Interim Results From the Phase 1B and Phase 2 TORREY Open-label Extension Study of Seralutinib in Pulmonary Arterial Hypertension

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Disclosures

Financial Relationships with “ineligible companies” within the past 24 months:

Company name: AOP Orphan
Type of relationship: Advisory Committee, Lecturer, Research grant

Company name: Enzyvant
Type of relationship: Advisory Committee

Company name: Ferrer
Type of relationship: Advisory Committee, Lecturer, research grant

Company name: Gossamer Bio, Inc.
Type of relationship: Advisory Committee, Manuscript preparation

Company name: Janssen
Type of relationship: Advisory Committee, Lecturer, Research grant, Other

Company name: Liquidia
Type of relationship: Advisory Committee

Company name: MSD
Type of relationship: Advisory Committee, Lecturer, Research grant, Other

Company name: Respira
Type of relationship: Advisory Committee

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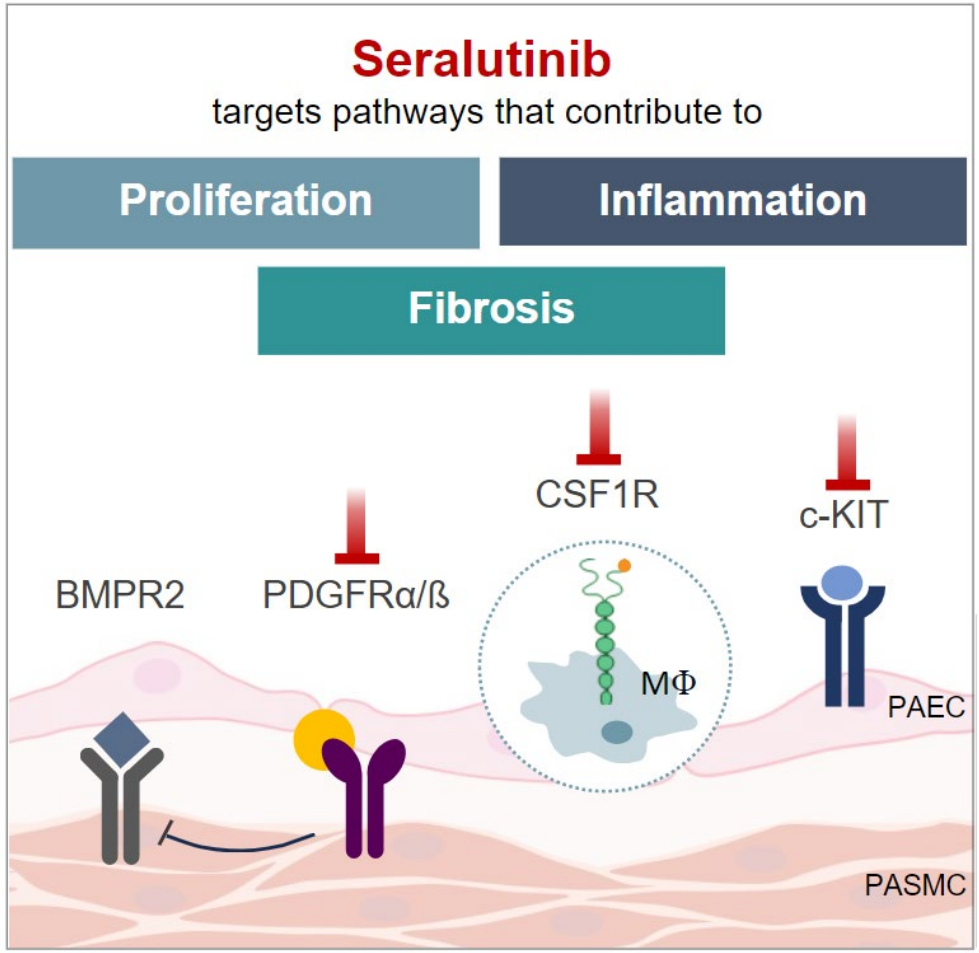
Type of relationship: Advisory Committee

Background

- **Inhibiting the PDGFR pathway** reverses pulmonary vascular remodeling in animal models of PAH[1,2]
- **Safety concerns with oral imatinib** in the IMPRES PAH trial led to efforts to develop novel TKIs with improved benefit-risk[3]
- **Seralutinib is a distinct next-generation TKI with greater potency and selectivity as compared to imatinib, targeting PDGFRα/ß, CSF1R, and c-KIT, thereby acting on inflammatory, proliferative, and fibrotic drivers of pulmonary vascular remodeling**[4]
- Seralutinib is the only TKI intentionally developed for PAH as an inhaled treatment



1 Schermuly et al. *J Clin Invest* 2005; 115:2811-21; **2** Antoniu *Expert Opin Ther Targets* 2012; 16:1055-63; **3** Hoeper et al. *Circulation* 2013; 127(10):1128-38; **4** Galkin et al. *Eur Respir J* 2022; 60:2102356.
Blunt arrows indicate inhibition. BMPR2, bone morphogenetic protein receptor type 2; c-KIT, mast/stem cell growth factor receptor kit; CSF1R, colony stimulating factor 1 receptor; MΦ, macrophage; PAEC, pulmonary artery endothelial cell; PAH, pulmonary arterial hypertension; PASMC, pulmonary artery smooth muscle cell; PDGFR, platelet-derived growth factor receptor; TKI, tyrosine kinase inhibitor.

The Phase 2 TORREY Study Met The Primary Endpoint of PVR Improvement

PVR			6MWD			NT-proBNP		
Overall	FC III	REVEAL ≥ 6	Overall	FC III	REVEAL ≥ 6	Overall	FC III	REVEAL ≥ 6
-14%*	-21%*	-23%*	+6.5m	+37.3m*	+21.9m	-408 ng/L*	-527 ng/L*	-732 ng/L*

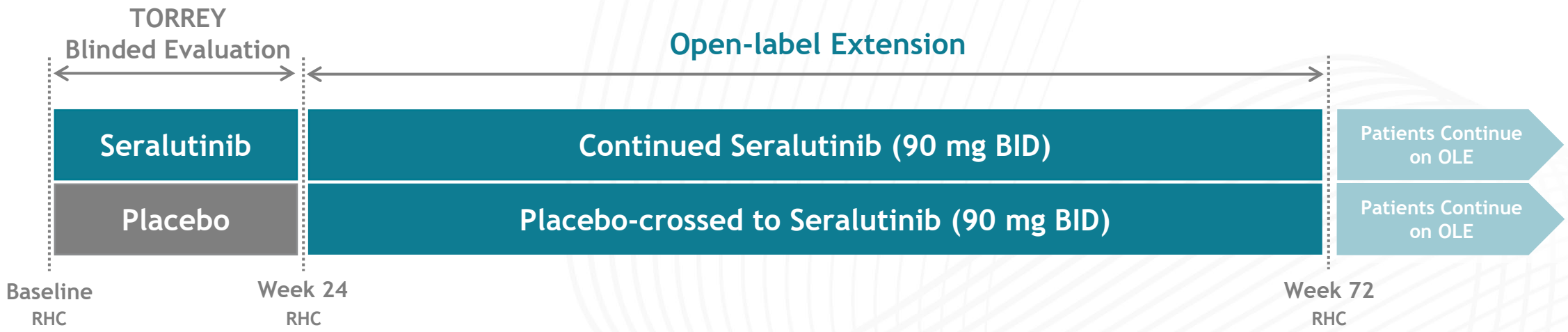
*p-value ≤ 0.05

- In prespecified analyses, the treatment effect on PVR and 6MWD was more pronounced in FC III and patients with REVEAL 2.0 risk score ≥ 6
- Inhaled seralutinib was well tolerated, avoiding many of the side effects observed with oral imatinib

Frantz et al. *Lancet Resp Med*; published online May 2, 2024. doi.org/10.1016/S2213-2600(24)00072-9
Phase 2 TORREY study: NCT04456998

6MWD, 6-minute walk distance; FC, functional class; NT-proBNP, N-terminal pro-brain natriuretic peptide; PVR, pulmonary vascular resistance.

Open-Label Extension: Methods



- Patient population: 73/80 patients who completed TORREY, 1/8 patients from a phase 1B study
- Objectives:
  - Ongoing, long-term safety & tolerability
  - Efficacy parameters, including hemodynamics at Week 72

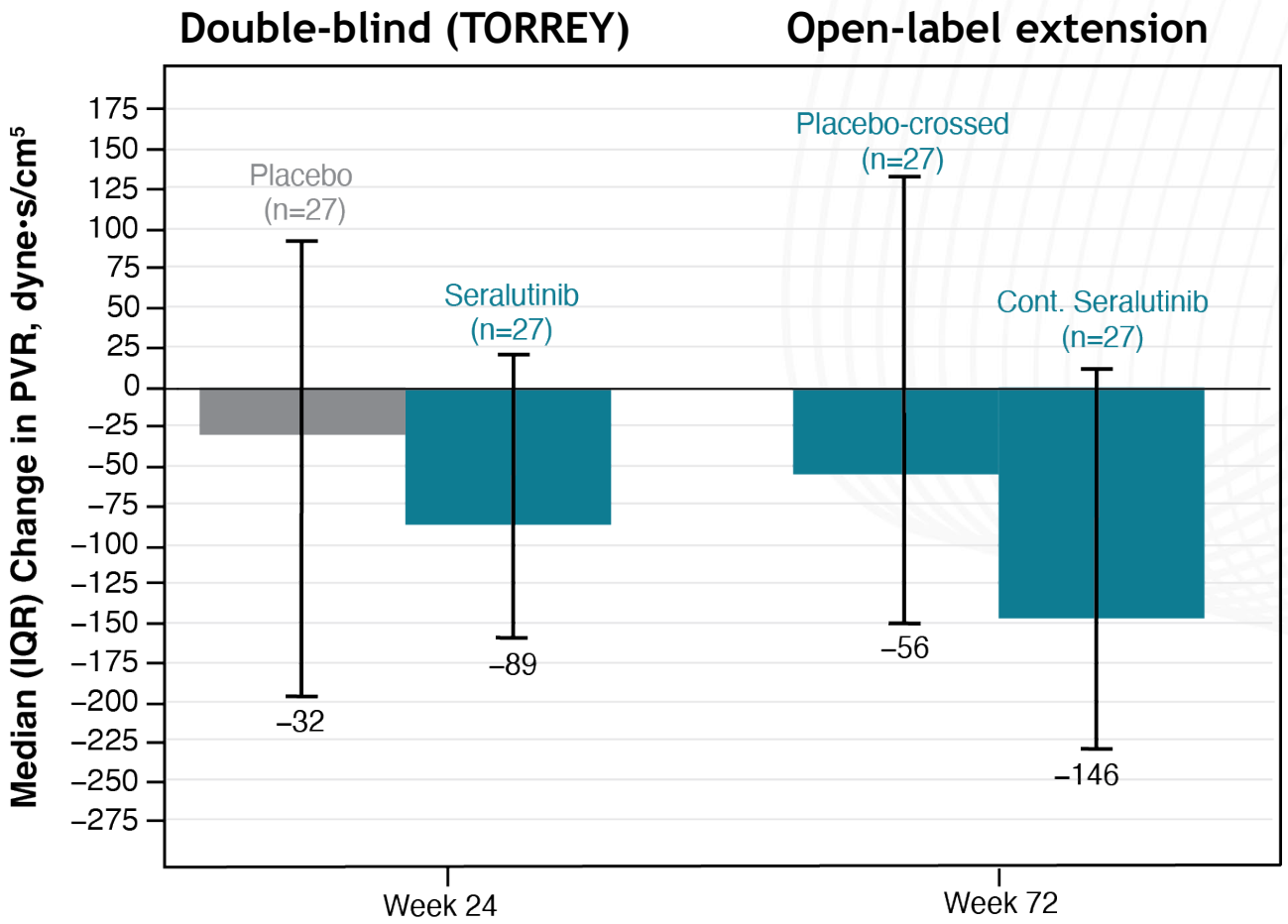
Cut-off date for data presented: March 4, 2024.
Phase 1B: NCT03926793; Phase 2 TORREY: NCT04456998; Open-label extension: NCT04816604.
BID, twice daily; OLE, open-label extension; RHC, right heart catheterization; TEAEs, treatment-emergent adverse events.

Baseline Disease Characteristics at Start of OLE

Characteristic	Placebo-crossed (n=40)	Cont'd seralutinib (n=34)	Total (N=74)
Age at PAH diagnosis, y	41.4 (11.85)	42.8 (15.67)	42.0 (13.66)
Years since PAH diagnosis	9.54 (7.336)	7.30 (6.412)	8.51 (6.972)
PAH classification, n (%)			
Idiopathic/Heritable	22 (55.0)/5 (12.5)	17 (50.0)/10 (29.4)	39 (52.7)/15 (20.3)
CTD / D and T, repaired CHD	9 (22.5)/4 (10.0)	2 (5.9)/5 (14.7)	11 (14.9)/9 (12.2)
Background PAH treatment, n (%)			
Double/triple therapy	16 (40.0)/22 (55.0)	13 (38.2)/20 (58.8)	29 (39.2)/42 (56.8)
Parenteral prostacyclins/PRA	19 (47.5)	15 (44.1)	34 (45.9)
WHO FC II, n (%)	17 (42.5)	25 (73.5)	42 (56.8)
WHO FC III, n (%)	17 (42.5)	6 (17.6)	23 (31.1)
WHO FC IV, n (%)	3 (7.5)	0	3 (4.1)
REVEAL 2.0 risk score ≥ 6, n (%)	21 (52.5)	14 (41.2)	35 (47.3)
PVR, dyne*s/cm^5	669.3 (257.71)	611.7 (279.75)	643.7 (267.36)
6MWD, m	408.7 (115.16)	422.3 (91.56)	415.0 (104.51)
NT-proBNP, ng/L	888.8 (1652.61)	464.1 (542.47)	691.4 (1274.22)

Data presented as mean (SD) unless otherwise noted. 6MWD, six-minute walk distance; CHD, congenital heart disease; CTD, connective tissue disease; D and T, drugs and toxins; FC, functional class; PRA, prostacyclin receptor agonist; PVR, pulmonary vascular resistance; OLE, open-label extension; REVEAL, Registry to Evaluate Early and Long-term PAH Disease Management; WHO, World Health Organization.

PVR Continues to Improve With Seralutinib in the OLE



Median PVR Values, dyne*s/cm^5

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

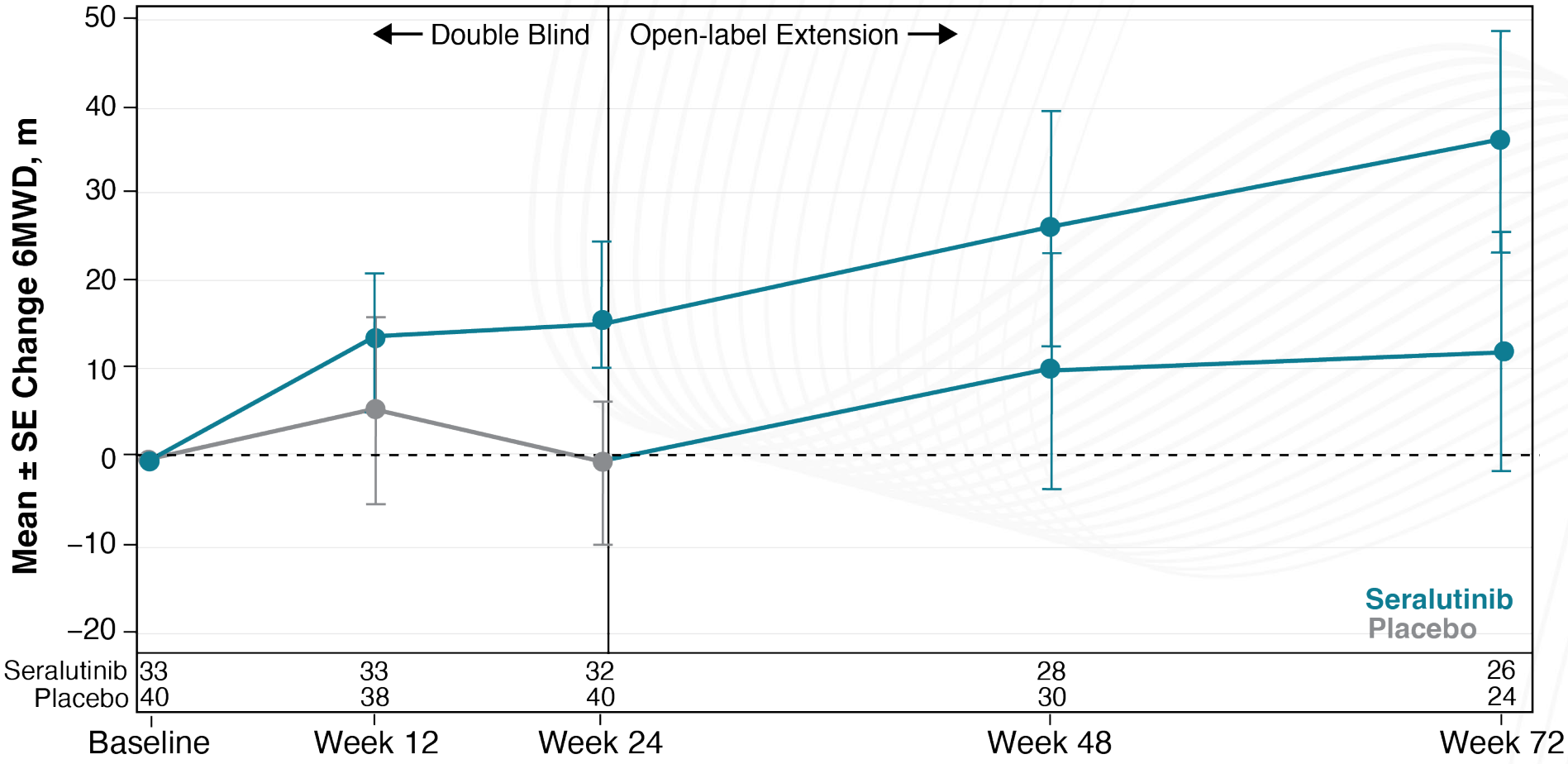
Note: OLE study is ongoing. Week 72 data are reflective of the database as of March 4, 2024.
IQR, interquartile range; OLE, open-label extension; PVR, pulmonary vascular resistance; RHC, right heart catheterization.

Favorable Cardiopulmonary Hemodynamics for OLE Patients Who Had RHC at Week 24 and Week 72

Median (IQR) n=27 Placebo n=27 Seralutinib	Placebo		Placebo-crossed	Seralutinib		Continued Seralutinib
	BL	Δ BL to W24	Δ BL to W72	BL	Δ BL to W24	Δ BL to W72
mPAP, mmHg	48.0 (44, 56)	0.0 (−6, 5)	−1.0 (−9, 5)	51.0 (42, 56)	−3.0 (−6, 0)	−4.0 (−8, 3)
CI, L/min/m^2	2.5 (2.1, 2.9)	0.0 (−0.3, 0.5)	0.0 (−0.3, 0.4)	2.6 (2.4, 3.0)	0.1 (−0.2, 0.4)	0.05 (−0.1, 0.6)
SVI, mL/m^2	36.36 (32.00, 42.59)	−2.33 (−6.55, 2.56)	0.25 (−4.73, 6.97)	37.93 (32.93, 43.06)	−0.35 (−4.43, 4.83)	0.81 (−4.64, 8.46)
mRAP, mmHg	8.0 (7,10)	1.0 (−3, 3)	0.0 (−3, 3)	8.0 (6, 11)	−1.0 (−2, 2)	−1.0 (−4, 1)

BL, baseline; CI, cardiac index; mPAP, mean pulmonary arterial pressure; mRAP, mean right atrial pressure; RHC, right heart catheterization; SVI, stroke volume index; W, week.

6MWD Increases in the OLE in the Continued-seralutinib Group and in the 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.

Favorable Safety and Tolerability Observed in up to 127 Weeks

- Seralutinib was generally well tolerated during the OLE treatment period
- Similar frequency of ≥ 3x hepatic enzyme elevation in the OLE (5/74, 6.8%) and in TORREY (3/44, 6.8%) with seralutinib
- No new safety signals associated with TKIs

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)

Note: OLE study is ongoing. Data are reflective of the database as of March 4, 2024.
AE, adverse event; OLE, open-label extension; TEAE, treatment-emergent adverse event; TKI, tyrosine kinase inhibitor.

Summary

- The open-label extension data demonstrate a **promising long-term efficacy profile up to 72 weeks**, with **continued improvement** in PVR and exercise capacity
- Seralutinib was **safe and well tolerated with no new safety signals** over the OLE treatment period to date (up to 2.4 years of exposure)
- These data support inhaled seralutinib as a novel **anti-proliferative therapy** in clinical development for PAH
- The phase 3 **PROSERA** study of seralutinib in patients with PAH is now enrolling (NCT05934526)