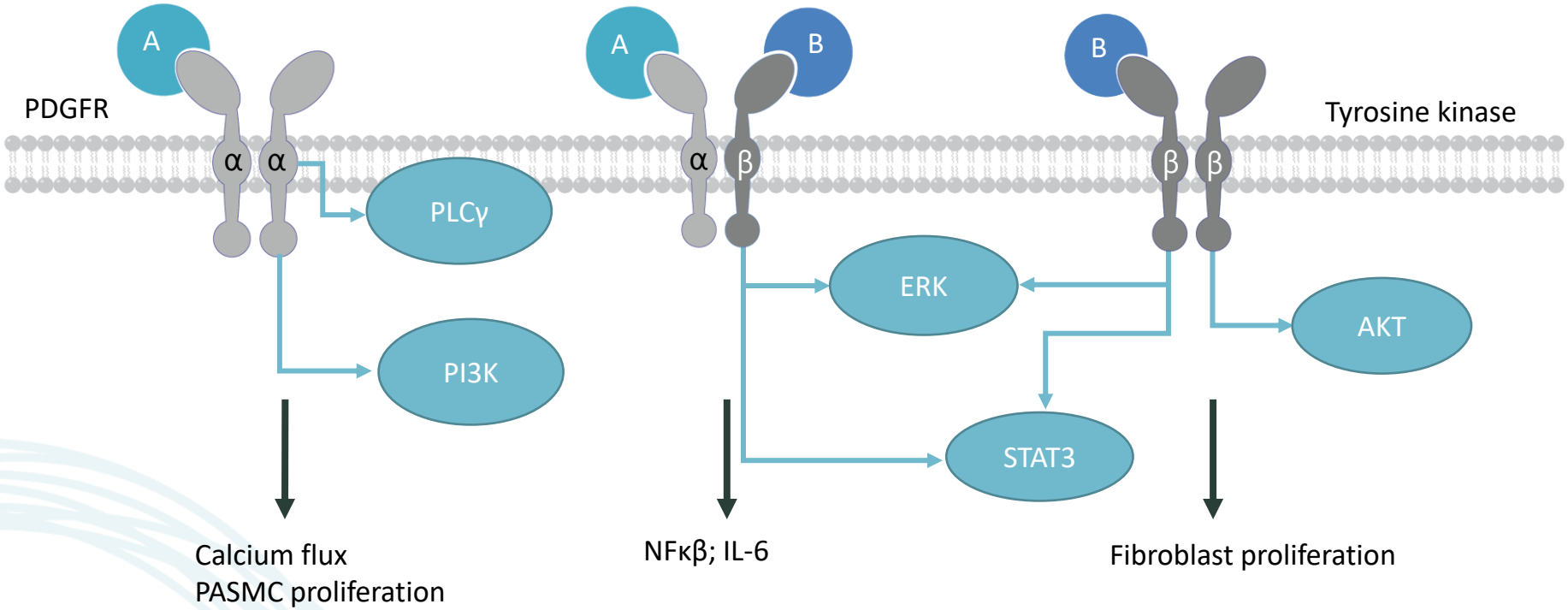
How Does PDGF / PDGFR Drive PAH?

Growth Factors



- In PAH, PDGFRα and PDGFRβ drive pulmonary arterial smooth muscle cell (PASMC) proliferation, while PDGFRβ plays a more prominent role in fibroblast proliferation
- PDGF is also secreted by c-KIT + cells, and CSF1R+ macrophages and its overexpression leads to fibrosis and extracellular matrix deposition

Source: Wu et al. *PLoS One* 2008;3:e3794

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c-KIT Has Also Been Identified as a Potential Driver of Vascular Remodeling

Inflammation

Growth Factors

Hypoxia-induced pulmonary artery adventitial remodeling and neovascularization: contribution of progenitor cells

N Davie, J Crossno Jr., M Frid, S Hofmeister, J Reeves, D Hyde, T Carpenter, J Brunetti, I McNiece, and K Stenmark

AJP Lung. 2004 286:4 L668-678

c-KIT–Positive cells accumulate in remodeled vessels of idiopathic pulmonary arterial hypertension

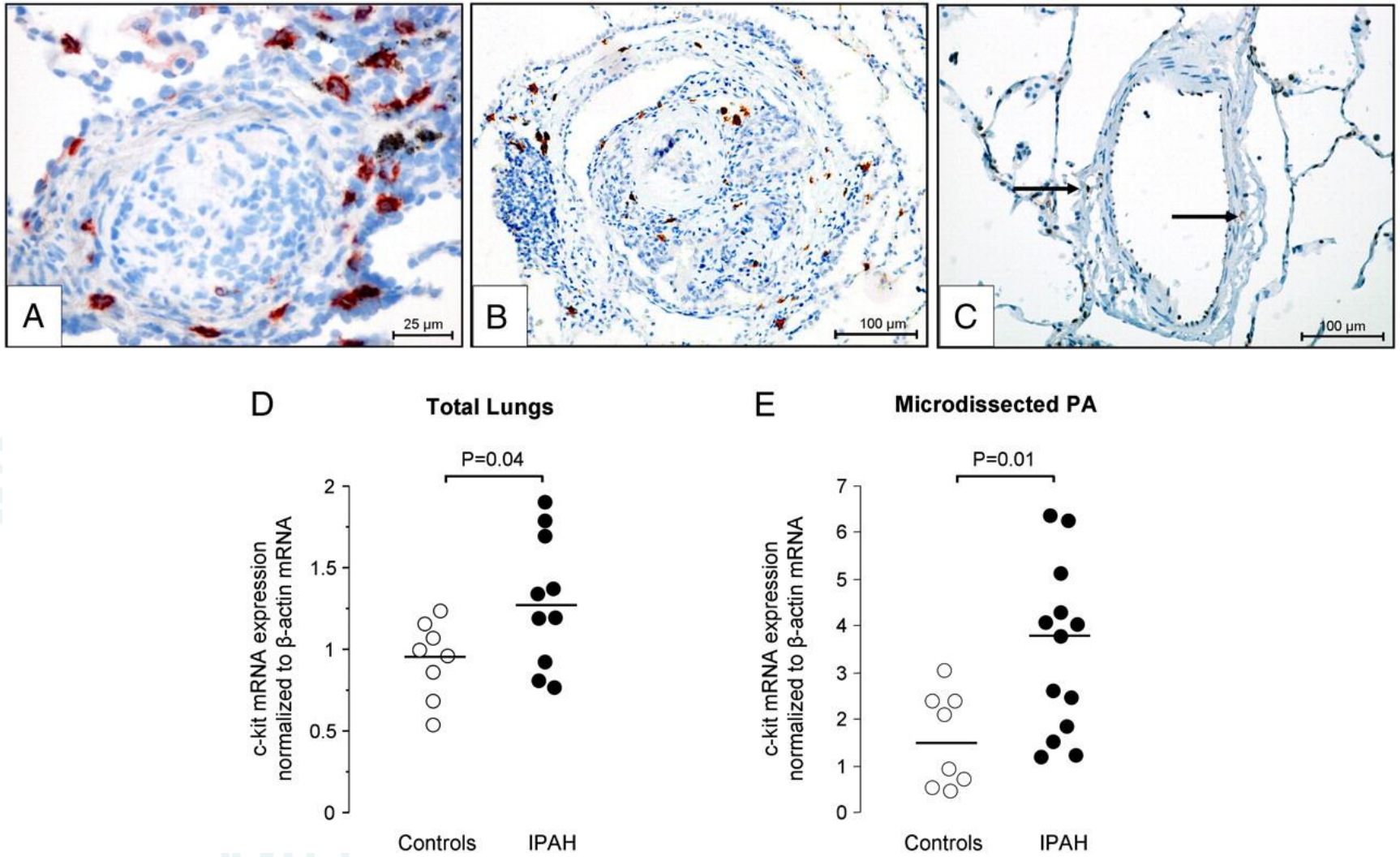
R Schermuly, E Dony, H D Montani, F Perros, N Gambaryan, B Girerd, P Dorfmuller, L Price, A Huertas, H Hammad, B Lambrecht, G Simonneau, JM Launay, S Cohen-Kaminsky, and M Humbert

Am J Respir Crit Care Med 2011, 184(1):116

c-KIT+ Cells Accumulate in Remodeled Vessels in PAH

Inflammation

Growth Factors



PA: pulmonary artery

Source: Montani, et al., *Am J Respir Crit Care Med* 2011, 184(1):116; Jonigk et al *Am J Path* 2011 179 67; Frid et al *AJ Physiol* 2009 297 L1059; Farkas et al *PloSOne* 2014 9 e89810; Mizuno et al *AJRCMB* 2012 47(5):679; Farha et al *Pulm Circ* 2012;12:220; Farha et al *Pulm Circ* 2014;4:452

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Growing Appreciation of the Role Macrophages Play in Vascular Remodeling in PAH

Inflammation

Growth Factors

Circulation

Circulation 2011 123;1986-1995

Early macrophage recruitment and alternative activation are critical for the later development of hypoxia-induced pulmonary hypertension

E Vergadi, MS Chang, C Lee, O Liang, X Liu, A Fernandez-Gonzalez, SA Mitsialis, S Kourembanas

JEM Journal of Experimental Medicine

J Exp Med 2014 Feb 10;211(2):263-80

Reduced BMPR2 expression induces GM-CSF translation and macrophage recruitment in humans and mice to exacerbate pulmonary hypertension

H Sawada, T Saito, N Nickel, TP Alastalo, J Glotzbach, R Chan, L Haghighat, G Fuchs, M Januszyk, A Cao, YJ Lai, V Perez, YM Kim, L Wang, PI Chen, E Spiekerkoetter, Y Mitani, G Gurtner, P Sarnow, and M Rabinovitch

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Macrophage-Mediated Inflammatory / Immunologic Response Contributes to Vascular Remodeling in PAH

Inflammation

Growth Factors

- CSF1R highly expressed on macrophages [1,2]
- Activated macrophages accumulate around pulmonary arterioles in PAH[3]; macrophage infiltration of lungs in PAH demonstrated in vivo with PET[4]
- Decreased BMPR2 induces GM-CSF and macrophage recruitment[5]
- In BMPR2 KO mice, pulmonary inflammation occurs due to activation of tissue macrophages[6]
- Inflammatory macrophages secrete PDGF and stimulate PASMC migration and proliferation in PAH[7]

Source: [1]Zhou et al *Cell* 2018;172:744; [2]Stanley & Chitu, *Cold Spring Harbor Perspect Biol* (2014) 6(6):a021857; [3]Savai, et al., *Am J Respir Crit Care Med* 2012, 186(9):897; [4]Park, et al, *Am J Respir Crit Care Med* 2020, 201(1):95; [5]Sawada, et al., *J Exp Med* (2014) 211 (2):263; 6Talati, et al, *PLoS One* (2014) 9(4):e94119; [7]Abid, et al, *Eur Respir J* 2019, 10;54(4):1802308

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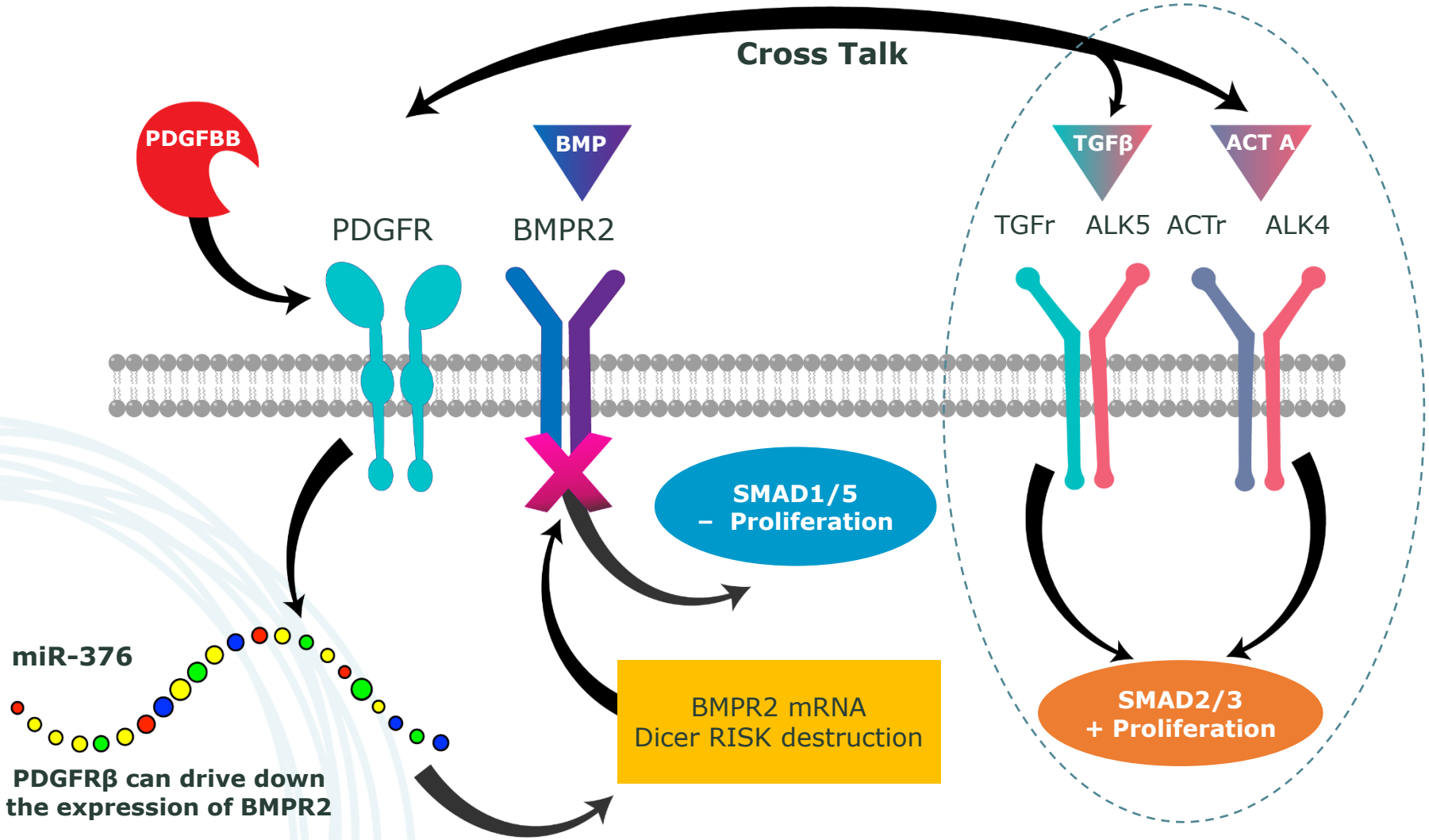
Crosstalk Between PDGF, BMPR2, and Activin Pathways

BMPR2/TGF Beta Signaling



Source: Adapted from Chen, et al. *BMC Genomics* 2016; Kudryashova et al. *Int J Molecular Sciences* 2018

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Summary of Novel PAH Treatment Approaches Discussed

Growth Factors: PDGFR and c-KIT

- PDGFRα/β drive PASMC and human lung fibroblast proliferation in neointimal PAH lesions
- c-KIT+ cells accumulate in remodeled vasculature and may secrete PDGF
- Relevance of targeting this pathway in PAH established in prior clinical studies

Inflammation

- Macrophages are a major component of perivascular inflammation
- CSF1R+ macrophages secrete PDGF and stimulate PASMC and fibroblast proliferation in pulmonary arteriolar lesions
- c-KIT positive cells contribute to perivascular inflammation

BMPR2/TGF Beta Signaling

- Significant cross-talk between PDGFR signaling and BMPR2; increased PDGF can lead to down-regulation of BMPR2 via micro-RNAs
- Potentially complimentary to other approaches targeting TGFβ /activin signaling

New therapeutic approaches are needed in PAH that address the disease's underlying pathogenesis of proliferation, inflammation, and fibrosis in a safe and tolerable way

Preclinical Insights and Early Development of Seralutinib

Larry Zisman, MD

Senior Director, Clinical Development

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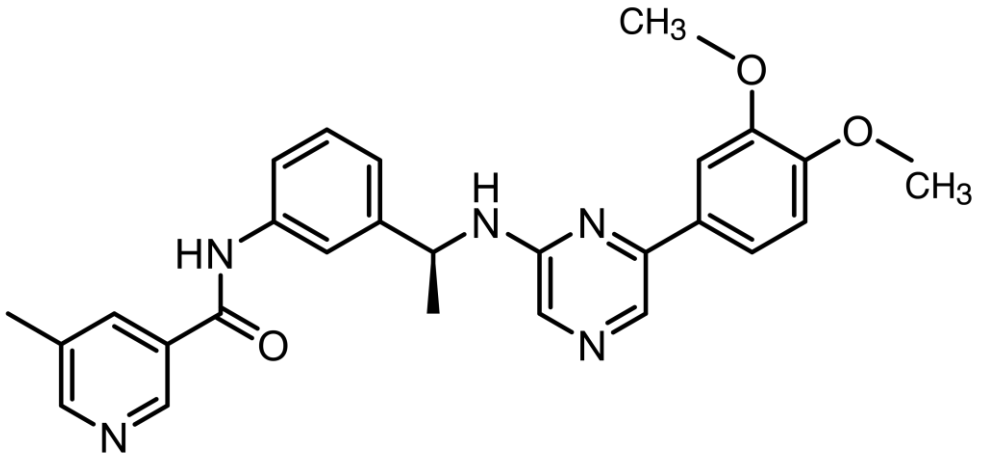
Overview of Seralutinib

- **Type of Drug:** Small molecule
- **Mechanism of Action:** PDGFRα and PDGFRβ, CSF1R, and c-KIT kinase inhibitor
- **Drug Properties:** Formulated as a dry powder for inhalation with excipient leucine; aerosol properties appropriate for deep lung deposition and retention
- **Stage of Development:** Phase 2
- **Therapeutic Area:** PAH (WHO Group 1 PH)
- **IP:** Patent protection to 2034[1]
- **Orphan Designation:** FDA and EMA



[1]Does not include available patent term extension. Corresponding patent(s) and patent application(s) with compound-specific claims.

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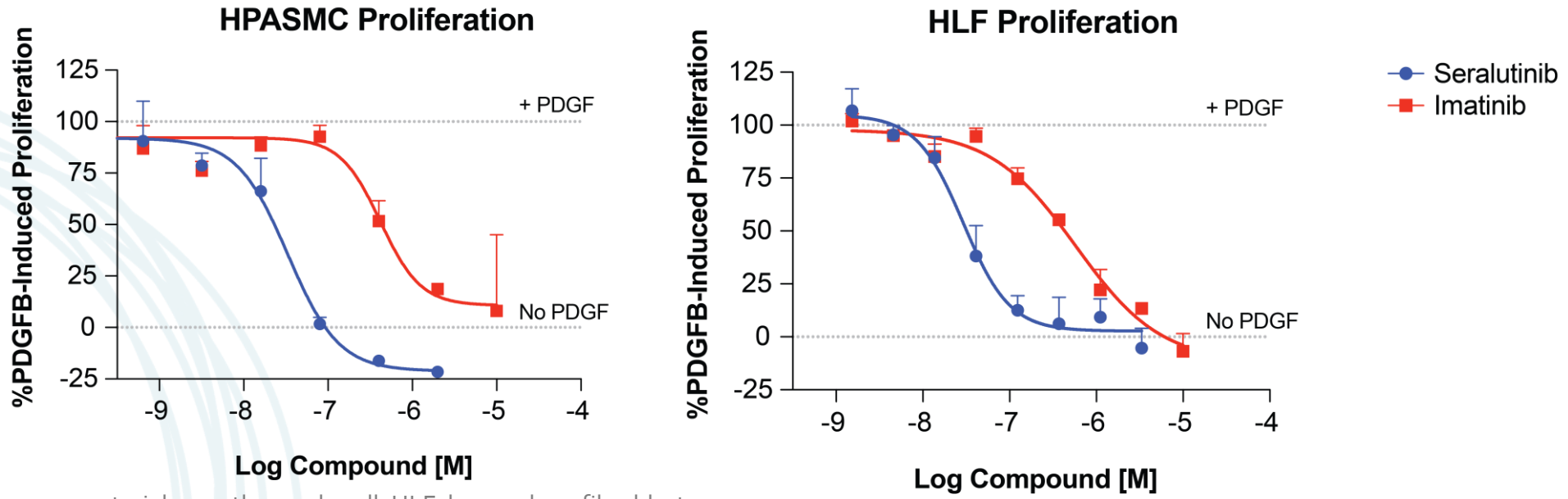
Seralutinib In Vitro Profile

Seralutinib is a potent PDGFR, CSF1R and c-KIT inhibitor

Compound	Cell Based IC50 (nM)				
	H1703 PDGFRα	HLF PDGFβ>α	PASMC PDGFRα=β	CSF1R	c-KIT
Seralutinib	32	29	33	8	14
Imatinib	62	579	419	1032	230

Seralutinib is highly potent in PASMC and HLF proliferation assays



HPASMC: human pulmonary arterial smooth muscle cell; HLF: human lung fibroblast

Source: Ten Freyhaus, *Arterioscler Thromb Vasc Biol* 2015, 35(5):1236; Barst, *J Clin Invest* 2005, 115(10):2691; Gomez-Arroyo, et al, *Am J Physiol* (2012) 302(10):L1014; Sawada, et al, *J Exp Med* (2014) 211 (2):263; Talati, et al, *PLoS One* (2014) 9(4):e94119; Abid, et al, *Eur Respir J* 2019, 10;54(4):1802308; Savai, et al., *Am J Respir Crit Care Med* 2012, 186(9):897; Montani, et al., *Am J Respir Crit Care Med* 2011, 184(1):116

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Kinome Screen: Seralutinib Selectivity Profile

Potential >70% inhibition at 1µM*

- EPHA5
- EPHA8
- EPHB2
- FGR
- PTK5
- FYN
- HCK
- KDR
- LCK
- LYN
- RET
- SRC N1

Imatinib >70% inhibition at 1µM Not Targeted by Seralutinib

- ABL1
- ABL2 (Arg) – 65%

Key Takeaways

- **Adverse effects related to potential off target kinase inhibition not observed in vivo to date**
  - **No adverse findings in chronic tox studies, including on pulmonary and cardiovascular systems; no hypertension**
  - **No adverse events related to potential off target kinase inhibition observed to date in clinical studies**
- Minimal systemic exposure reduces risk of adverse events
- Seralutinib shows no effect on pulmonary arterial endothelial cell function, in contrast to other tyrosine kinases inhibitors

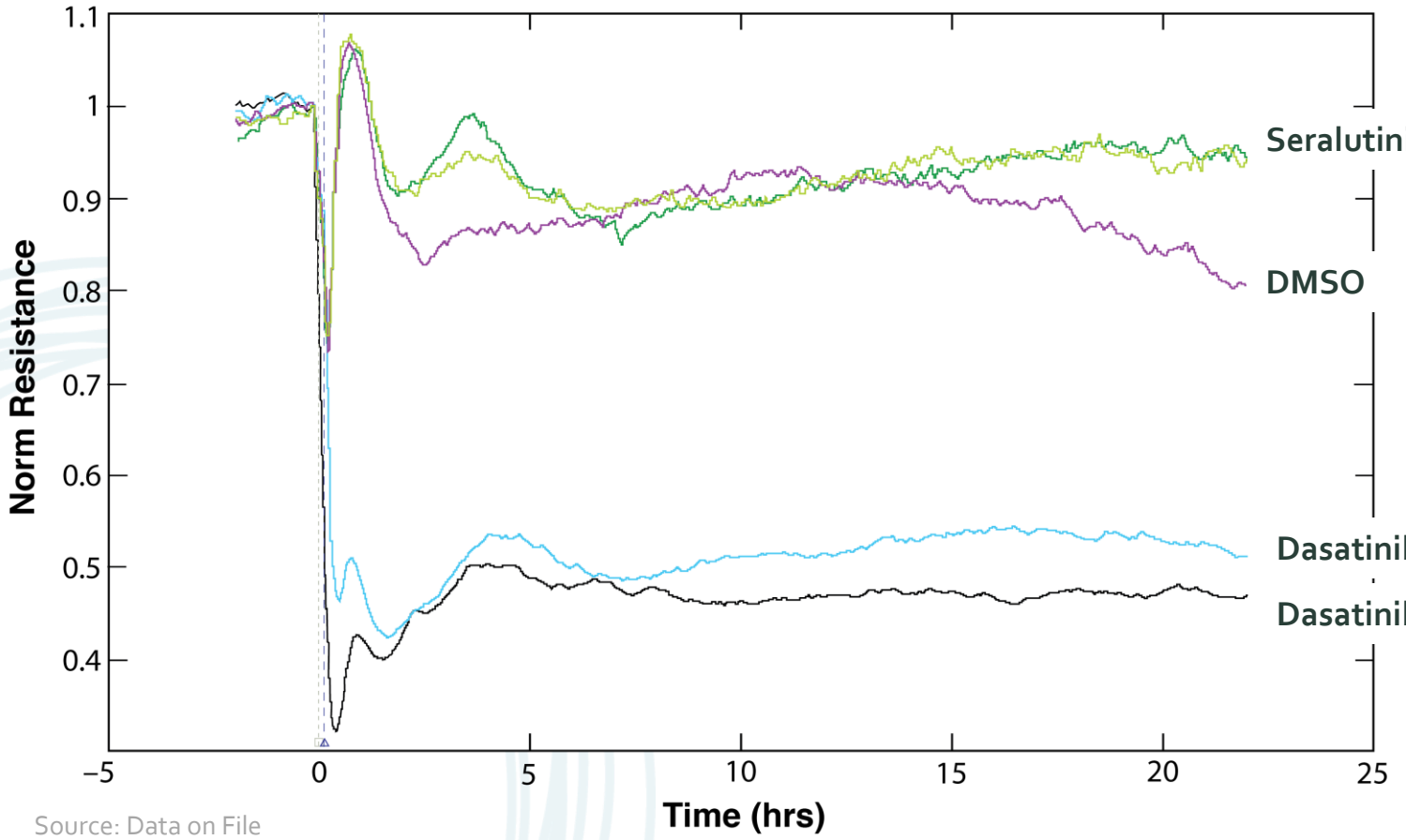
*Cell free assay at [ATP] Km; excludes PDGFRα, PDGFRβ, CSF1R, and c-KIT (selectivity in cellular assay confirmed and shown on prior page)

Source: Data on File

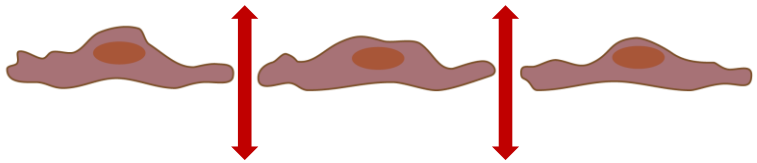
Seralutinib Has No Adverse Effect on Normal Endothelial Barrier Function

Transendothelial resistance assay:

- Seralutinib maintains normal pulmonary arterial endothelial barrier function, while tyrosine kinase inhibitor dasatinib has severe adverse effect



Normal endothelial cell barrier



Damaged endothelial cells

Source: Data on File

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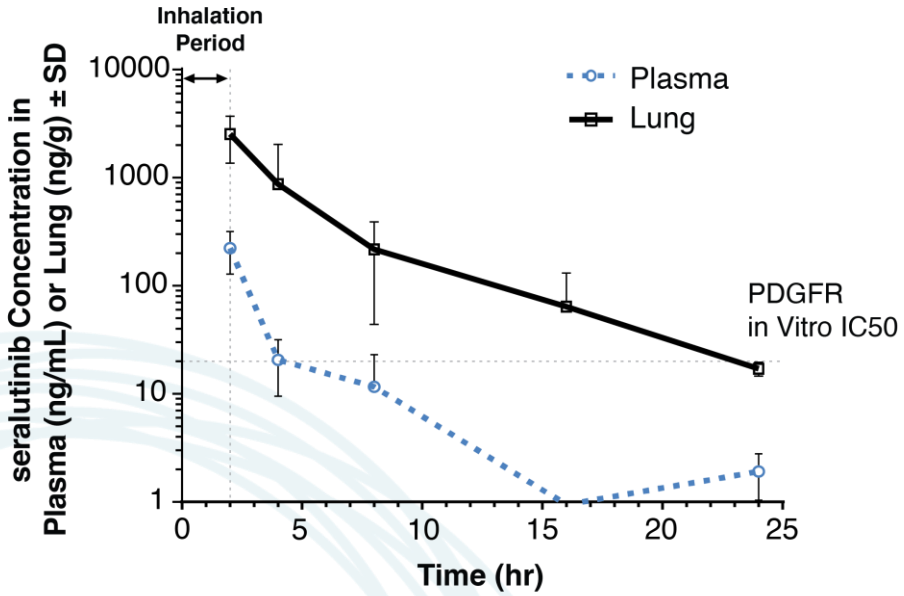
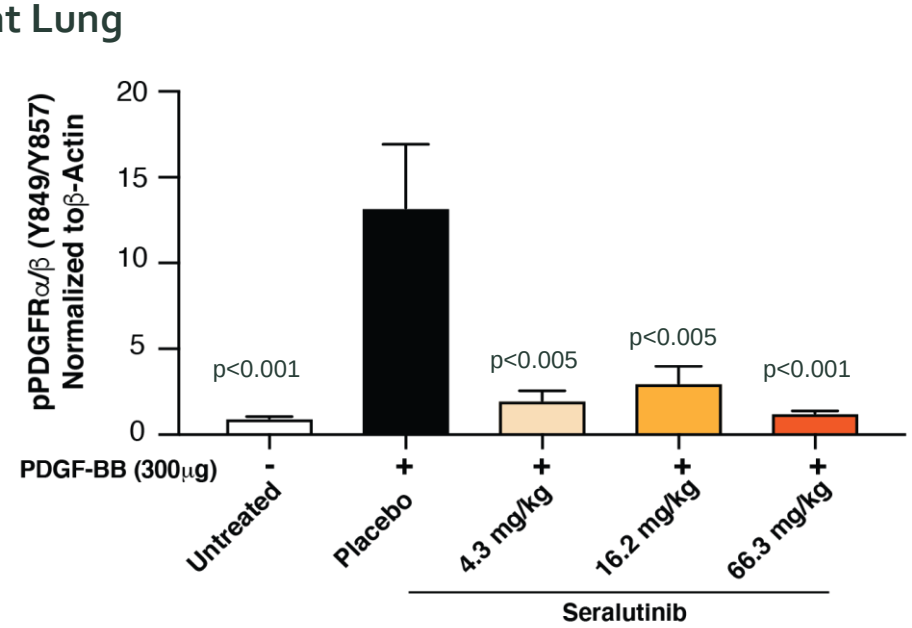
Inhaled Seralutinib Has Sustained Lung Concentrations and Engages Target in Lung

Seralutinib* Displays ~ 30X Rat Lung-to-Plasma Exposure Ratio



Seralutinib Inhibits PDGFR Phosphorylation In Vivo



- Seralutinib designed for deep lung deposition and rapid systemic clearance to minimize systemic adverse events
- Systemic PK profile from human single ascending dose study similar to systemic profile in rat
- Extensive PK/PD modeling projected BID (twice daily) dosing to sustain target coverage

* Seralutinib delivered at 4.3 mg/kg via 2hr passive inhalation

Source: Data on File

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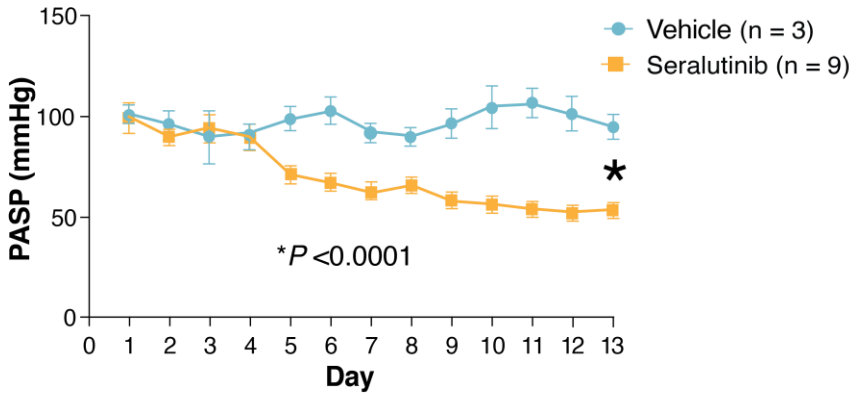
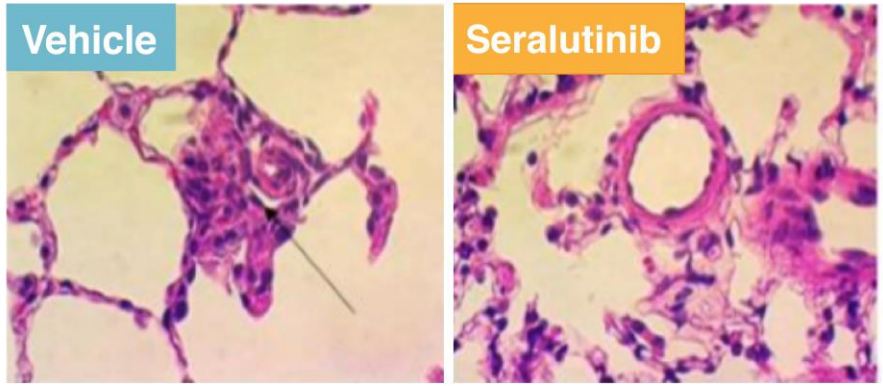
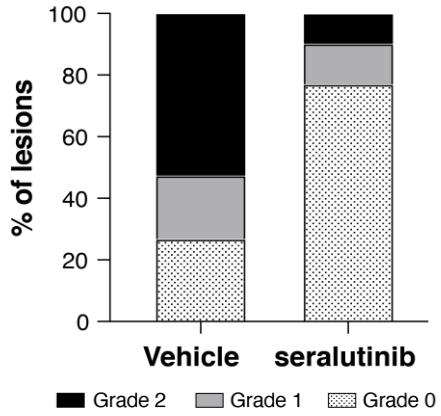
Seralutinib Demonstrates Efficacy in the SU5416/Hypoxia and MCT/PN Models

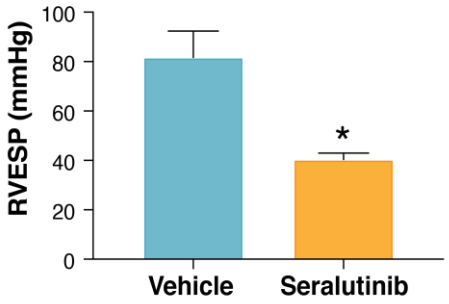
SU5416/H telemetry study

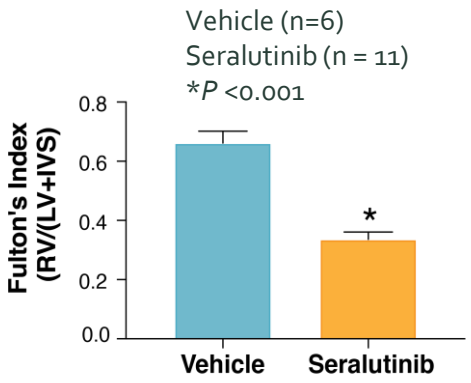


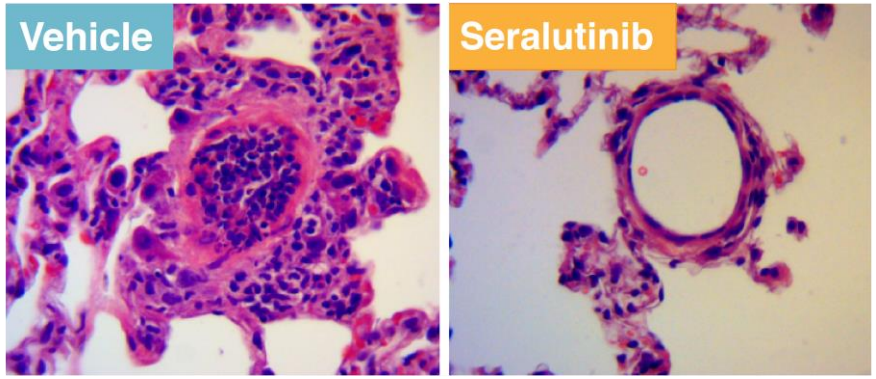


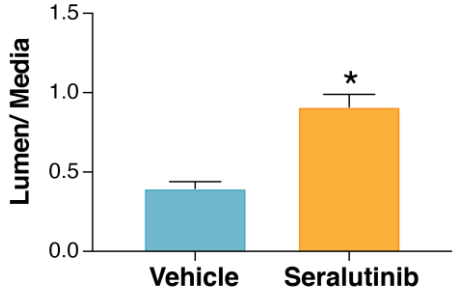


MCT/PN study









SU5416: Sugen 5416 MCT/PN: monocrotaline pneumonectomy; PASP: pulmonary artery systolic pressure; RVESP: right ventricular end-systolic pressure-volume; RV/(LV+IVS): right ventricular weight/weight of left ventricle plus interventricular septum

Source: Galkin, et al., Manuscript in preparation; Sitapara, et al., *Circulation* 2019;140: A12947.

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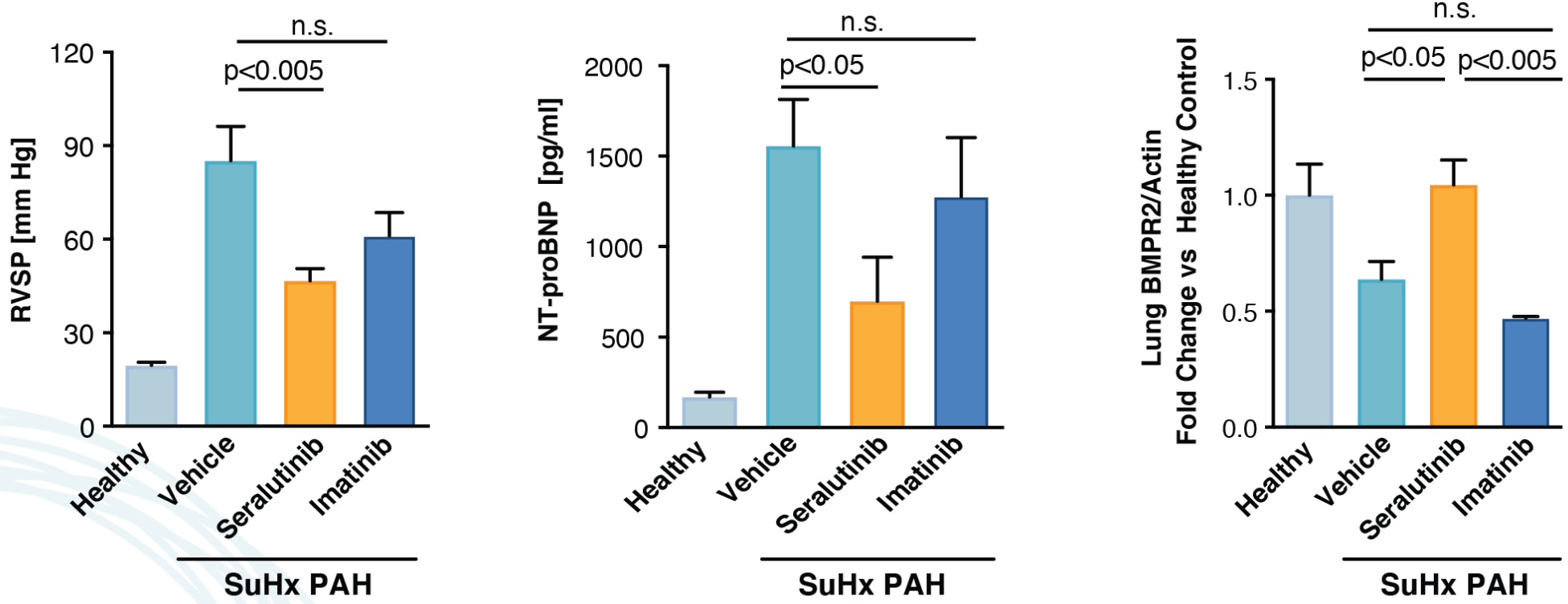
Inhaled Seralutinib Outperformed Oral Imatinib in a Head-to-Head Preclinical SuHx PAH Study



Data presented as Mean +/- SEM. Statistical analysis was performed using one-way ANOVA with Dunnett's multiple comparisons test (Healthy n=8; Vehicle n=7; Seralutinib n=9; Imatinib n=7)

- Seralutinib treatment led to a significant improvement in RVSP
- Seralutinib reduced circulating levels of NT-proBNP and increased lung BMPR2 protein expression

SuHx: Sugen hypoxia; RVSP: right ventricular systolic pressure
Source: Galkin, et al. Circulation 2019, 140: A11102

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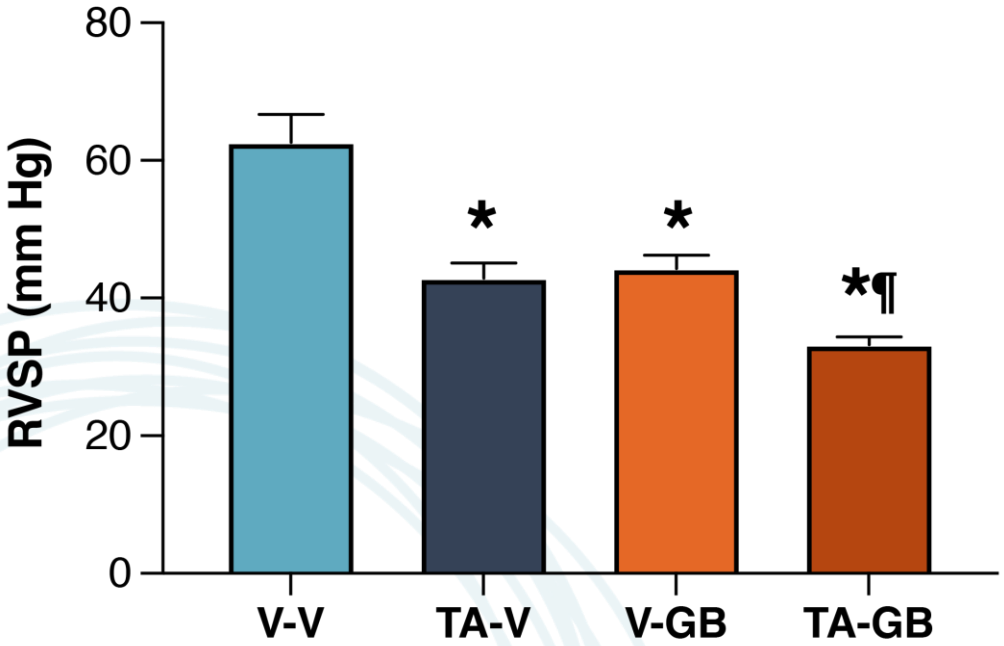
Additive Benefit of Seralutinib When Combined With Tadalafil and Ambrisentan in an Animal Model of PAH

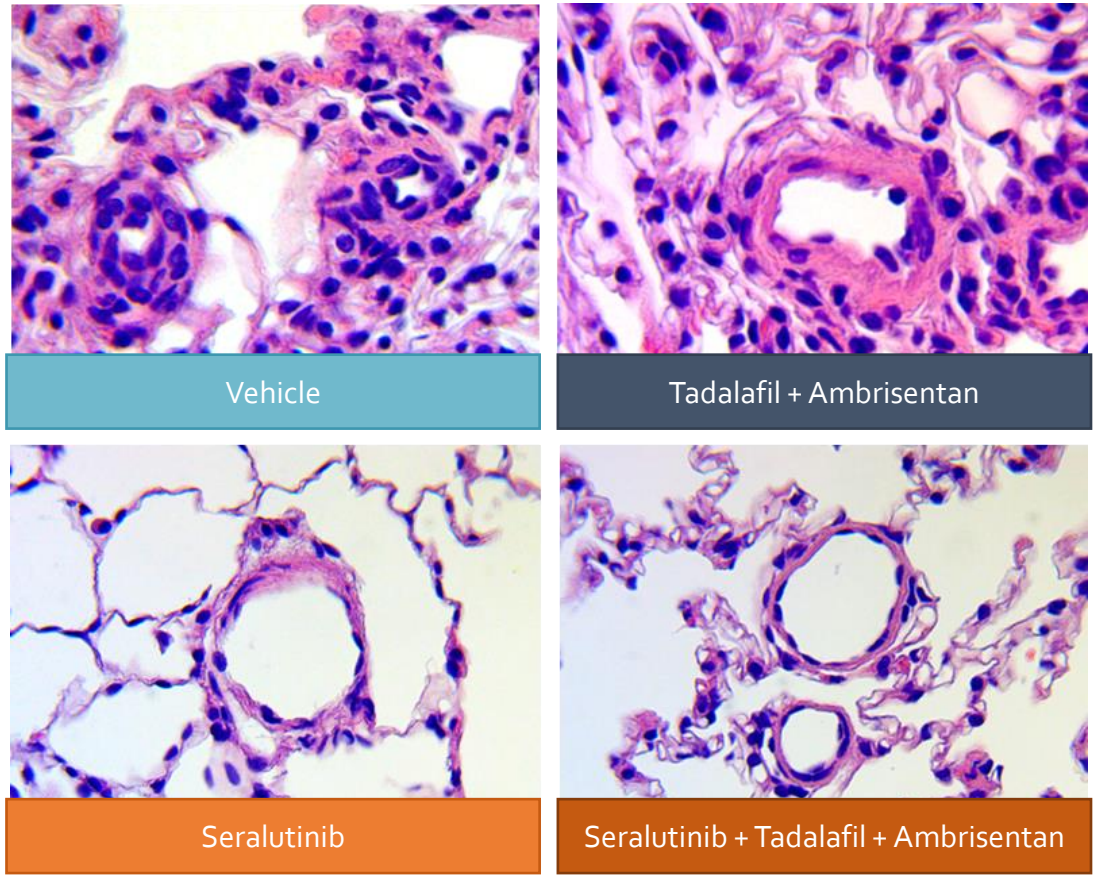
Seralutinib when added to tadalafil + ambrisentan resulted in further improvement in right ventricular systolic pressure



V=vehicle, TA=tadalafil + ambrisentan, GB=seralutinib

*p<0.01, compared with V-V; ¶ p<0.01, compared with TA-V and V-GB.

Seralutinib provided greater improvement in pulmonary vascular remodeling than tadalafil + ambrisentan



Source: Sitapara, et al., *Am J Respir Crit Care Med* 2017, 195:A6897

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Seralutinib is a Promising Candidate for the Treatment of PAH

- ✓ Targets several kinases central to PAH pathobiology, potential to reverse remodeling in PAH
  - PDGFRα/β
  - CSF1R
  - c-KIT
- ✓ Seralutinib is more potent in cell-based assays compared to imatinib, could overcome some of the limitations observed with imatinib in PAH clinical trials.
- ✓ No adverse effects on normal endothelial cell function
- ✓ Designed for delivery by oral inhalation
  - In rats, inhaled seralutinib results in approximately 30-fold higher lung exposure compared to systemic exposure
- ✓ Demonstrates positive effects in animal models of PAH
  - Preclinical efficacy with seralutinib has been demonstrated in several animal models of severe PAH, with superior performance compared to oral imatinib
  - Seralutinib when combined with tadalafil and ambrisentan showed additive benefit in a preclinical model of PAH

Seralutinib Clinical Development Program

Robert Roscigno, PhD

Vice President,
Clinical Development

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Seralutinib Clinical Development Program

Formulation and Delivery System

Review of Clinical Data to Date

- Phase 1a
- Phase 1b

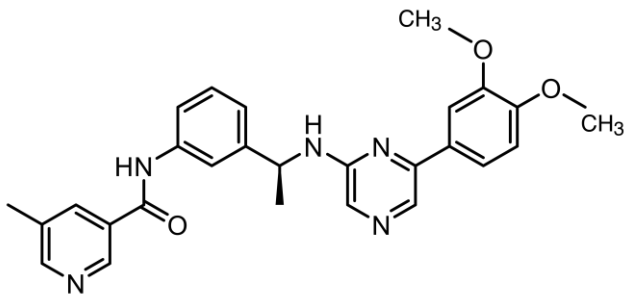
Overview of Phase 2 Program

TORREY STUDY

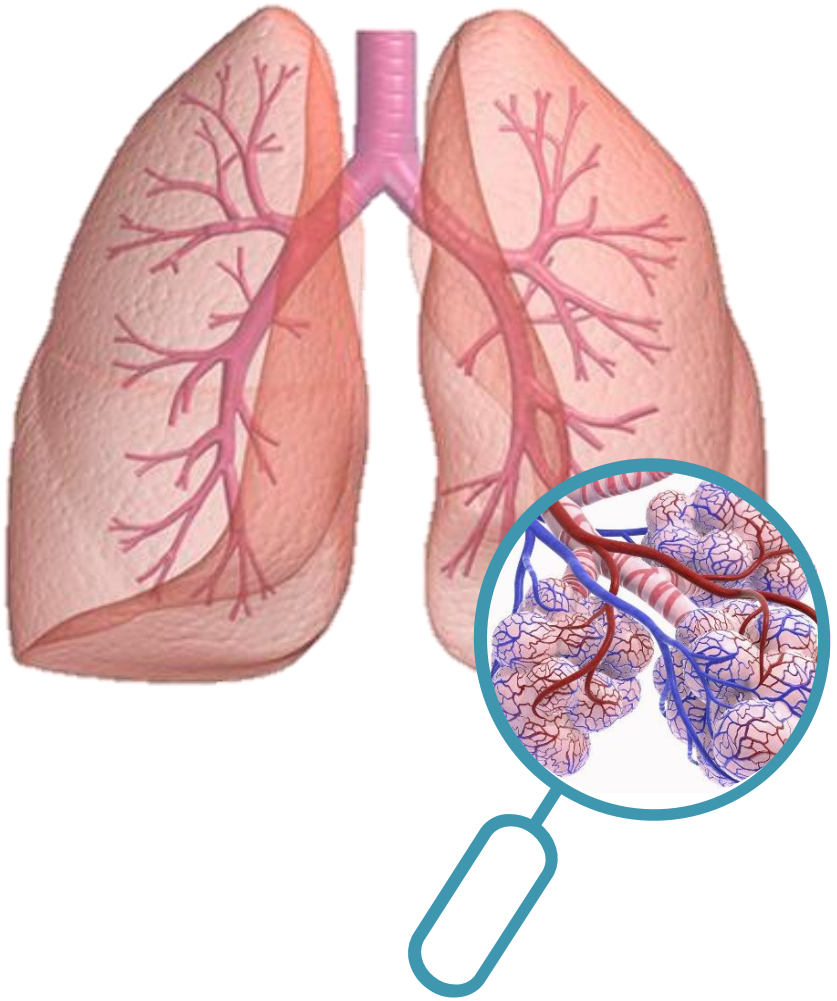
Seralutinib Overview

- Seralutinib is a small molecule platelet-derived growth factor receptor (PDGFR), colony stimulating factor 1 receptor (CSF1R), and c-KIT kinase inhibitor being developed as an inhaled treatment for PAH
- Good potency and kinase specificity profile
- Formulated for deep lung delivery via dry powder inhaler with convenient BID administration

Seralutinib structure



Dry Powder Inhaler from Plastiape



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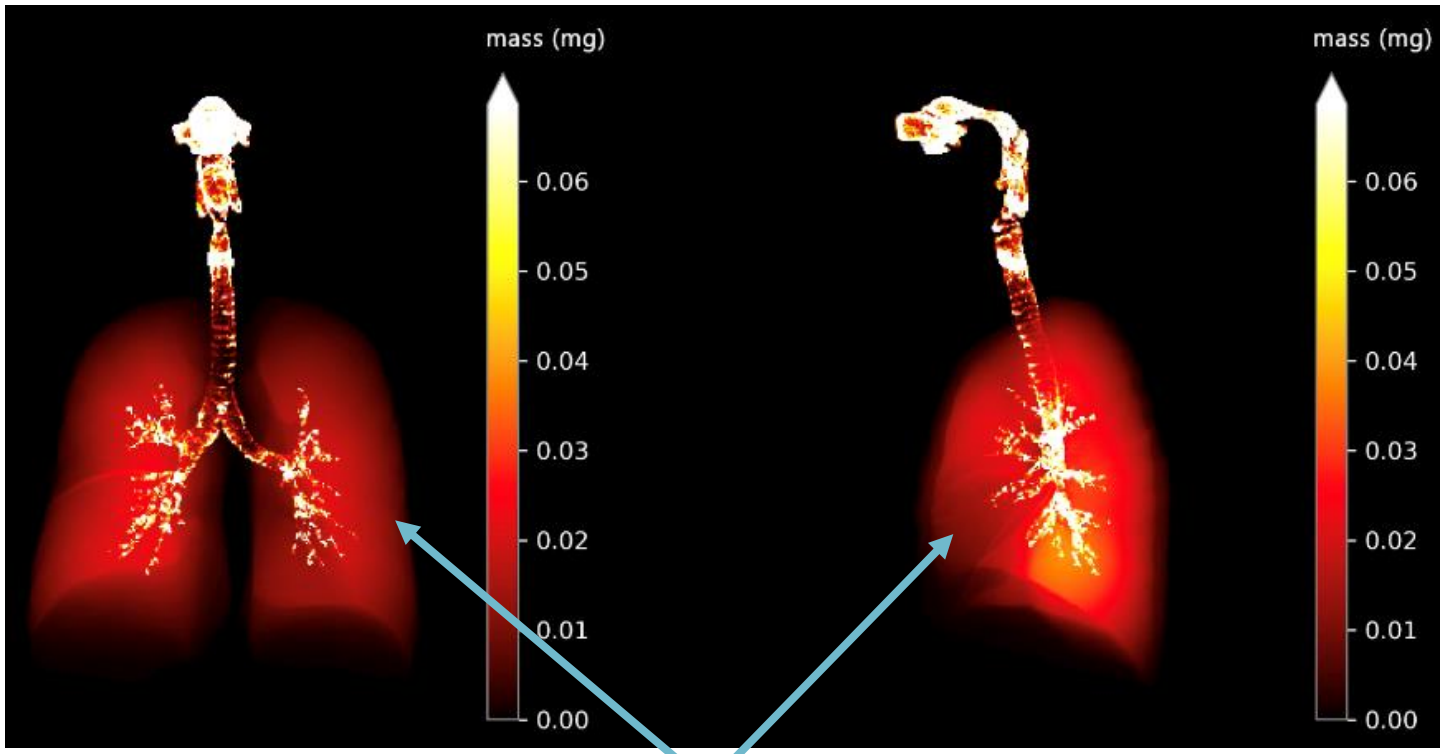
Seralutinib Formulation Engineered for Deep Lung Deposition

- Seralutinib particle characteristics carefully controlled in manufacturing process to optimize deep lung deposition

- Deposition modeled using Computational Fluid Dynamic Simulation (inputs were key particle characteristics and used CT scans from normal lungs)

Computational Fluid Dynamic Simulations Demonstrate Deep Lung Deposition



Red signal indicates deep lung deposition of seralutinib

Source: Data on File

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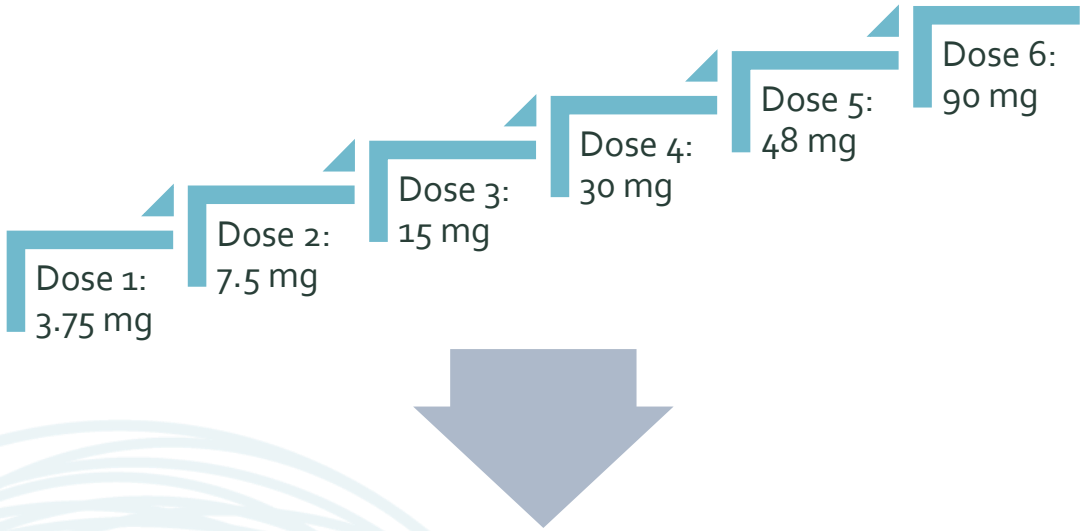
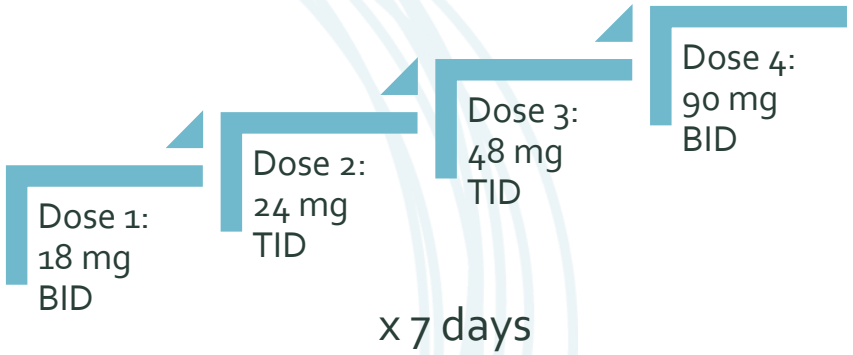
Phase 1a SAD and MAD Clinical Trial in Healthy Human Volunteers

Part A: Single Ascending Dose



Part B: Multiple Ascending Dose



- Randomized, placebo-controlled Ph 1a study: Seralutinib was administered to 62 healthy adult subjects in single doses of 3.75 to 90 mg and multiple doses of 18 to 90 mg twice daily (BID) for 7 days.
- Subjects were healthy, non-smoking adults, 18-55 years of age, body mass index 18-32 kg/m^2
- Seralutinib or matching placebo powder was delivered by inhalation using Plastiape Inhaler RS01
- Part A comprised the single ascending dose study, in which subjects received one of five dose levels (Figure 1)
- In Part B, seralutinib dose and schedule was determined by safety and PK data from Part A
- Within each dose level, six subjects were to receive active drug (seralutinib) and two subjects were to receive placebo

Source: Li, et al., Presented at ATS 2020, Poster A2907

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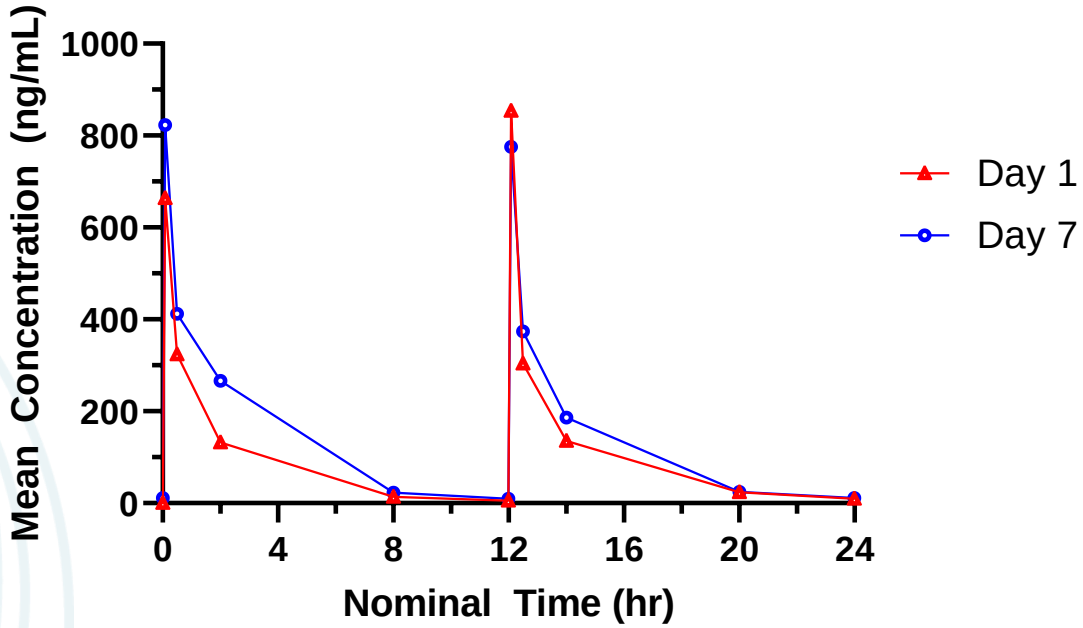
Phase 1a SAD and MAD: *Pharmacokinetics in Healthy Human Volunteers*

- **Seralutinib was dose proportional and well-tolerated at all doses tested**
- Following single and multiple oral inhalations, seralutinib was rapidly absorbed into the systemic circulation; median time to maximum concentration (T_{max}) ranged from 3 to 5 minutes post-dose
- Seralutinib plasma concentrations declined rapidly. Mean terminal elimination half-life ranged from 3.1 to 5.8 hours.

Mean Plasma GB002 Concentration vs Time Profiles, Days 1 and 7: 90 mg Twice Daily x 7 Days



Source: Li, et al., Presented at ATS 2020, Poster A2907

Phase 1a SAD and MAD: *Safety Outcomes in Healthy Human Volunteers*

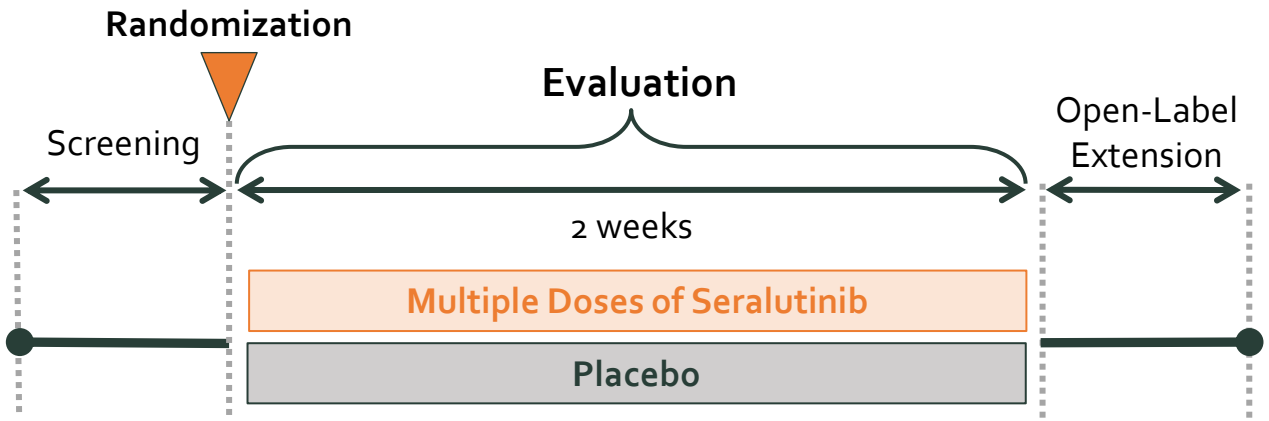
- No serious adverse events (SAEs) were reported
- No reported adverse events (AEs) led to study drug discontinuation
- No dose-limiting toxicities
- The most common adverse events were throat irritation and cough, which were mild in severity and similar in incidence to placebo
- No clinically significant abnormal laboratory values

Phase 1a SAD and MAD Conclusions

- Following single and multiple oral inhalations, seralutinib was rapidly absorbed into and cleared from the systemic circulation
  - Seralutinib exposure increased in a dose-proportional manner following single and multiple dose administration
  - After C_{max}, seralutinib plasma concentrations declined rapidly
- No SAEs or withdrawals due to treatment emergent adverse events (TEAEs) reported for this study
  - Seralutinib was observed to be well tolerated at doses of up to 90 mg BID, with only mild TEAEs

Seralutinib was well-tolerated at doses up to 90 mg BID (the highest dose tested)

Phase 1b Study (GB002-1001) in Patients with PAH



- First patient enrolled Q1:20; prior to pandemic-related site closures, 5 patients (4 active and 1 placebo) completed two weeks of treatment
- Study was re-opened with COVID precautions in Q3:20, allowing enrollment of 3 additional patients (N = 8 total)

Study Objectives

Primary

- To evaluate the safety and tolerability of inhaled seralutinib

Secondary

- To evaluate pharmacokinetics (PK) of seralutinib

Exploratory

- To evaluate pharmacodynamic (PD) biomarker analysis on blood samples and/or circulating cells and/or airway samples

Key Inclusion Criteria

- **Diagnosis PAH,** WHO group 1, FC II-IV
- Prior cardiac catherization data c/w PAH
- Baseline 6MWT >100 m
- On PAH background medications

Dosing

- 45 mg to 90 mg BID dose escalation at PI discretion

Source: clinical trials.gov/NCT03926793

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Phase 1b Summary of Demographics and Baseline Characteristics

	N = 8
Demographics	
Age (Range):	30 - 63 years old
Female / Male:	7 patients / 1 patient
NYHA Functional Classification at Baseline	
Functional Class II:	6 patients
Functional Class III:	2 patients
PAH Etiology	
Idiopathic:	4 patients
Heritable:	2 patients
Scleroderma:	1 patient
Systemic Sclerosis:	1 patient
Background PAH Medications	
Double Therapy:	3 patients
Triple Therapy:	5 patients
PGI or IP Receptor Agonist:	5 patients

Enrolled patients' baseline characteristics representative of target population for seralutinib

Source: Data on File

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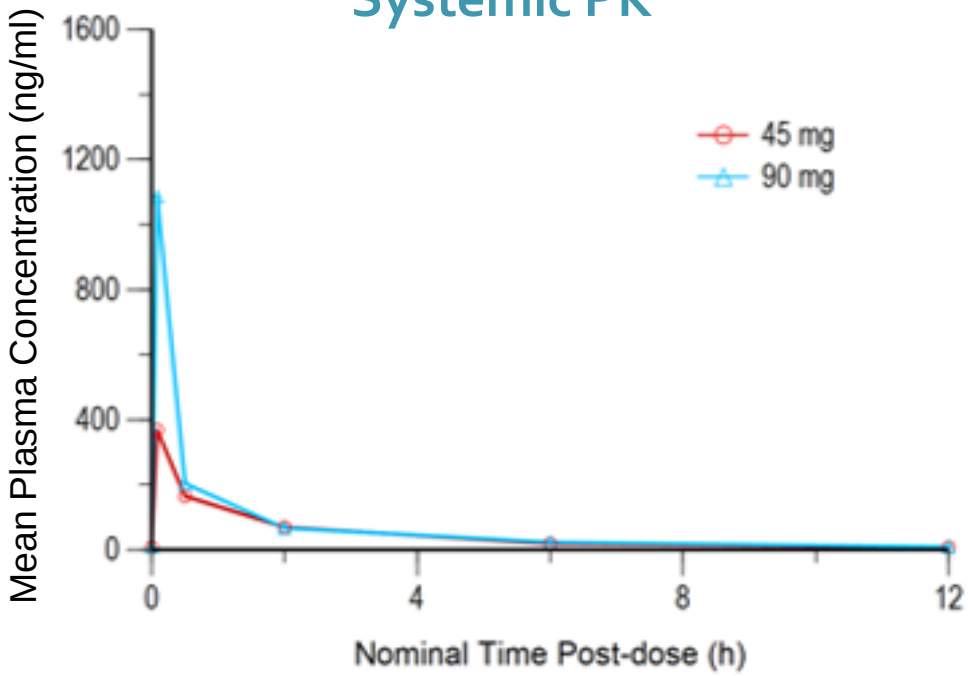
Preliminary Phase 1b Results: *Safety and Pharmacokinetics*

- Seralutinib generally well tolerated in PAH patients
- All 8 subjects completed the 2-week study
- No SAEs were reported
- The most frequently reported AEs were:
  - Cough (mild-moderate)
  - Headache (mild)
- There were no clinically significant changes in labs, ECGs, PFTs, and vital signs.
- PK in PAH patients consistent with PK data from Healthy Volunteers
- Systemic PK characterized by low systemic exposure and rapid clearance

Systemic PK



- Profile is consistent with an inhaled therapy and the potential for a favorable therapeutic index

ECG: electrocardiogram; PFT: pulmonary function test
Source: Data on File

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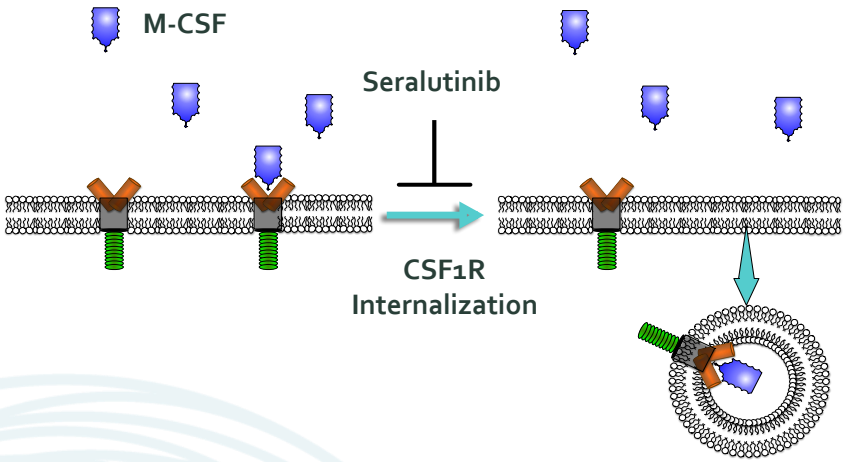
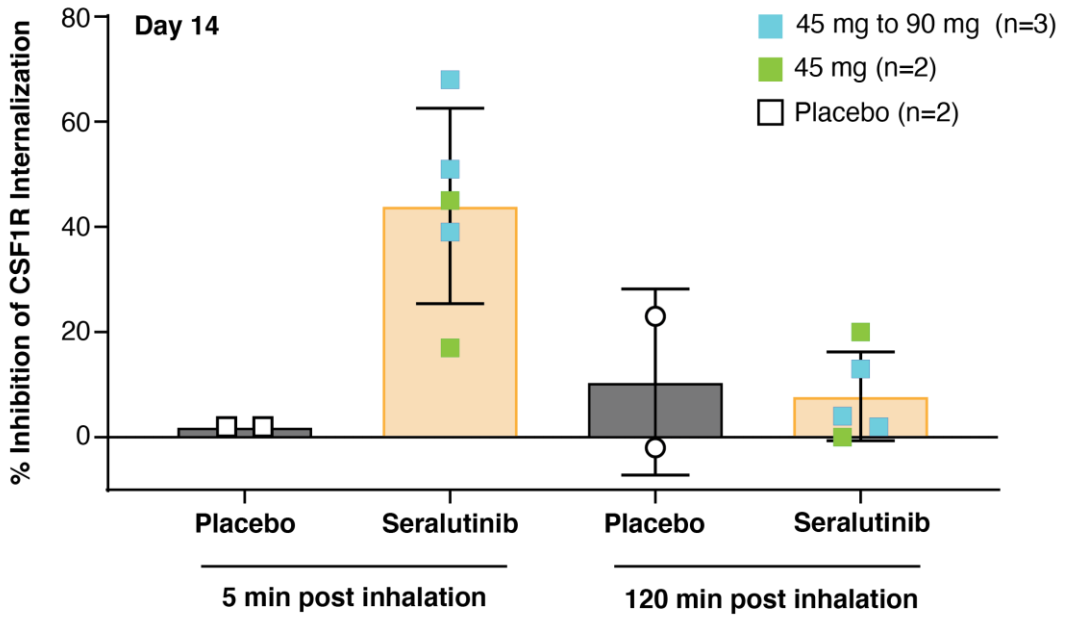
Seralutinib Target Engagement Confirmed in Whole Blood CSF1R Stabilization Assay Across All Dose Levels in PAH Patients





- M-CSF induces activation and subsequent internalization of CSF1R in blood monocytes
- Seralutinib blocks CSF1R internalization at 5 min post inhalation demonstrating successful Target Engagement
- Seralutinib rapid clearance from circulation is associated with reduced inhibition 120 min post inhalation

M-CSF: macrophage colony-stimulating factor;
Source: Data on File

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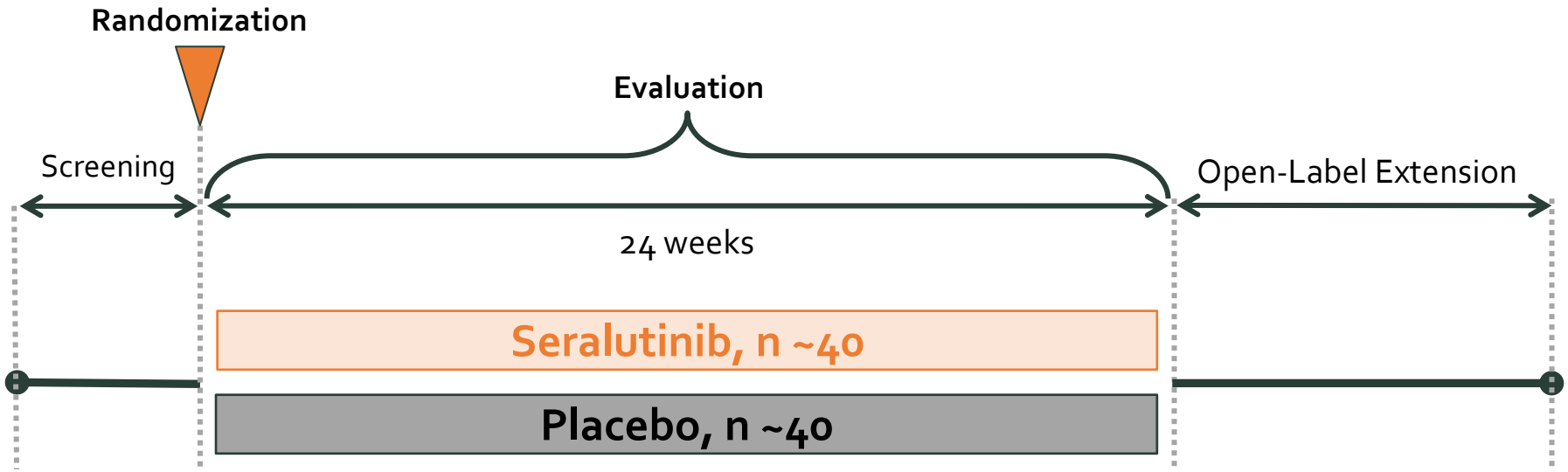
Phase 1b Study Summary: Seralutinib Promising Preliminary Results

- ✓ Well tolerated in PAH patients
- ✓ PK profile:
  - Consistent with Phase 1a healthy volunteer results
  - Consistent with an inhaled therapy
- ✓ Demonstrated target engagement (CSF1R)

Seralutinib has a promising profile, ready for Phase 2

TORREY: *Phase 2 Study of Seralutinib in Patients With Functional Class II and III PAH*

TORREY STUDY



Patient Population	Functional Class II and III PAH patients on standard background therapy (including triple therapy); PVR >/= 400 dyne*s/cm^5
Endpoints	**Primary:** PVR Change from Baseline at Week 24 **Key Secondary:** 6MWD Change from Baseline at Week 24

PVR: pulmonary vascular resistance; 6MWD: six-minute walk distance
Source: clinical trials.gov/NCT04456998

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TORREY Study: *Phase 2 Study Objectives and Endpoints*

Objectives

Primary

- Determine the effect of seralutinib on improving pulmonary hemodynamics in subjects with World Health Organization (WHO) Group 1 PAH who are WHO Functional Class (FC) II or III

Secondary

- Determine the effect of seralutinib on improving exercise capacity in this population

Safety

- Evaluate the safety of seralutinib in this population

End Points

Primary

- Change in pulmonary vascular resistance (PVR) using right heart catheterization (RHC) from Baseline to Week 24

Secondary

- Change in distance achieved on the six-minute walk test (6MWT, Δ6MWD) from Baseline to Week 24

Safety

- Incidence of treatment-emergent adverse events (TEAEs), serious TEAEs (SAEs), and treatment-emergent adverse events of special interest (AESIs)

Exploratory

- Change in WHO Functional Class & Risk Score, right ventricle (RV) function by imaging (echocardiography), European Quality of Life, NT-proBNP, disease modification sub-studies

Source: clinical trials.gov/NCT04456998

TORREY Study: *Key Inclusion Criteria*

- A current diagnosis of symptomatic PAH classified by one of the following:
  - iPAH, HPAH, PAH-CTD
  - PAH associated with anorexigen or methamphetamine use
  - Congenital heart disease with simple systemic to pulmonary shunt at least 1 year after surgical repair
- 6MWD ≥ 150 meters and ≤ 550 meters at screening
- WHO FC II or III
- Treatment with standard of care PAH background therapies, including prostacyclins
- RHC data consistent with the diagnosis of PAH and PVR ≥ 400 dyne·s/cm^5

RHC: right heart catheterization
Source: clinical trials.gov/NCT04456998

TORREY Study: *Key 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; if on coumadin or NOAC, these drugs can be withdrawn, if clinically appropriate, during the screening period and should have normal coagulation parameters prior to randomization

Source: clinical trials.gov/NCT04456998

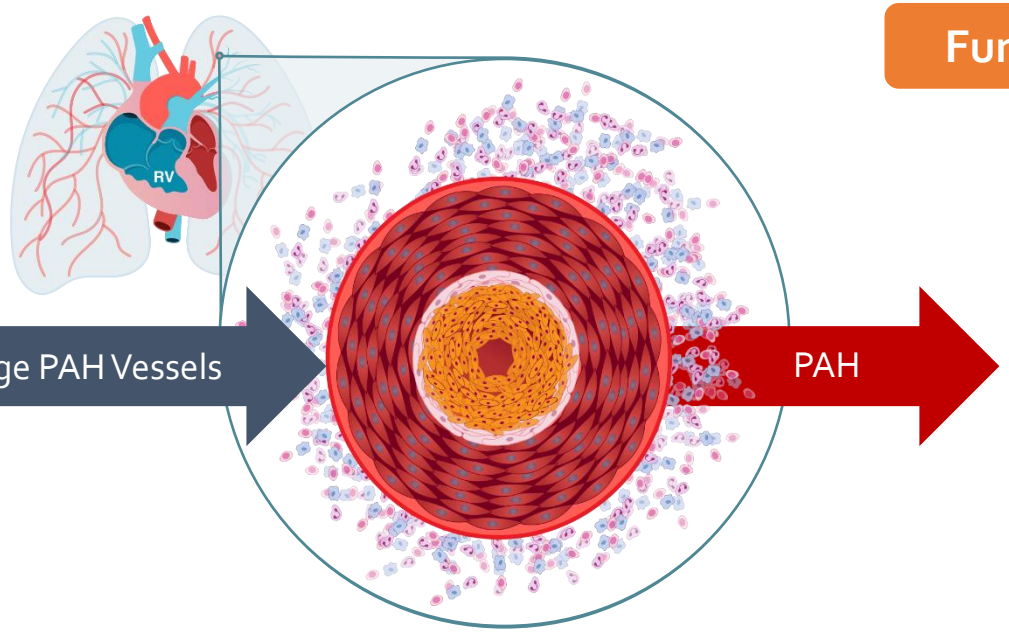
TORREY Study: *Operational Considerations*

- Anticipated Enrollment:
  - 80 Subjects (1:1 randomization, 40/group)
  - WHO Group 1 PAH (WHO FC II and III)
- Investigational Sites: ~70
  - Upsized to give optionality based on COVID-19 continued impact
  - North America, Europe, Australia
- Covid-19 Contingencies Built Into Protocol:
  - Opportunity for home health nurse at certain visits for AE assessment, lab draws, and other study related procedures
  - Visit windows relaxed at certain visits to allow greater flexibility

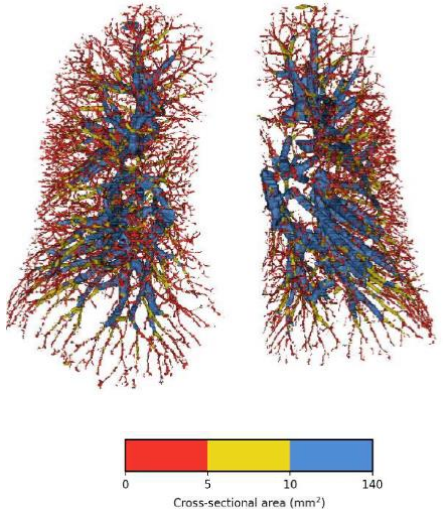
Source: Data on File

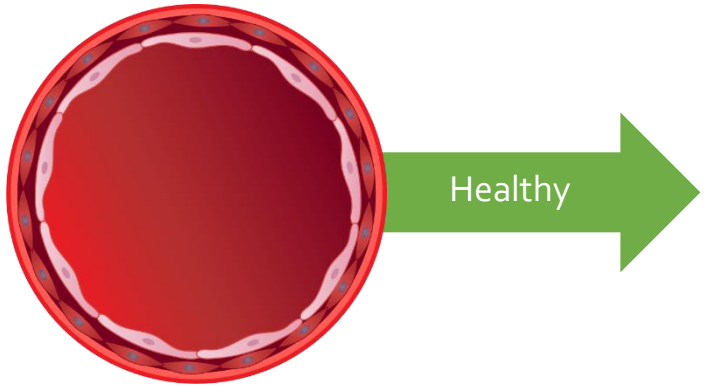
FLUIDDA CT Sub-Study: *Investigational Imaging Modality to Assess Pulmonary Vascular Remodeling in PAH*

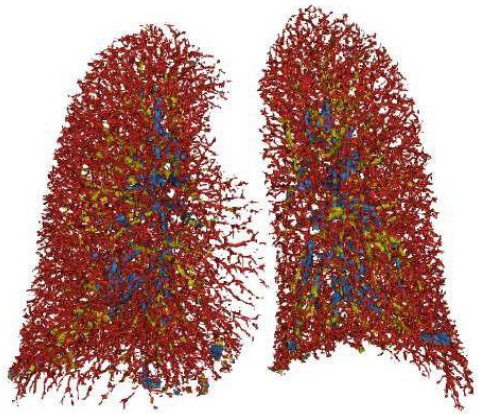
High Resolution CT



Functional Respiratory Imaging







- **Purpose:** Demonstrate pulmonary arterial reverse remodeling by seralutinib
- **Endpoint for Phase 2:** Change in pulmonary arterial vascular volume for vessels with cross-sectional area week 24 vs baseline

Source: Data on File

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Seralutinib Heart Rate (HR) Sub-Study

HR Sub-Study Goal:

Assessment of HR during and after the 6MWT to determine if various HR biomarkers provide insight into prognosis or treatment effect beyond standard 6MWT, of seralutinib compared to placebo

- Assess relationship of HRE (heart rate expenditure) acquired during 6MWT to baseline and subsequent changes in RV (right ventricular) function to determine if HRE is a more sensitive measure of response to therapy than 6MWT alone
- Assess HRE on a beat-by-beat basis to determine absolute beat decrement and rate of HR decline at pre-specified and exploratory timepoints and their relationship to baseline hemodynamics and ECHO metric of RV function
- Show how HR and HRE provide insight into disease burden and response to therapy

Source: Data on File

Commercial Opportunity

Mario Orlando

Vice President,
Commercial, New Product Planning

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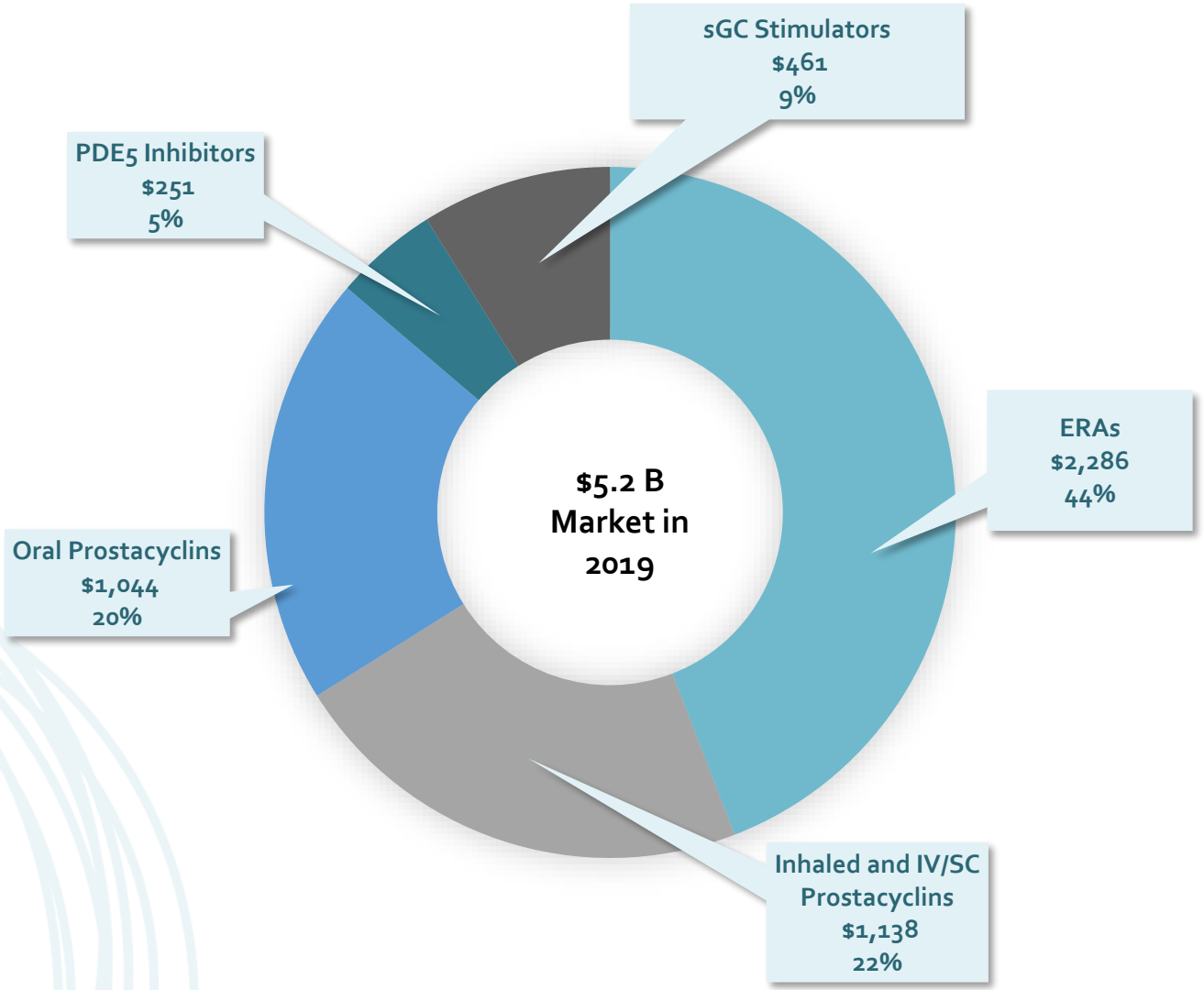
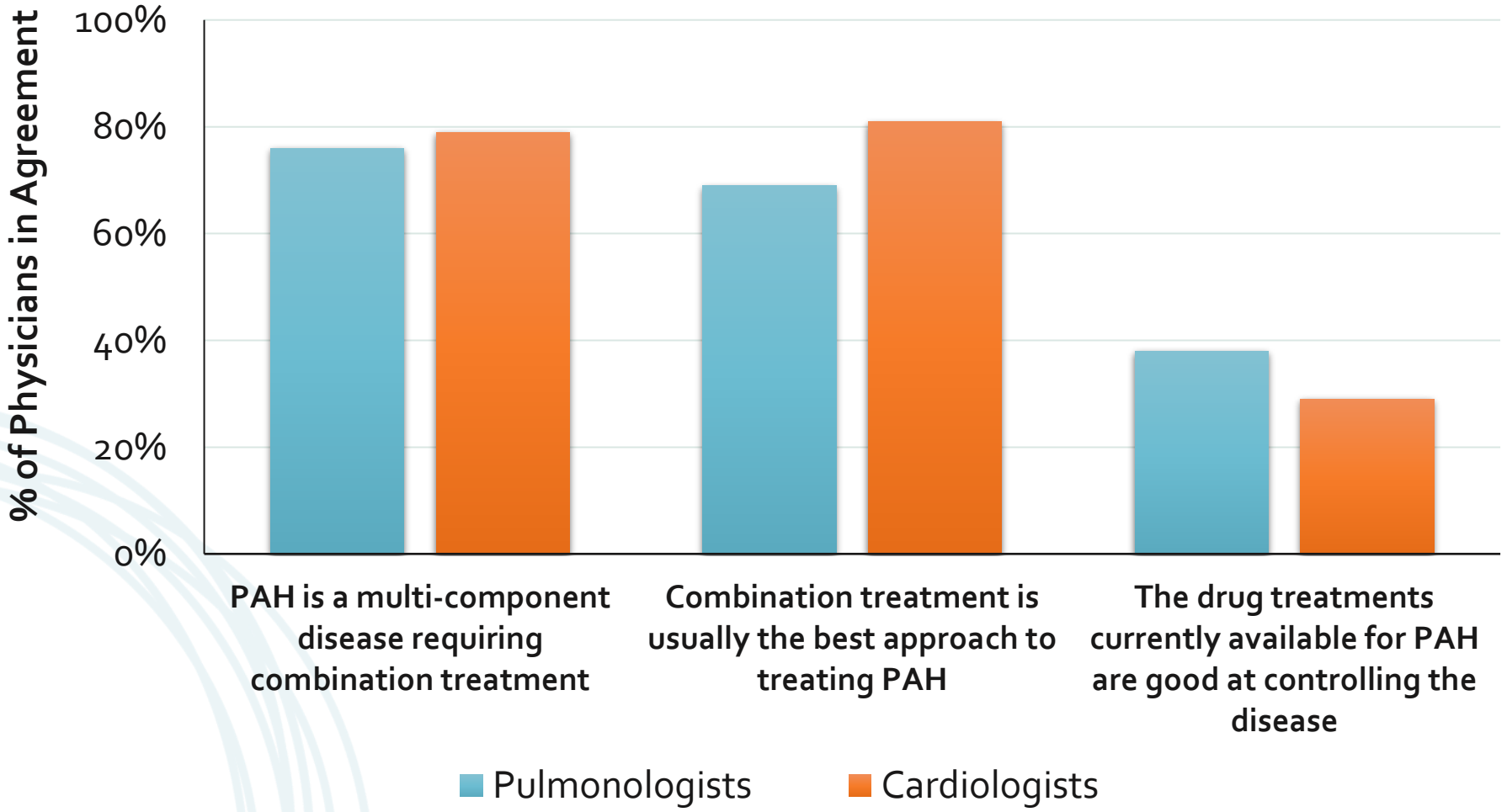
The PAH Therapeutic Market Generated ~$5.2B in Revenue in 2019



WW PAH Market by Class (2019)
Millions of dollars

Source: Company full year 2019 filings

Treaters Largely Agree That PAH is a Multi-Component Disease That Should Be Treated With Combo Therapy, but There is an Unmet Need for New Therapies



Source: Adelphi PAH DSP II (2019) Physician Survey data from USA PAH physicians (n=103)

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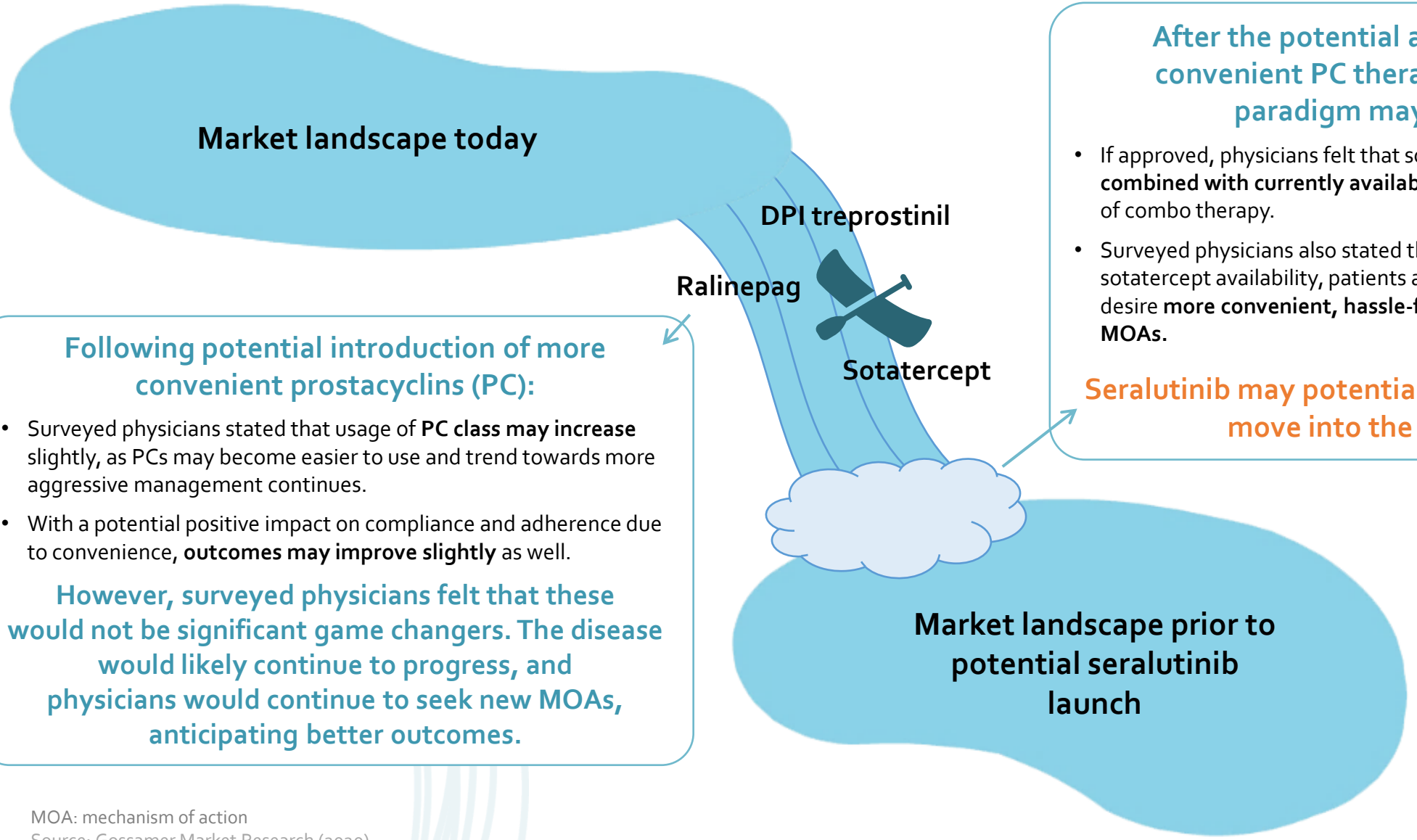
In Recent Market Research, Physicians Consistently Cited a Need for Therapies to Treat the Underlying Pathology of PAH



Following potential introduction of more convenient prostacyclins (PC):

- Surveyed physicians stated that usage of **PC class may increase** slightly, as PCs may become easier to use and trend towards more aggressive management continues.
- With a potential positive impact on compliance and adherence due to convenience, **outcomes may improve slightly** as well.

However, surveyed physicians felt that these would not be significant game changers. The disease would likely continue to progress, and physicians would continue to seek new MOAs, anticipating better outcomes.

After the potential availability of more convenient PC therapy, the treatment paradigm may shift again:

- If approved, physicians felt that sotatercept would likely be **combined with currently available therapies,** increasing the use of combo therapy.
- Surveyed physicians also stated that beyond potential sotatercept availability, patients and doctors would continue to desire **more convenient, hassle-free therapies with unique MOAs.**

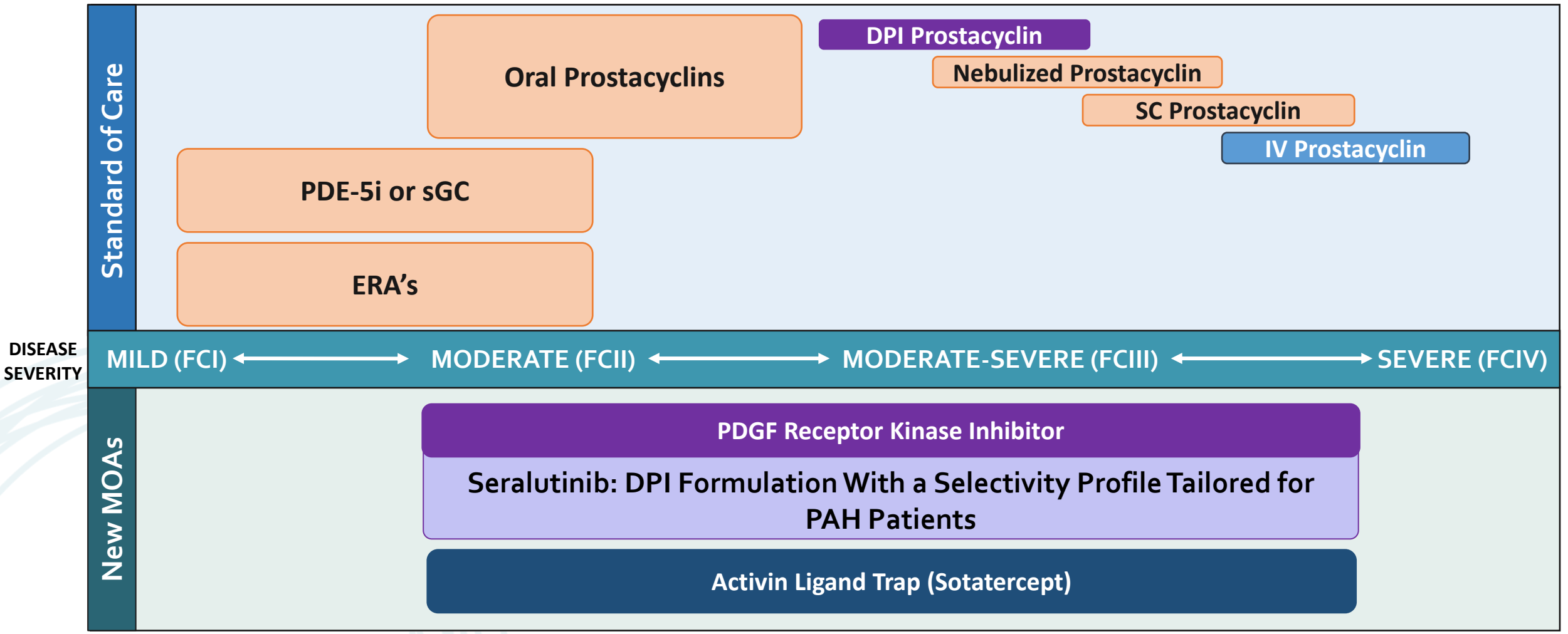
Seralutinib may potentially be well positioned to move into the PAH market.

MOA: mechanism of action
Source: Gossamer Market Research (2020)

Seralutinib Value Story

- Current standard of care in PAH does not fully address underlying pathological mechanisms of disease
  - Even for PAH patients on maximal standard of care therapy (triple combo with parenteral prostacyclins), unmet needs remain high with significant morbidity and mortality
- Seralutinib is a unique inhaled small molecule kinase inhibitor with an innovative selectivity profile targeting PDGFR α/β, c-KIT, and CSF1R, and modulating BMPR2. Targeting of these pathways is proposed to address underlying fibrotic, inflammatory, and proliferative pathological mechanisms that characterize PAH
- Seralutinib is self-administered via convenient DPI inhalation
- Seralutinib has the potential to be additive to standard of care therapies, extending efficacy beyond what is currently attainable with maximal combination therapy

Seralutinib Offers a New, Multifaceted Approach to Treating PAH, Differentiating it From the Competitive Landscape



Seralutinib is being evaluated on-top of background therapy (≥1 therapy)

*Hypothesized positioning based on internal analysis

KEY

- Approved Self-Admin. Tx
- Novel Self-Admin. Tx*
- Approved Physician Admin. Tx
- Novel Physician-Admin. Tx*

Q&A

Robert Roscigno, PhD

Vice President,
Clinical Development

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Closing Remarks

Faheem Hasnain

Co-Founder, Chairman
and Chief Executive Officer

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Thank you for joining us today

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