

#### **Corporate Presentation**

August 2024

### Forward Looking Statements

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### I. Seralutinib Overview

### Phase 3 Pulmonary Hypertension Program Partnered with Chiesi

PROGRAM	CLASS (Route of Admin.)	INDICATION	PHASE 1	PHASE 2	PHASE 3	Partner
Seralutinib	PDGFR, CSF1R,	Pulmonary Arterial Hypertension (PAH)	Ph. 3 PROSEI  Completed Phase 2  Met Primary Endpoint  Well-Tolerated	RA Study Ongo	oing	<ul> <li>Chiesi</li> <li>50 / 50 US Profit Split</li> <li>Gossamer to receive</li> </ul>
(GB002)	c-KIT Inhibitor Pulmonary Hypertension Associated with Interstitial Lung Disease (PH-ILD)		Future Develo	opment se 3 Expected Mid-20.	25	mid-to-high teens royalties on ex-US sales  • \$146mm regulatory & \$180 sales milestones  • Gossamer leads global development & US commercialization in PAH & PH-ILD

# Seralutinib is Poised to be a Potential Paradigm-Shifting Therapy in PAH

- Seralutinib is a novel inhaled kinase inhibitor, currently in an ongoing registrational Phase 3 for the treatment of PAH
- In the Phase 2 TORREY study, seralutinib demonstrated statistically significant<sup>3</sup>:
  - Reduction in pulmonary vascular resistance (PVR primary endpoint)
  - Reduction in NT-proBNP, a biomarker of right heart strain
  - Changes in right heart structure & function
- In an open-label extension study, seralutinib showed a continued reduction in PVR, with a near doubling of improvement from Week 24 to Week 72<sup>4</sup>
- Seralutinib has been generally well tolerated to date
  - No reports of GI or CNS bleeding events<sup>4</sup>
- PROSERA Phase 3 study initiated Q4:23; topline results expected Q4:25
- Patent protection to 2039<sup>5</sup>; Orphan Drug Designation from FDA and EMA





Low long-term survival (5-year: 57%<sup>2</sup>)

#### PAH Has High Unmet Need & Significant Disease Burden

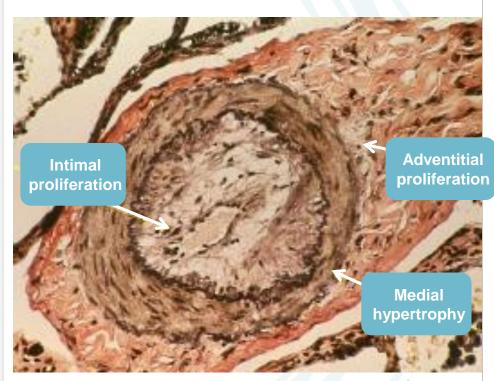
#### Pulmonary Arterial Hypertension (PAH)

- 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
- Progressive disease and often fatal
- Heart works harder to pump blood to the lungs, potentially leading to right heart failure

#### **Symptoms**

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

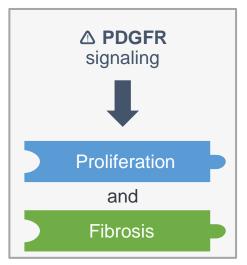
### PAH is Characterized by Vascular Remodeling

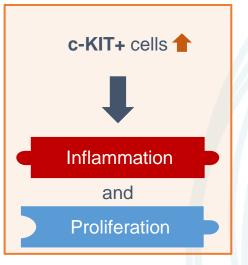


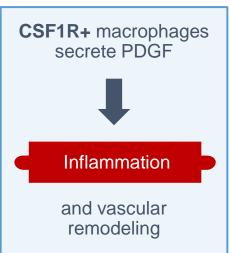
Muscular pulmonary artery from iPAH patient<sup>1</sup>

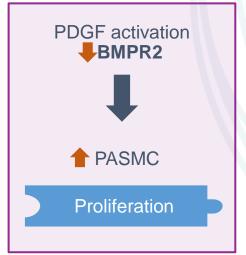
### Contributing Factors to Vascular Remodeling

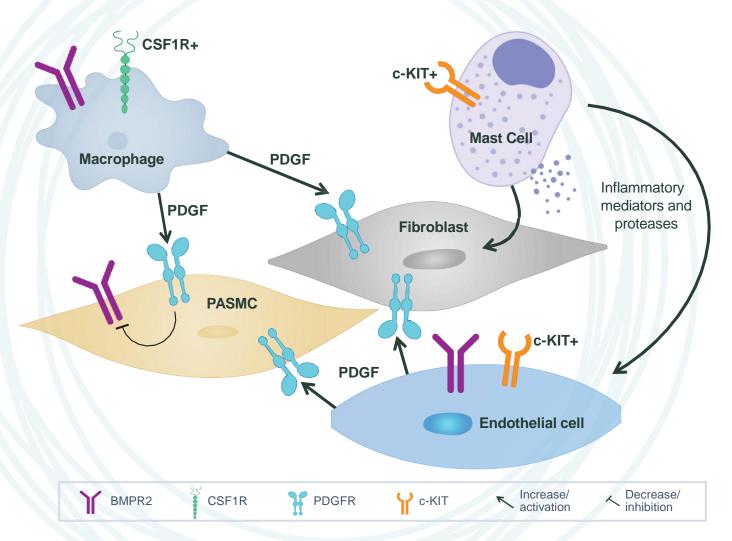
Role of PDGFR, CSF1R, c-KIT and Interactions with BMPR2











### In the Phase 3 IMPRES Study of Imatinib in PAH, Safety Liabilities Outweighed Clinically Meaningful Efficacy





#### **Clinical Efficacy Results**

**Phase 3 IMPRES Study** 

- Primary Endpoint:
  - 6-Minute Walk Distance (6MWD)
  - 32-meter improvement (pbo-adj.)\*
- Secondary Endpoint:
  - Pulmonary Vascular Resistance (PVR)
  - 32% reduction (pbo-adj.)\*

#### Clinical Safety / Tolerability

**Phase 3 IMPRES Study** 

- Adverse Events:
  - High rate of GI side effects
  - 44% SAE rate for imatinib group
  - 8 subdural hematomas across study and extension
- Discontinuations:
  - 33% for imatinib group, with most occurring in first 8 weeks of trial

# Seralutinib Employs Multiple Strategies to Mitigate Imatinib's Liabilities

## Molecule Specifically Designed for PAH

- Imatinib was developed & approved as an anti-cancer therapy
- Seralutinib utilized Phase 3 IMPRES learnings and targets underlying biology of PAH, including PDGFR $\alpha/\beta$ , CSF1R and c-Kit
- Seralutinib avoids c-ABL inhibition

# Improved Selectivity Against Targets of Interest

- Increased potency\* across target kinases v. imatinib
  - Increased potency against the PDGFRα isoform
  - Greater than ten-fold higher potency against PDGFRβ, c-Kit, and CSF1R

#### Designed for Inhalation

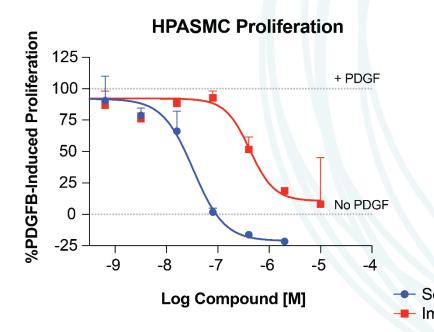
- Inhalation limits systemic exposure to mitigate systemic AEs, while directly getting drug to site of disease
- As part of inhalation process, some drug product is inevitably swallowed
  - Swallowed / ingested drug can enter systemic concentration
  - Seralutinib designed to have limited oral bioavailability (~5%)

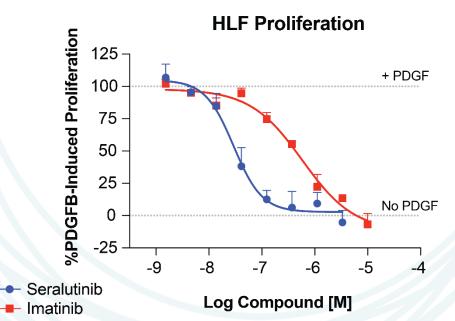
### Seralutinib In Vitro Profile

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

		Cell Based IC50 (nM)				
Compound	<b>H1703</b> PDGFRα	<b>HLF</b> PDGFβ>α	<b>PASMC</b> PDGFRα=β	CSF1R	c-KIT	
Seralutinib	32	29	33	8	8	
Imatinib	62	579	419	1032	301	

#### Seralutinib is highly potent in PASMC and HLF proliferation assays





### Seralutinib Utilizes Convenient Dry Powder Inhaler



### A Well-Suited Partner

 Global biopharmaceutical group with international R&D and commercialization infrastructure & operations, headquartered in Italy



- Over 85 years of experience, operations in >30 countries, >7,000 employees world-wide, including ~700 in R&D, and >€3 billion in revenue in 2023
- Chiesi's therapeutic focus perfectly aligns with seralutinib: AIR (respiratory disease), RARE (rare diseases), & CARE (specialty care, including cardiovascular disease)
- Global reach & areas of focus position Chiesi to enhance seralutinib's access to pulmonary hypertension (PH) patients across the globe



Encompasses products & services for the treatment of respiratory diseases among patients of all ages, from newborns to the elderly.

Asthma • COPD • PAH • IPF



Focusing on the treatment of patients living with rare or ultra-rare diseases.

Rare Immunologic Diseases



Combines products & services that support special care provided by medical professionals, as well as consumer healthcare/over the counter.

**Cardiovascular Diseases** 

gossamerbio

### Value of Partnership to Gossamer

Provides Adequate Capital & Global Commercial Partner for Investment in Commercial Launch of PAH

- Bolstered Gossamer cash balance
- Gossamer & Chiesi can confidently invest in commercial planning during PROSERA study (expected Q4:25 topline readout)
- Chiesi is a global partner with significant commercial pulmonary & rare disease infrastructure

Accelerates Seralutinib into a Phase 3 Study in PH-ILD

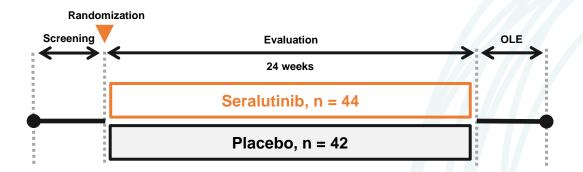
- Pivotal Phase 3 Study in PH-ILD expected to begin in mid-2025, cutting years off potential development timeline
- Adds multi-billion-dollar peak sales opportunity in indication with high unmet medical need, strong biological rationale, & limited competition

Retained Strategic Optionality & Experienced, Motivated Partner

- Gossamer retains control over US commercialization & global development in PAH & PH-ILD
- Gossamer & Chiesi are committed to smart expansion into indications of unmet need that overlap with areas of expertise

# II. Completed TORREY Phase 2 Study

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





Patient **Population** 

Stable FC II & III PAH patients on background therapy, including double & triple therapy

**Endpoints** 

Primary: △PVR at Week 24

Key Secondary: ∆6MWD at Week 24<sup>†</sup> Exploratory: Includes NT-proBNP, Echo

Dosing Regimen

Titrated up to 90mg BID

(Started at 60mg BID; protocol allowed for down-titration to 45mg BID)

Enrolled relatively low-risk PAH patient population; most wellcontrolled PAH pop. to meet primary efficacy endpoint\*

Met primary endpoint; seralutinib treatment benefit observed across primary, secondary and exploratory endpoints

Treatment well tolerated - vast majority of patients able to achieve and maintain 90mg BID dosing

<sup>\*</sup>As determined by baseline PVR & 6MWD, we believe that TORREY enrolled the most well-controlled PAH patient trial population to meet its primary efficacy endpoint. FC = Functional Class; OLE = open label extension; PVR = pulmonary vascular resistance; 6MWD = six-minute walk distance; BID = twice-daily dosing. Source: clinical trials.gov/NCT04456998

#### Selected Baseline Disease Characteristics

(ITT Population)

Characteristic	Placebo (N=42)	Seralutinib <sup>(N=44)</sup>	Total (N=86)
Number of PAH background therapies – n (%)			
1	2 (4.8)	1 (2.3)	3 (3.5)
2	16 (38.1)	18 (40.9)	34 (39.5)
3	24 (57.1)	25 (56.8)	49 (57.0)
WHO FC – n (%)			
Class II	20 (47.6)	30 (68.2)	50 (58.1)
Class III	22 (52.4)	14 (31.8)	36 (41.9)
PVR (dyne*s/cm <sup>5</sup> ) – mean (SD)	661.3 (164.91)	675.8 (240.35)	668.7 (205.90)
6MWD (m) - mean (SD)	407.1 (107.02)	408.6 (75.11)	407.9 (91.54)
NT-proBNP (ng/L) - mean (SD)	645.6 (1158.75)	611.0 (714.58)	628.3 (956.83)

Heavily pre-treated patient population

Hit Primary Endpoint
Despite FC Imbalance in
Drug & Pbo Arms

Mildest baseline
PAH disease to see
treatment effect\*

STELLAR Trial Phase 3 NT-proBNP mean baseline was 1,121.1ng/L; PVR was 763.7 dyne\*s/cm<sup>5</sup> (1)

#### Full Baseline Characteristics Available in Appendix

<sup>1)</sup> Source: <a href="https://doi.org/10.1056/NEJMoa2213558">https://doi.org/10.1056/NEJMoa2213558</a>.

<sup>\*</sup>As determined by baseline PVR & 6MWD, we believe that TORREY enrolled the most well-controlled PAH patient trial population to meet its primary efficacy endpoint.

6MWD = six-minute walk distance; FC = Functional Class; NT-proBNP = N-terminal pro B-type natriuretic peptide; PVR = pulmonary vascular resistance; WHO = World Health Organization; ITT = intention-to-treat; SD = standard deviation; Pbo = placebo.

### TORREY Study Phase 2 Topline Results

- Met Primary Endpoint: Statistically significant reduction in PVR in heavily-treated study population
- Consistent, favorable PVR benefit seen in all pre-specified sub-groups in favor of seralutinib with enhanced effects in patients with more severe disease at baseline§

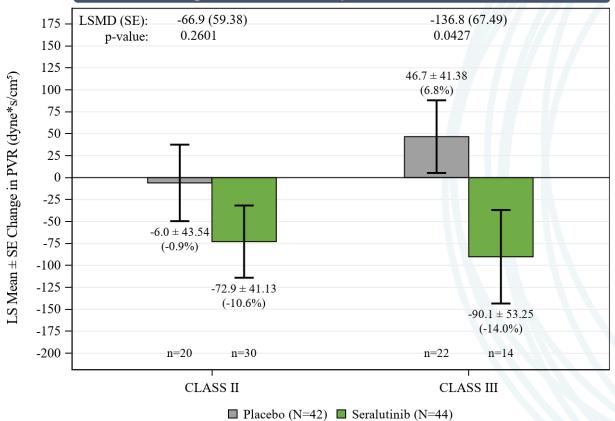
				Pre	-Specified TO	RREY Subgrou	ıps	
Overall Study Population		lation	Functional Class III		REVEAL 2.0 Risk Score ≥ 6			
PVR	NT-proBNP	6MWD	PVR	NT-proBNP	6MWD	PVR	NT-proBNP	6MWD
-14%*	-408 ng/L*	+6.5m	-21%*	-527 ng/L*	+37.3m*	-23%*	-732 ng/L*	+21.9m
p = 0.0310	p = 0.0012	p = 0.5972	p = 0.0427	p = 0.0055	p = 0.0476	p = 0.0134	p = 0.0002	p = 0.2482
Primary Endpoin	t							

- Consistently favorable results for hemodynamic and ECHO endpoints
- Well-tolerated, avoiding side effect profile associated with systemic imatinib in PAH

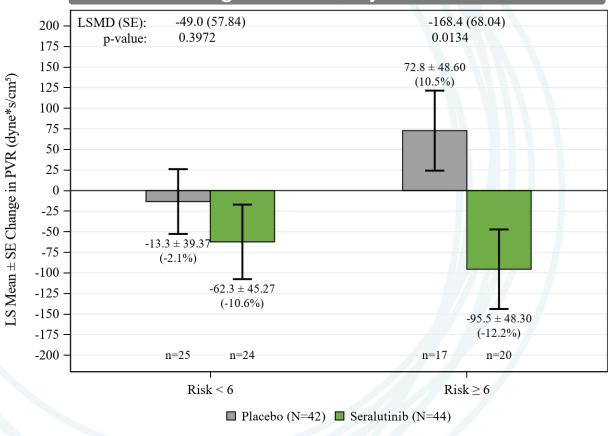
<sup>\* =</sup> p-value ≤ 0.05. All p-values in this presentation are nominal, aside from primary endpoint (overall study population delta in PVR). § At baseline, as determined by Functional Class and REVEAL 2.0 Risk Score (pre-specified subgroups).

# Seralutinib's Effect on PVR was More Pronounced in Patients with More Severe Disease at Baseline (ITT Population)

## WHO Functional Class Change in PVR, by Functional Class

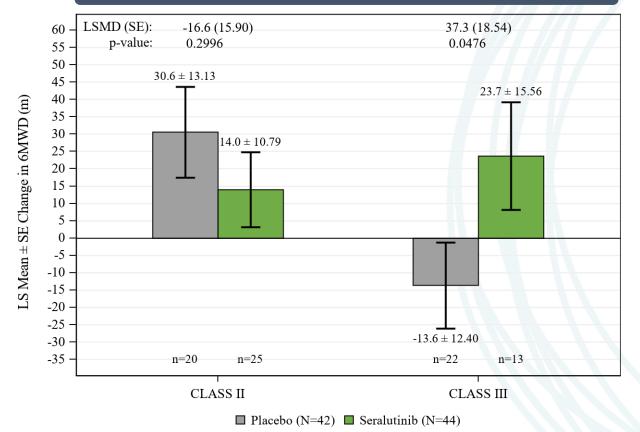


## REVEAL 2.0 Risk Score Change in PVR, by Risk Score

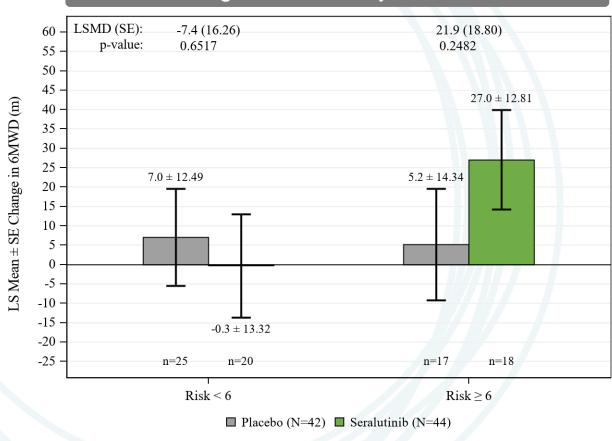


# Change in 6MWD by Functional Class and REVEAL 2.0 Risk Score (ITT Population)

### Functional Class Change in 6MWD, by Functional Class

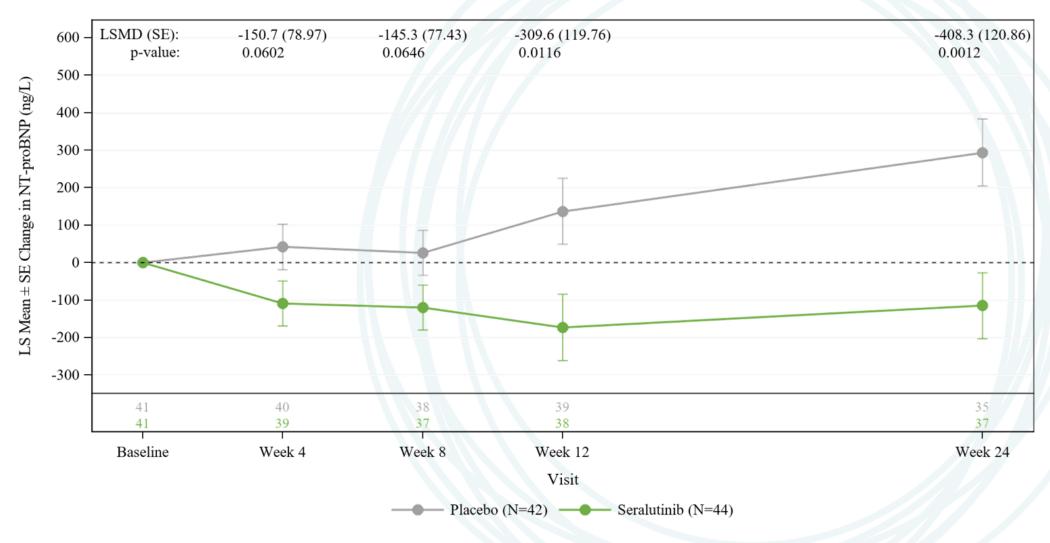


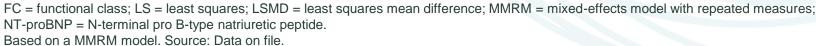
### REVEAL 2.0 Risk Score Change in 6MWD, by Risk Score



6MWD = six-minute walk distance; FC = Functional Class; LS = least squares; LSMD = least squares mean difference; MMRM = mixed-effects model with repeated measures; WHO = World Health Organization.

# Seralutinib Treatment Led to Statistically Significant Reduction in NT-proBNP (ITT Population)





# Centrally-Read RHC and ECHO Results at Week 24 Consistently Favored Seralutinib (ANCOVA – Observed Cases)

Endpoint	LS Mean Difference (95% CI)	Statistically Significant Result Favoring Seralutinib (p ≤ 0.05)	Point Estimate Favoring Seralutinib	p-value
Right Atrium Area (cm²)	-1.99 (-3.783, -0.206)			0.0293*
RV Free Wall Strain (%)	-2.64 (-5.172, -0.098)			0.0420*
PA Compliance (mL/mmHg)	0.22 (0.009, 0.423)			0.0410*
RV Systolic Pressure (mmHg)	-8.10 (-13.877, -2.317)			0.0067*
PA Systolic Pressure (mmHg)	-6.98 (-12.774, -1.187)			0.0189*
PA Diastolic Pressure (mmHg)	-3.43 (-6.211, -0.643)			0.0165*
RV Fractional Area Change	2.62 (-1.405, 6.652)	\\		0.1983
PVR index (dyne*s/cm <sup>5</sup> /m <sup>2</sup> )	-160.42 (-333.970, 13.138)			0.0695
mRAP (mmHg)	-0.99 (-2.350, 0.367)			0.1503
Stroke Volume Index (mL/m²)	2.19 (-0.917, 5.299)			0.1644
Cardiac Index (L/min/m²)	0.13 (-0.100, 0.359)			0.2658

<sup>\*</sup>  $p \le 0.05$ .

Source: Data on file.

mRAP = mean right atrial pressure; PA = pulmonary artery; PVR = pulmonary vascular resistance; RV = right ventricle; LS = least squares; RHC = right heart catheterization; ECHO = echocardiography.

### Top AEs From Imatinib IMPRES Study Not Observed at High Incidence in TORREY

Preferred Term <sup>a</sup>
Nausea
Peripheral edema b
Diarrhea
Vomiting
Periorbital edema <sup>c</sup>
Dyspnea
Hypokalemia
Anemia
Face edema <sup>d</sup>
Muscle spasms

IMPRE	IMPRES Study (Phase 3) Imatinib		
Placebo (N=98)	Imatinib (N=103)		
23 (24)	57 (55)		
20 (20)	45 (44)		
19 (19)	36 (35)		
10 (10)	31 (30)		
7 (7)	30 (29)		
13 (13)	19 (18)		
3 (3)	16 (16)		
3 (3)	14 (14)		
1 (1)	10 (10)		
2 (2)	10 (10)		

TORREY Study (Phase 2) Seralutinib			
Placebo (N=42)	Seralutinib (N=44)		
6 (14)	5 (11)		
1 (2)	2 (5)		
3 (7)	6 (14)		
3 (7)	2 (5)		
0 (0)	1 (2)		
5 (12)	4 (9)		
1 (2)	2 (5)		
0 (0)	1 (2)		
0 (0)	1 (2)		
0 (0)	1 (2)		

AE = adverse event; MedDRA = Medical Dictionary for Regulatory Activities; PT = preferred term.

Note: AEs in IMPRES with an incidence ≥ 10% in Imatinib and ≥5% higher in Imatinib than Placebo are summarized for both IMPRES and TORREY.

Note: The above tables are for illustrative purposes only and are not a head-to-head comparison. Differences exist between study designs and methodologies, and caution should be exercised when comparing data across studies.

<sup>&</sup>lt;sup>a</sup> Coded using MedDRA (v 24.0 in TORREY).

b Includes AE PTs of oedema, oedema peripheral, and peripheral swelling in TORREY.

<sup>&</sup>lt;sup>c</sup> Includes AE PT of periorbital edema in IMPRES and AE PT of periorbital swelling in TORREY.

d Includes AE PT of face edema in IMPRES and AE PT of swelling face in TORREY. Source: Data on file.

# Incidence of TEAEs by Preferred Term: ≥ 5% in Seralutinib (Safety Population)

Preferred Term <sup>a</sup>	Placebo (N=42)	Seralutinib (N=44)
Number of subjects with a TEAE	36 (85.7)	41 (93.2)
Cough	16 (38.1)	19 (43.2)
COVID-19	7 (16.7)	6 (13.6)
Diarrhea	3 (7.1)	6 (13.6)
Headache	8 (19.0)	6 (13.6)
Dizziness	2 (4.8)	5 (11.4)
Fatigue	3 (7.1)	5 (11.4)
Nausea	6 (14.3)	5 (11.4)
Dyspnea	5 (11.9)	4 (9.1)
Nightmare	1 (2.4)	4 (9.1)
Abdominal pain lower	0	3 (6.8)
Arthralgia	1 (2.4)	3 (6.8)
Back pain	2 (4.8)	3 (6.8)
Chest discomfort	1 (2.4)	3 (6.8)
Nasal congestion	1 (2.4)	3 (6.8)
Nasopharyngitis	0	3 (6.8)
Rash	1 (2.4)	3 (6.8)
Throat irritation	0	3 (6.8)

#### All TEAEs in the table above were mild or moderate in severity.

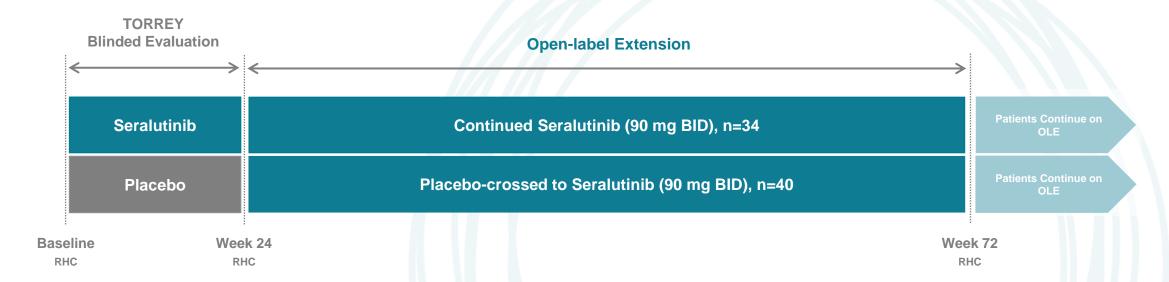
MedDRA = Medical Dictionary for Regulatory Activities; TEAE = treatment-emergent adverse event.

Source: Data on file.

<sup>&</sup>lt;sup>a</sup> Coded using MedDRA v 24.0

# III. Ongoing TORREY OLE Trial

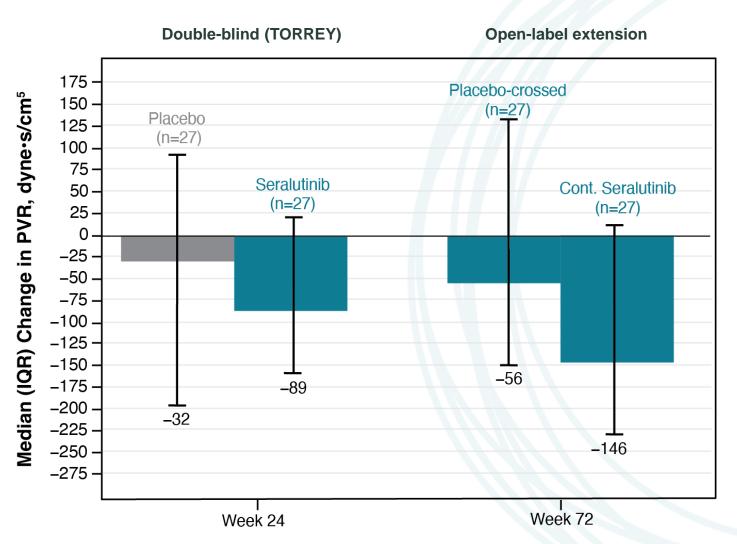
### Ongoing TORREY Open-Label Extension



- Patient population: 73/80 patients who completed TORREY, 1 patient from a phase 1B study
- Objectives:
  - Ongoing, long-term safety & tolerability
  - Efficacy parameters, including hemodynamics at Week 72

Source: https://www.gossamerbio.com/wp-content/uploads/Poster-ATS24b.pdf

### PVR Continues to Improve With Seralutinib in the OLE



Median PVR Values, dyne\*s/cm<sup>5</sup>

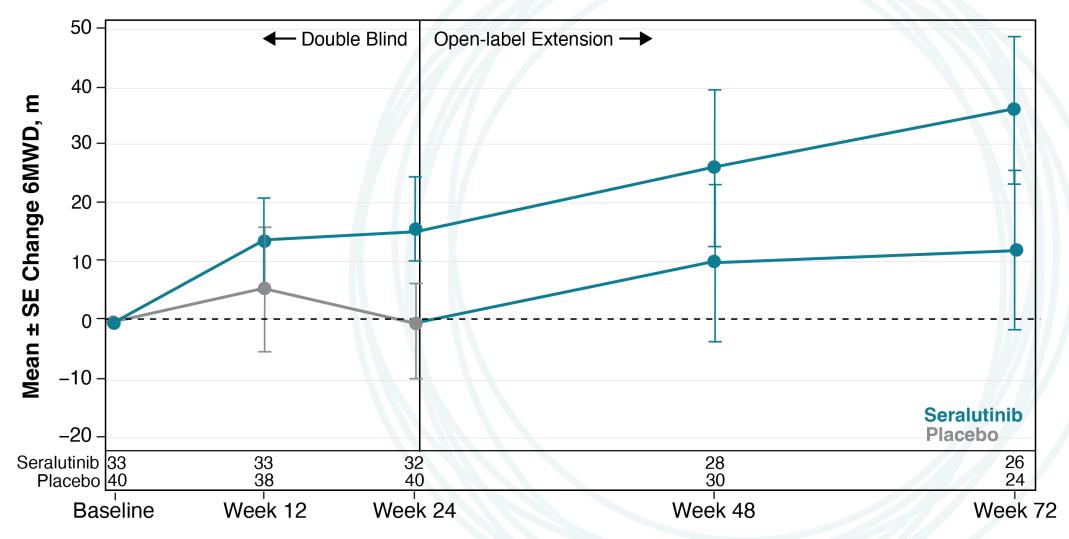
Visit	Placebo/ Placebo- Crossed	Seralutinib/ Cont Seralutinib
Baseline	650.0	620.0
Week 24	647.0	505.0
Week 72	603.0	475.0

Note: OLE study is ongoing. Week 72 data are reflective of the database as of March 4, 2024.

IQR = interquartile range; OLE = open-label extension; PVR = pulmonary vascular resistance; RHC = right heart catheterization.

Source: <a href="https://www.gossamerbio.com/wp-content/uploads/Poster-ATS24b.pdf">https://www.gossamerbio.com/wp-content/uploads/Poster-ATS24b.pdf</a>

# 6MWD Increases in Continued-Seralutinib Group & Placebo-Crossed Group



Note: OLE study is ongoing. Week 48 and 72 data are reflective of the database as of March 4, 2024. 6MWD = six-minute walk distance; OLE = open-label extension; SE = standard error. Source: https://www.gossamerbio.com/wp-content/uploads/Poster-ATS24b.pdf



### Favorable Safety and Tolerability Observed

 No new safety signals associated with TKIs

 Seralutinib was generally well tolerated during the OLE treatment period Incidence of TEAEs by preferred term: ≥ 10%

	Total (N=74)
Subjects with a TEAE, n (%)	71 (95.9)
Headache	19 (25.7)
Cough	18 (24.3)
COVID-19	17 (23.0)
Diarrhoea	15 (20.3)
Dyspnoea	13 (17.6)
Nausea	13 (17.6)
Nasopharyngitis	10 (13.5)
Arthralgia	9 (12.2)
Fatigue	8 (10.8)
Pyrexia	8 (10.8)
Rash	8 (10.8)

# IV. Ongoing Phase 3 PROSERA Study

### Ongoing PROSERA Phase 3 Study



Double Blind Placebo-Controlled Treatment Period (24 weeks)

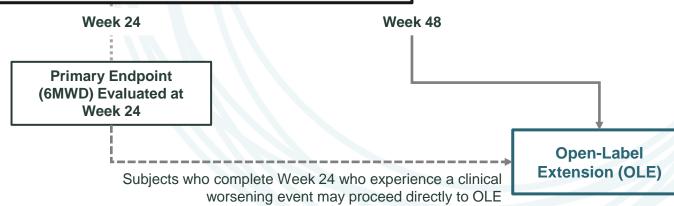
Extended Double Blind
Treatment Period
(up to an additional 24 weeks)\*

Screening (up to 4 weeks) Seralutinib 90mg BID + Background PAH Therapy N = 175

Placebo BID + Background PAH Therapy N = 175 • Adults ≥ 18 and ≤ 75 years old

**PROSERA Key Inclusion Criteria** 

- WHO Group 1 PAH
- WHO Functional Class II or III
- PVR ≥ 400 dyne•s/cm<sup>5</sup>
- Baseline 6MWD 150 475m\*
- Either REVEAL Lite 2 Risk Score ≥ 5 **or** NT-proBNP ≥ 300 ng/L **or** PVR ≥ 800 dyne•s/cm<sup>5</sup>\*
- Stable treatment with at least one SOC background therapy



<sup>\*</sup> Key enrichment criteria.

### V. Seralutinib in PH-ILD

### Seralutinib's Next Frontier: What is PH-ILD?

- WHO Group 3 PH is pulmonary hypertension due to lung diseases and / or hypoxia
  - PH associated with interstitial lung disease (PH-ILD) is a subgroup of Group 3 PH
  - PH-ILD includes PH related to idiopathic pulmonary fibrosis (IPF)
     & PH related to connective tissue disease-associated interstitial lung disease (CTD-ILD)
- Characterized by pulmonary vascular pathology associated with PH, in addition to thickening & scarring of the lung interstitium resulting from ILD
- Only Tyvaso® is approved for PH-ILD, & only in the US
- Patients have poor disease prognosis & increased mortality rate as compared to PAH patients (40% 3-year survival rate<sup>2</sup>)







### PH-ILD is an Ideal Next Indication for Seralutinib

Biologic Rationale:

Demonstrated Positive Impact on Reducing Pulmonary Hypertension



- The pulmonary hypertension in PH-ILD is caused by the same proliferative, inflammatory, & fibrotic pathways as PAH
- Seralutinib demonstrated statistically significant improvement in PVR, right heart function/structure measures, & NT-proBNP in TORREY

2

**Clinical Trial Patient Dynamics are Favorable** 



- Lack of therapeutic options has fostered strong patient demand for clinical trials
- PH-ILD clinical trial patients have increased exercise impairment, as compared to PAH studies
  - Mean BL STELLAR (PAH) 6MWD: 401m
  - Mean BL INCREASE (PH-ILD) 6MWD: 260m
- Seralutinib demonstrated a stat. sig. pbo-controlled 38m increase in 6MWD in baseline FC III PAH patients\* in TORREY (mean BL 6MWD = 367m)

3

**High Unmet Need** 



- Only Tyvaso is approved for PH-ILD, & only in the US
  - No approved therapies in EU or Japan
- Patient population is potentially double the PAH population
- Patients have a high mortality rate, even compared to PAH

Phase 3 design to be discussed after interactions with global regulatory authorities

### Seralutinb MoA Aligned with Underlying Pathophysiology of Group 3 PH

Disease Process	Cell Type / Mechanism	Potentially Relevant Pathway
Vascular Inflammation	Macrophages & ECs	• CSF1R • KIT
Vascular fibrosis	Fibroblasts / myofibroblasts	• PDGFR
Pulmonary vasculopathy (plexiform lesions)	Endothelial-to-mesenchymal transition	• PDGFR
Pulmonary arteriolar hypertrophy / hyperplasia	Pulmonary arteriole vascular smooth muscle cells	<ul><li>PDGFR</li><li>BMPR2</li></ul>
Parenchymal interstitial lung	Fibroblasts	• PDGFR • CSF1R
inflammation & fibrosis	Epithelial-to-mesenchymal transition	• PDGFR
Shunt/hypoxia	V/Q mismatch	Multiple

Seralutinib Was Rationally Designed For PH & Is Highly Relevant For Targeted Indications

### PH-ILD Presents a Significant Market Opportunity

	PAH	PH-ILD
US Prevalence	~30-50k <sup>1</sup>	~60-100k+ <sup>3</sup>
Competitive intensity	16 marketed products	1 marketed product (US Only)
5-year survival rate	57% <sup>2</sup>	23%4
Generics	8 generic products	0 generic products

#### Patients living with PH-ILD are deeply underserved



### Financial Overview

### Financial Overview

Cash, Cash Equivalents and Marketable Securities (As of 6/30/24)

~\$354mm

Principal of Convertible Notes Outstanding

(As of 6/30/24; 5% annual interest; matures May 2027; conversion price: \$16.23)

~\$200mm

Common Shares Outstanding

(As of 8/7/24)

~226mm

### Appendix



## FLUIDDA CT Sub-Study in Phase 2 TORREY Study: Assessing Pulmonary Vascular Remodeling in Patients Treated on Seralutinib

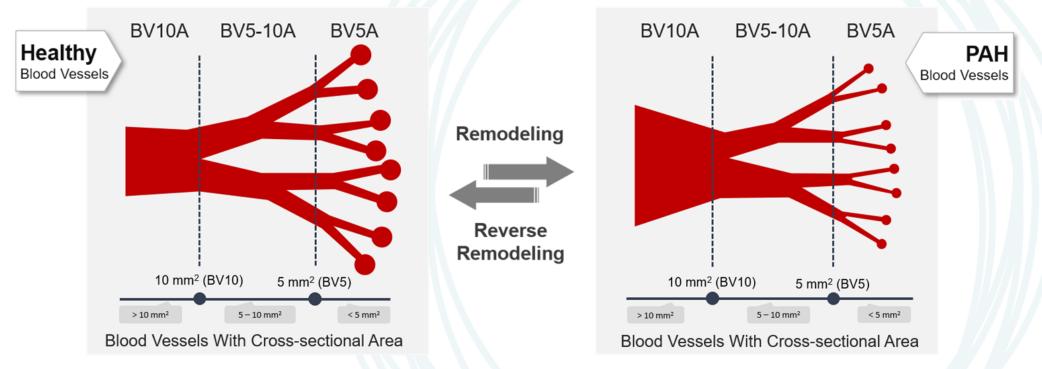
- Purpose: Provide evidence consistent with a reverse remodeling effect of seralutinib
- Hypothesis: volume of distal pulmonary arteries relative to volume of proximal pulmonary arteries will be increased by seralutinib as expressed by the ratio of BV5A to BV10A (BV510ARatio)
- Available data: Baseline and Week 24 HRCTs with pulmonary vascular reconstruction in 7 seralutinibtreated subjects and 12 placebo subjects

Thin Slice CTs with Pulmonary Vascular Segmentation at Baseline and Week 24



See publication - presented at ERS International Congress 2023 in Milan, Italy: "Seralutinib improves pulmonary arterial blood vessel volume distribution in pulmonary arterial hypertension (PAH): Results of the TORREY Phase 2 imaging substudy"

## Pulmonary Vascular Volume of Small Distal Arterial Vessels is Decreased in PAH, Leading to Dilation of Larger Proximal Vessels

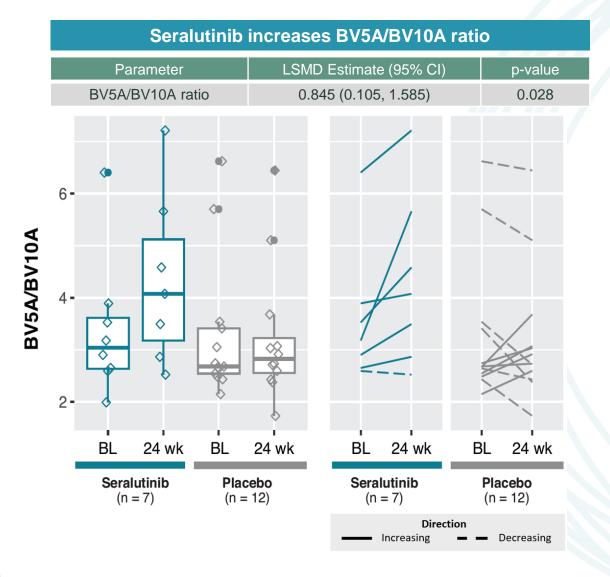


CT imaging can quantify these changes: BV5A: BVV of pulmonary arteries with a CSA < 5 mm2; BV5-10A: BVV of pulmonary arteries with a CSA between 5-10 mm2; BV10A: BVV of pulmonary arteries with a CSA > 10 mm2; BV510ARatio: BV5A/BV10A

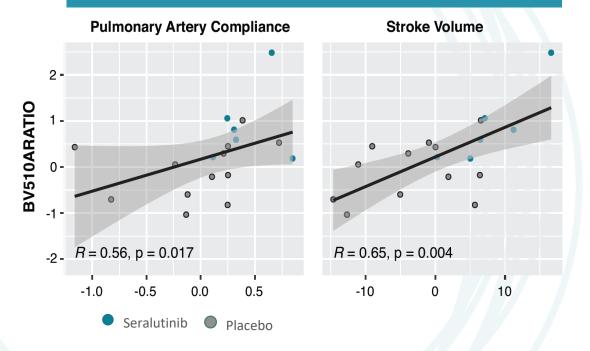
Pulmonary vascular pruning on CT correlates with histologic pulmonary vascular remodeling<sup>1</sup>



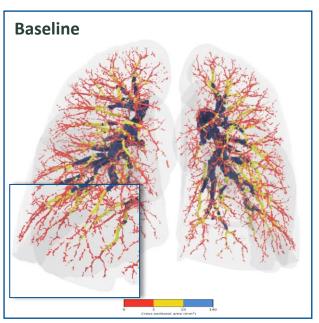
# Seralutinib Treatment Increases the BV5A/BV10A Ratio & Supports Blood Volume Redistribution Hypothesis

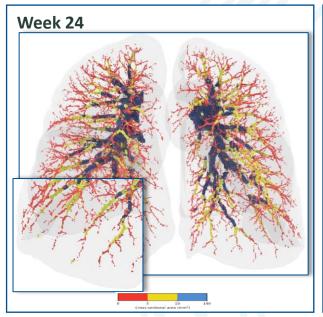


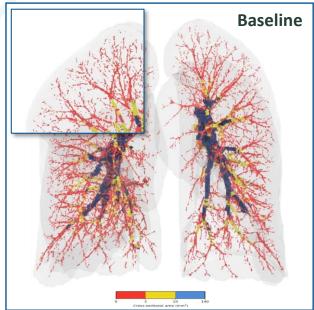
Change in BV5A/BV10A ratio from BL to Week 24 correlates with change in hemodynamics

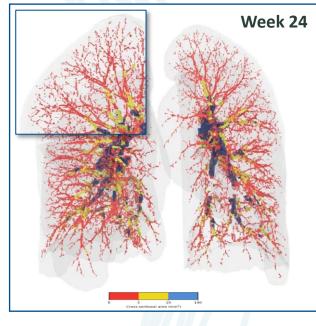


### Examples of Imaging: Placebo vs. Seralutinib









Place	bo I	patie	ent
			444

Female, 24 y, iPAH, FC II, treated with PDE5-i + prostacyclin

PVR change, dyne\*s/cm<sup>5</sup> (%) 283 (+65.4)

ΔBV510ARatio (% change) -0.70 (-28.9)

#### **Seralutinib** patient

Female, 58 y, iPAH, FC II, treated with ERA + PDE5-i + prostacyclin

PVR change, dyne\*s/cm<sup>5</sup> (%)

-159 (-39.0)

ΔBV510ARatio (% change)

+2.5 (+78.0)

# TORREY Phase 2 - Baseline Demographics (ITT Population)

Characteristic	Placebo (N=42)	Seralutinib (N=44)	Total (N=86)	
Age (years) – mean (SD)	49.5 (11.81)	48.3 (12.70)	48.8 (12.22)	
Sex - n (%)				
Female	38 (90.5)	40 (90.9)	78 (90.7)	
Male	4 (9.5)	4 (9.1)	8 (9.3)	
Race - n (%)				
White	37 (88.1)	37 (84.1)	74 (86.0)	
Black or African American	1 (2.4)	0	1 (1.2)	
Asian	2 (4.8)	4 (9.1)	6 (7.0)	
Other	2 (4.8)	3 (6.8)	5 (5.8)	
Ethnicity – n (%)				
Hispanic or Latino	6 (14.3)	8 (18.2)	14 (16.3)	
Not Hispanic or Latino	34 (81.0)	36 (81.8)	70 (81.4)	
Not reported	2 (4.8)	0	2 (2.3)	
Region – n (%)				
North America	30 (71.4)	29 (65.9)	59 (68.6)	
Western Europe	10 (23.8)	11 (25.0)	21 (24.4)	
Asia Pacific	1 (2.4)	4 (9.1)	5 (5.8)	
Eastern Europe	1 (2.4)	0	1 (1.2)	

# TORREY Phase 2 - Baseline Background PAH Medication Use(ITT Population)

Characteristic	Placebo (N=42)	Seralutinib (N=44)	Total (N=86)	
Number of background therapies – n (%)				
1	2 (4.8)	1 (2.3)	3 (3.5)	
2	16 (38.1)	18 (40.9)	34 (39.5)	
3	24 (57.1)	25 (56.8)	49 (57.0)	
Prostacyclin/Prostacycin Receptor Agonist use – n (%)				
None	13 (31.0)	15 (34.1)	28 (32.6)	
Monotherapy	1 (2.4)	1 (2.3)	2 (2.3)	
Double therapy	4 (9.5)	3 (6.8)	7 (8.1)	
Triple therapy	24 (57.1)	25 (56.8)	49 (57.0)	
Parenteral Prostacyclin	19 (45.2)	19 (43.1)	38 (44.2)	
Oral	10 (23.8)	10 (22.7)	20 (23.3)	

# TORREY Phase 2 - Baseline Disease Characteristics (ITT Population)

Characteristic	Placebo (N=42)	Seralutinib (N=44)	Total (N=86)	
Age at PAH diagnosis (years) – mean (SD)	41.2 (11.65)	40.7 (15.84)	40.9 (13.87)	
Years since PAH diagnosis – mean (SD)	8.78 (7.218)	8.07 (7.074)	8.41 (7.111)	
PAH classification – n (%)				
Idiopathic	22 (52.4)	20 (45.5)	42 (48.8)	
Heritable	5 (11.9)	10 (22.7)	15 (17.4)	
Associated with:				
CTD	11 (26.2)	6 (13.6)	17 (19.8)	
Anorexigen use	0	1 (2.3)	1 (1.2)	
Methamphetamine use	4 (9.5)	4 (9.1)	8 (9.3)	
Corrected congenital shunts	0	3 (6.8)	3 (3.5)	
WHO FC – n (%)				
Class II	20 (47.6)	30 (68.2)	50 (58.1)	
Class III	22 (52.4)	14 (31.8)	36 (41.9)	
REVEAL 2.0 Risk Score ≥ 6 – n (%)	17 (40.5)	20 (45.5)	37 (43.0)	
PVR (dyne*s/cm <sup>5</sup> ) – mean (SD)	661.3 (164.91)	675.8 (240.35)	668.7 (205.90)	
6MWD (m) - mean (SD)	407.1 (107.02)	408.6 (75.11)	407.9 (91.54)	
NT-proBNP (ng/L) - mean (SD)	645.6 (1158.75)	611.0 (714.58)	628.3 (956.83)	

6MWD = six-minute walk distance; CTD = connective tissue disease; FC = functional class; NT-proBNP = N-terminal pro B-type natriuretic peptide; PAH = pulmonary arterial hypertension; PVR = pulmonary vascular resistance; WHO = World Health Organization; ITT = Intention-to-treat.



# TORREY Phase 2 - Baseline Demographics and Disease Characteristics by Baseline WHO FC (ITT Population)

	Baseline WHO FC Class II			Base	Baseline WHO FC Class III		
Characteristic	Placebo (N=20)	Seralutinib (N=30)	Total (N=50)	Placebo (N=22)	Seralutinib (N=14)	Total (N=36)	
Age (years) – mean (SD)	47.6 (11.69)	47.7 (13.42)	47.7 (12.63)	51.1 (11.94)	49.4 (11.40)	50.4 (11.60)	
Female - n (%)	19 (95.0)	27 (90.0)	46 (92.0)	19 (86.4)	13 (92.9)	32 (88.9)	
Race, White - n (%)	19 (95.0)	24 (80.0)	43 (86.0)	18 (81.8)	13 (92.9)	31 (86.1)	
Region, North America – n (%)	13 (65.0)	20 (66.7)	33 (66.0)	17 (77.3)	9 (64.3)	26 (72.2)	
Years since PAH diagnosis – mean (SD)	9.60 (7.262)	8.40 (6.961)	8.88 (7.034)	8.02 (7.263)	7.36 (7.527)	7.76 (7.266)	
PAH classification – n (%)							
Idiopathic	11 (55.0)	16 (53.3)	27 (54.0)	11 (50.0)	4 (28.6)	15 (41.7)	
Heritable	4 (20.0)	6 (20.0)	10 (20.0)	1 (4.5)	4 (28.6)	5 (13.9)	
Associated with CTD	5 (25.0)	5 (16.7)	10 (20.0)	6 (27.3)	1 (7.1)	7 (19.4)	
REVEAL 2.0 Risk Score ≥ 6 - n (%)	4 (20.0)	11 (36.7)	15 (30.0)	13 (59.1)	9 (64.3)	22 (61.1)	
PVR (dyne*s/cm <sup>5</sup> ) – mean (SD)	638.3 (161.85)	689.9 (265.72)	669.3 (229.34)	682.2 (168.62)	645.7 (179.29)	668.0 (171.25)	
6MWD (m) - mean (SD)	455.5 (63.96)	425.5 (62.98)	437.5 (64.45)	363.2 (120.05)	372.4 (87.97)	366.8 (107.43)	
NT-proBNP (ng/L) – mean (SD)	406.8 (798.39)	609.9 (715.31)	525.3 (749.58)	873.0 (1403.06)	613.3 (742.17)	773.7 (1187.34)	
On 3 background therapies – n (%)	11 (55.0)	18 (60.0)	29 (58.0)	13 (59.1)	7 (50.0)	20 (55.6)	
ERA + PDE-5i + Prostacyclins/PRA	8 (40.0)	16 (53.3)	24 (48.0)	10 (45.5)	6 (42.9)	16 (44.4)	
ERA + sGC + Prostacyclins/PRA	3 (15.0)	2 (6.7)	5 (10.0)	3 (13.6)	1 (7.1)	4 (11.1)	