



ATS 2021 INTERNATIONAL CONFERENCE

**ACCELERON INVESTOR AND ANALYST CALL
MAY 19, 2021**



Accelaron Forward-Looking Statements



THIS PRESENTATION CONTAINS FORWARD-LOOKING STATEMENTS ABOUT THE COMPANY’S STRATEGY, FUTURE PLANS AND PROSPECTS, including statements regarding the development and commercialization of sotatercept in pulmonary arterial hypertension (“PAH”) and of the Company’s other compounds, the timeline for clinical development and regulatory approval of the Company’s compounds and the expected timing for reporting of data from ongoing clinical trials. The words “anticipate,” “believe,” “could,” “estimate,” “expect,” “goal,” “intend,” “may,” “plan,” “potential,” “project,” “should,” “target,” “will,” “would,” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

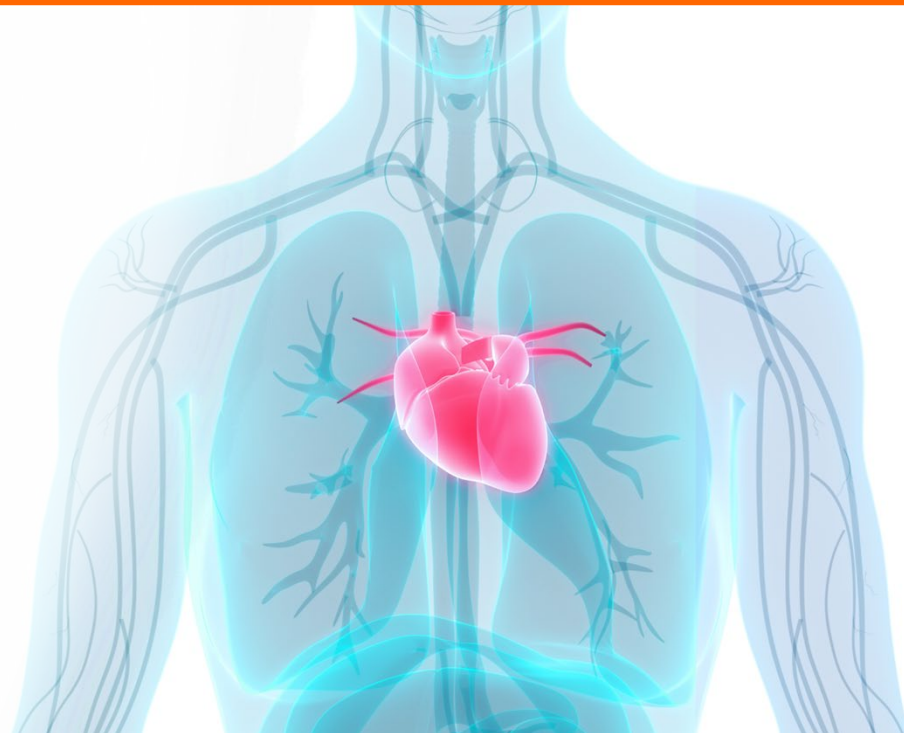
ACTUAL RESULTS COULD DIFFER MATERIALLY FROM THOSE INCLUDED IN THE FORWARD-LOOKING STATEMENTS DUE TO VARIOUS factors, risks and uncertainties, including, but not limited to, that preclinical testing of the Company's compounds and data from clinical trials may not be predictive of the results or success of ongoing or later clinical trials, that regulatory approval of the Company's compounds in one indication or country may not be predictive of approval in another indication or country, that the development of the Company's compounds may take longer and/or cost more than planned, that the Company may be unable to successfully complete the clinical development of the Company's compounds, that the Company may be delayed in initiating, enrolling or completing any clinical trials, that the Company's compounds may not receive regulatory approval or become commercially successful products, and that Breakthrough Therapy or Priority Medicines (PRIME) designation may not expedite the development or review of sotatercept. These and other risks and uncertainties are identified under the heading "Risk Factors" included in the Company's most recent Annual Report on Form 10-K and other filings that the Company has made and may make with the SEC in the future.

THE FORWARD-LOOKING STATEMENTS CONTAINED IN THIS PRESENTATION ARE BASED ON MANAGEMENT’S CURRENT VIEWS, PLANS, estimates, assumptions and projections with respect to future events, and the Company does not undertake and specifically disclaims any obligation to update any forward-looking statements.



HABIB DABLE
CHIEF EXECUTIVE OFFICER

BACKBONE THERAPY IN PAH





JAY BACKSTROM, MD, MPH
HEAD OF RESEARCH &
DEVELOPMENT



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Clinical Presentations



PULSAR Study Open-Label Extension: Interim Results from a Phase 2 Study of the Efficacy and Safety of Sotatercept When Added to Standard of Care for the Treatment of Pulmonary Arterial Hypertension (PAH)



The SPECTRA Study: A Phase 2a Single-Arm, Open-Label, Multicenter Exploratory Study to Assess the Effects of Sotatercept for the Treatment of Pulmonary Arterial Hypertension (PAH)

Preclinical Presentations

Sotatercept Analog RAP-011 Alleviates Cardiopulmonary Remodeling and Inflammation in a Model of Heritable PAH Arising from Bmpr2 Haploinsufficiency

Sotatercept Analog RAP-011 Reduces Right Ventricular Hypertrophy and Alleviates Pulmonary Hypertension in A ZSF1 Rat Model of Heart Failure with Preserved Ejection Fraction

■ Clinical Presentations:

— PULSAR

- Clinical efficacy was maintained or enhanced up through 48 weeks
- Placebo crossover patients also achieved similar improvement in efficacy measures

— SPECTRA

- In this preliminary analysis of patients in the ongoing SPECTRA study, encouraging results in hemodynamics, invasive cardiopulmonary exercise testing (iCPET), and 6-minute walk distance (6MWD) were seen
- Sotatercept was generally well tolerated; adverse events were consistent with previously published data on sotatercept in clinical trials in PAH and in other diseases

■ Non-Clinical Presentations:

- Preventative treatment of RAP-011¹ significantly reduced measures of elevated right ventricular pressures (RV) and reversed right ventricular hypertrophy (RVH) in an experimental genetic model of pulmonary hypertension (PH)
- RAP-011¹ reduced elevated pulmonary pressures and reversed right ventricular (RV) remodeling in an experimental model of Group 2 PH

¹ Murine version of sotatercept
Sotatercept is an investigational therapy that is not approved for any use in any country.



JANETHE PENA, MD, PhD
HEAD OF PULMONARY MEDICAL
RESEARCH



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Welcome

PULSAR study open-label extension: Interim results from a Phase 2 study of the efficacy and safety of sotatercept when added to standard of care for the treatment of pulmonary arterial hypertension (PAH)

**David B. Badesch¹, Simon R. Gibbs²,
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Rogerio Souza⁷, Aaron Waxman⁸,
Solaiappan Manimaran⁹, Jennifer Barnes^{9*},
Janethe de Oliveira Pena⁹ and Marc Humbert¹⁰**

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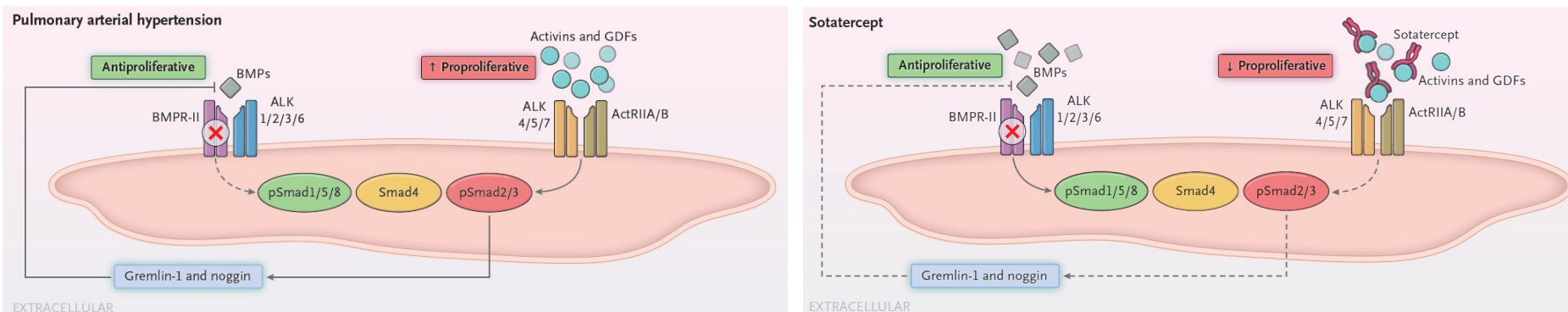
⁴Department of Respiratory Medicine, Hannover Medical School and German Center of Lung Research, Hannover, Germany; ⁵University of Michigan, Ann Arbor, MI, USA; ⁶Tufts Medical Center, Boston, MA, USA; ⁷InCor - University of São Paulo Medical School, São Paulo, Brazil;

⁸Brigham and Women's Hospital, Boston, MA, USA; ⁹Accelaron Pharma, Cambridge, MA, USA; ¹⁰University of Paris-Saclay, Assistance Publique Hopitaux de Paris, INSERM U999, Le Kremlin-Bicetre, France

*previous employee

Pulmonary arterial hypertension and sotatercept

- Pulmonary arterial hypertension (PAH) is characterized by pulmonary vascular remodeling, resulting in increased pulmonary artery pressure and progressive right ventricular dysfunction¹



- Sotatercept is a first-in-class selective ligand trap proposed to rebalance pro- (ActRIIA-mediated) and anti- (BMPR-II-mediated) proliferative signaling, thereby having the potential to reverse the characteristic vascular remodeling that underlies PAH pathology²⁻⁴

Sotatercept is an investigational product that is not approved for any use in any country.

ActRIIA/B: activin receptor type 2A/B; ALK: activin receptor-like kinase; BMP: bone morphogenetic protein; BMPR-II: bone morphogenetic protein receptor type 2; GDF: growth differentiation factor; PAH: pulmonary arterial hypertension; pSmad: phosphorylated Smad.

1. Lai YC et al. *Circ Res*. 2014; 115: 115–30; 2. Humbert M, et al. *N Engl J Med*. 2021; 384: 1204–15; 3. Cappellini MD, et al. *Haematologica*. 2019; 104: 477–84; 4. Yung L-M, et al. *Sci Transl Med*. 2020; 12: eaaz5660.

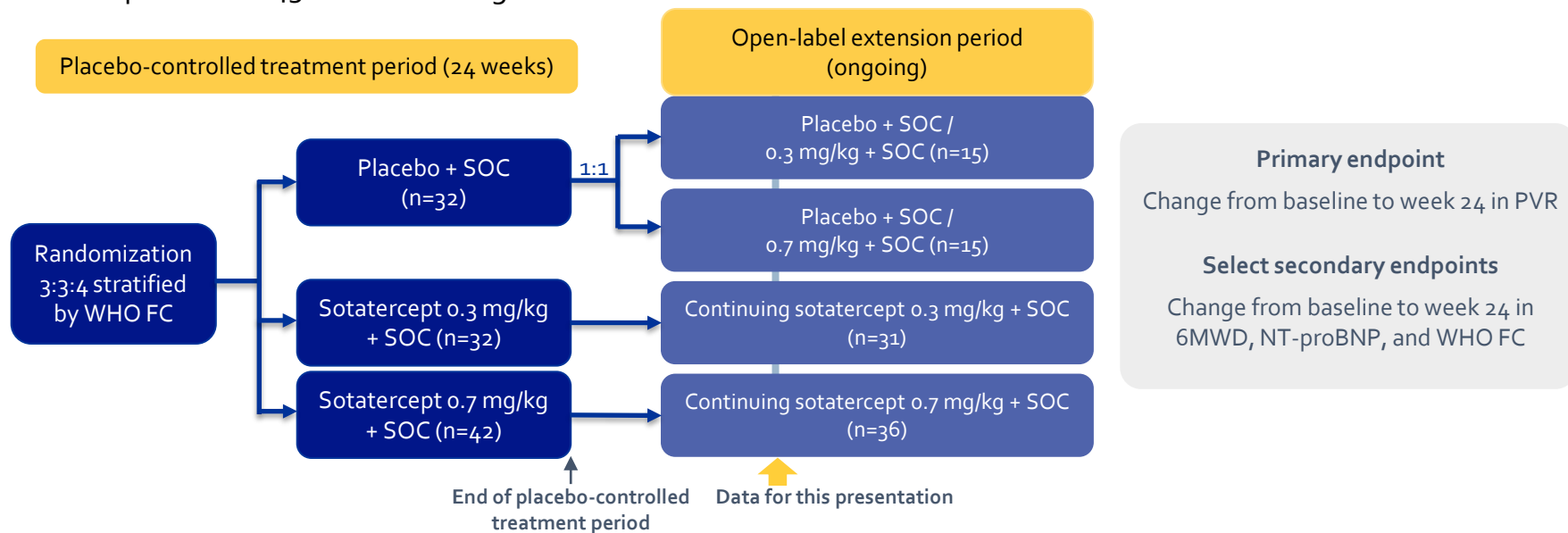


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PULSAR: Study design

- A Phase 2, randomized, double-blind, placebo-controlled study to compare the safety and efficacy of sotatercept versus placebo when added to standard of care (SOC) for the treatment of PAH in 106 patients at 43 sites across eight countries



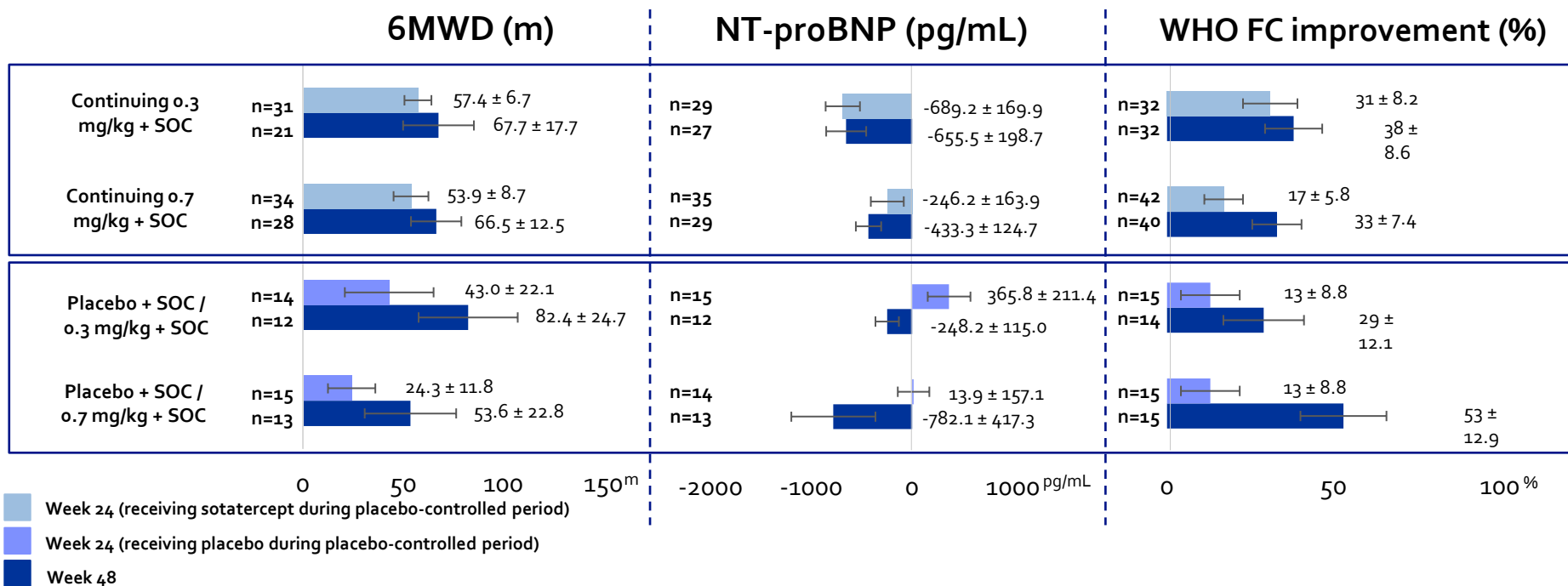
6MWD: 6-minute walk distance; FC: functional class; NT-proBNP: N-terminal pro-brain natriuretic peptide; PAH: pulmonary arterial hypertension; PVR: pulmonary vascular resistance; SOC: standard of care; WHO: World Health Organization.
1. Humbert M, et al. *N Engl J Med*. 2021; 384: 1204–15.



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PULSAR: Change from baseline at week 24 and change from baseline at week 48



Interim extension analysis data cut-off date: 14 September 2020.

Data presented as mean ± SE change from baseline for 6MWD and NT-proBNP; percentage of patients ± SE who improved by ≥1 WHO FC; not all data for in-person assessments (6MWD, NT-proBNP) were available due to COVID-19 delays and missing visits.

Per the statistical methods for calculating WHO FC, missing data for reasons other than COVID-19 are recorded as non-responders and therefore the overall n is different for WHO FC.

6MWD: 6-minute walk distance; FC: functional class; NT-proBNP: N-terminal pro-brain natriuretic peptide; SE: standard error; SOC: standard of care; WHO: World Health Organization.



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PULSAR: Overall safety experience including open-label extension

- As of the interim data cut, 103/106 (97%) patients reported treatment-emergent adverse events (TEAEs)
- Serious TEAEs occurred in 30/106 (28%) patients
- Overall, 9/106 (9%) patients had TEAEs that led to study discontinuation; 2/106 (2%) died (cardiac arrest, brain abscess) and deaths were not considered related to study drug by the investigators
- The safety profile of sotatercept was consistent with the placebo-controlled treatment period

TEAEs during the OLE period only, n (%)	Continuing 0.3 mg/kg + SOC (n=31)	Continuing 0.7 mg/kg + SOC (n=36)	Placebo + SOC / 0.3 mg/kg + SOC (n=15)	Placebo + SOC / 0.7 mg/kg + SOC (n=15)
TEAEs	29 (94)	33 (92)	13 (87)	15 (100)
TEAEs of special interest*	1 (3)	2 (6)	5 (33)	0 (0)
Serious TEAEs	8 (26)	4 (11)	4 (27)	2 (13)
Serious related TEAEs	1 (3)	0 (0)	1 (7)	0 (0)
TEAEs leading to treatment discontinuation	1 (3)	0 (0)	0 (0)	0 (0)
TEAEs leading to study discontinuation	1 (3)	1 (3)	0 (0)	0 (0)
TEAEs leading to death	0 (0)	1 (3)	0 (0)	0 (0)

Interim extension analysis data cut-off date: 14 September 2020.

*TEAEs of special interest defined as any adverse event of leukopenia, neutropenia, or thrombocytopenia.

OLE: open-label extension; SOC: standard of care; TEAE: treatment-emergent adverse event.



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Conclusions

- In this first interim report from the open-label extension period of PULSAR, clinical efficacy was maintained or enhanced with sotatercept treatment across multiple study endpoints for up to 48 weeks
- Improvements observed in patients re-randomized from the placebo group to sotatercept treatment align with the initial results from the placebo-controlled treatment period
- Safety findings were consistent with previous reports in PAH and other patient populations
- Final data from the open-label extension period are forthcoming and sotatercept will be further evaluated in a Phase 3 program¹⁻³
 - The randomized, double-blind, placebo-controlled STELLAR study is currently recruiting (NCT04576988) and the HYPERION study in newly diagnosed intermediate- and high-risk patients with PAH is now active (NCT04811092)

PAH: pulmonary arterial hypertension.

1. ClinicalTrials.gov. A study of sotatercept for the treatment of pulmonary arterial hypertension (STELLAR). <https://clinicaltrials.gov/ct2/show/NCT04576988> [Accessed 24 March 2021]; 2. ClinicalTrials.gov. A long-term follow-up study of sotatercept for PAH treatment (SOTERIA). <https://clinicaltrials.gov/ct2/show/NCT04796337> [Accessed 24 March 2021]; 3. ClinicalTrials.gov. Study of sotatercept in newly diagnosed intermediate- and high-risk PAH patients (HYPERION). <https://clinicaltrials.gov/ct2/show/NCT04811092> [Accessed 24 March 2021].

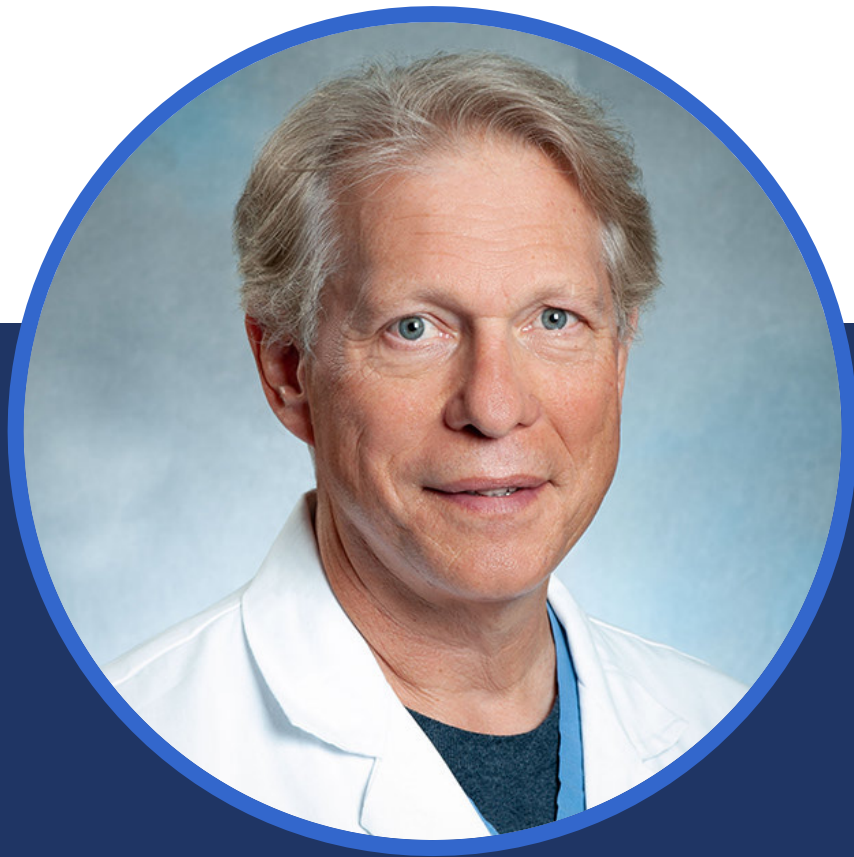


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Acknowledgments

- We thank all the patients, their families, and all the PULSAR study investigators and coordinators who participated in the trial
 - PULSAR study investigators: Y. Adir, H. Alnuaimat, M. Andrade-Lima, J. Arakaki, R. Argula, A. Balaira, D. Baratz, J. Barberá, A. Bar-Shai, C. Berastegui, L. Bertoletti, M. Delcroix, D. Blanco, A. Bourdin, F. Campos, M. Chakinala, C. Church, J. Cifrian Martinez, J. Coghlan, T. Demarco, S. Eisenmann, P. Engel, P. Escribano-Subias, J. Feenstra, J. Feldman, M. Halank, L. Howard, O. Hussein, A. Keogh, M. Kramer, T. Lange, M. Lavender, M. Lazaro Salvador, G. Meyer, J. Michaelson, D. Montani, W. Nseir, K. Olsson, C. Opitz, C. Pison, D. Poch, F. Rahaghi, Y. Raviv, G. Reeves, F. Rischard, J. Robinson, Z. Safdar, R. Saggat, J. Schreiber, M. Segel, J. Segovia Cubero, D. Shitrit, N. Sood, L. Spikes, S. Steiglit, J. Vachier, J. Wheatley, H. Wirtz
- The study was sponsored by Acceleron Pharma, Cambridge, MA, USA
- The authors received editorial assistance from InterComm International Ltd., supported by Acceleron Pharma



BRIGHAM HEALTH



BRIGHAM AND
WOMEN'S HOSPITAL



HARVARD
MEDICAL SCHOOL

Aaron Waxman, MD, PhD

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Brigham and Women's Hospital;
Associate Professor of Medicine, Harvard Medical School*

*Principal investigator in the SPECTRA trial and a paid
consultant to Acceleron*



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Welcome

The SPECTRA study: A Phase 2a single-arm, open-label, multicenter exploratory study to assess the effects of sotatercept for the treatment of pulmonary arterial hypertension (PAH)

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⁴Accelaron Pharma, Cambridge, MA; ⁵University of Arizona, Tucson, AZ

Disclosure to learners

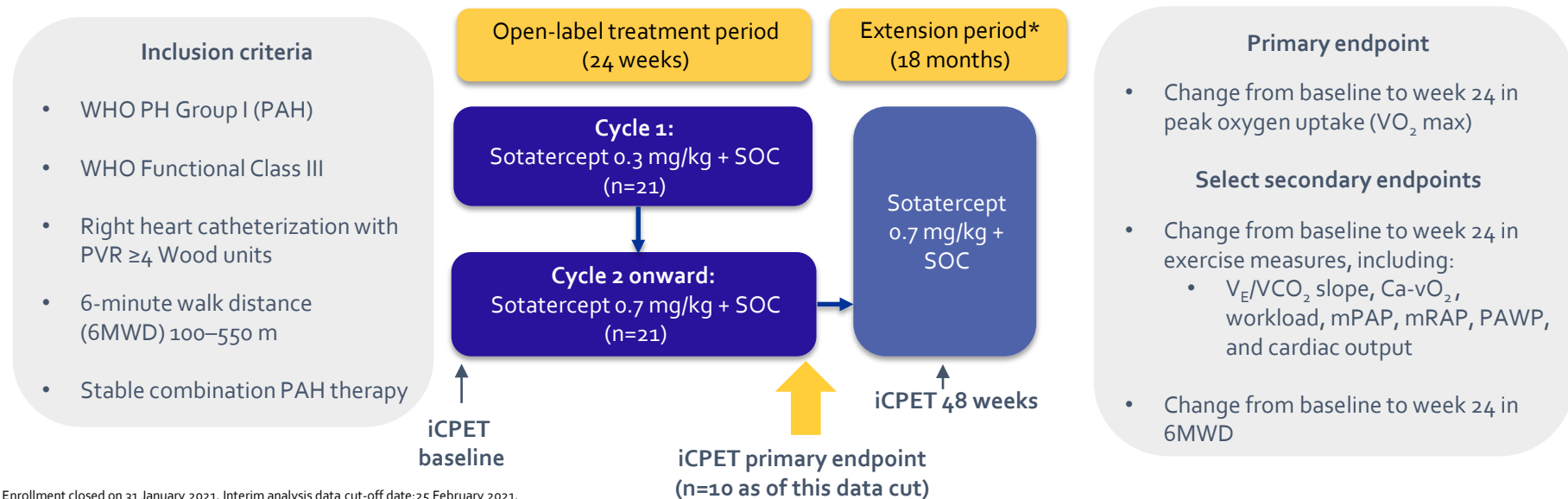
Financial relationships with relevant companies within the past 24 months:

Company name: Acceleron
Type of relationship: Research support/Consultant



SPECTRA: Study design

- A Phase 2a single-arm, open-label, multicenter exploratory study to assess the effects of sotatercept for the treatment of PAH in 21 patients at four sites across the USA



Enrollment closed on 31 January 2021. Interim analysis data cut-off date: 25 February 2021.

*Extension period followed by 8-week post-treatment follow-up.

6MWD: 6-minute walk distance; $Ca-vO_2$: arteriovenous O_2 content difference; iCPET: invasive cardiopulmonary exercise testing; mPAP: mean pulmonary arterial pressure; mRAP: mean right atrial pressure; PAH: pulmonary arterial hypertension; PAWP: pulmonary arterial wedge pressure; PH: pulmonary hypertension; PVR: pulmonary vascular resistance; SOC: standard of care; V_E/VCO_2 : ventilatory efficiency; VO_2 : peak oxygen uptake; WHO: World Health Organization.



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SPECTRA: Baseline characteristics

	Total patients enrolled n=21	Evaluable patients at week 24 n=10
Female, n (%)	17 (81)	6 (60)
Age, median (range), years	44 (21–70)	45 (25–66)
Time since diagnosis, median (range), years	4.9* (0.6–15.0)	3.2 (0.6–13.1)
PAH classification, n (%)		
Idiopathic	13 (62)	5 (50)
Heritable	1 (5)	1 (10)
Associated with connective-tissue disease	6 (29)	4 (40)
Missing	1 (5)	0 (0)
Standard-of-care PAH therapy, n (%)		
Prostacyclin infusion therapy	12 (57)	7 (70)
Double therapy	12 (57)	6 (60)
Triple therapy	9 (43)	4 (40)
6MWD, median (range), m	402 (254–525)	359 (254–506)

Interim analysis data cut-off date: 25 February 2021.

*n=20; evaluable patients at week 24 defined as those with primary endpoint assessment at both baseline and week 24/early EOT before 24 weeks entered in the database.

6MWD: 6-minute walk distance; EOT: end of treatment; PAH: pulmonary arterial hypertension.



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SPECTRA: Supine resting hemodynamics

- At rest, reductions were seen in mean change from baseline to week 24 in PVR and mPAP

	Supine resting		
	Baseline n=10	Week 24 n=10	Mean change at week 24 n=10
PVR, dynes-sec/cm ⁵	576.4 (139.2)	369.2 (121.1)	-207.3 (146.4)
mPAP, mmHg	43.4 (9.7)	30.6 (9.7)	-12.8 (7.1)
PAWP, mmHg	10.0 (4.0)	9.1 (4.8)	-0.9 (3.4)
Cardiac output, L/min	4.7 (0.7)	4.8 (1.4)	0.1 (1.4)

Interim analysis data cut-off date: 25 February 2021.

Data presented as mean (SD).

mPAP: mean pulmonary arterial pressure; PAWP: pulmonary arterial wedge pressure; PVR: pulmonary vascular resistance.



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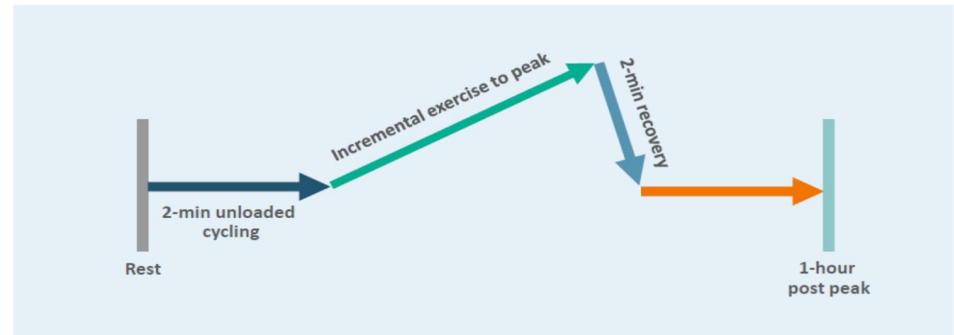
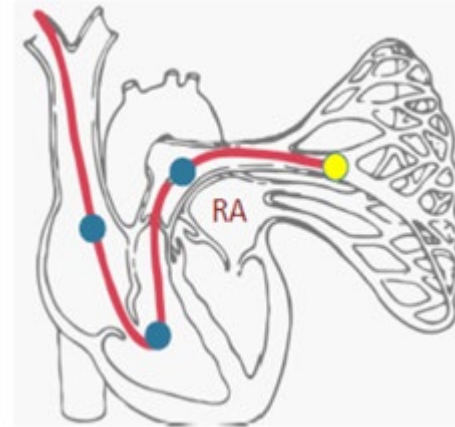
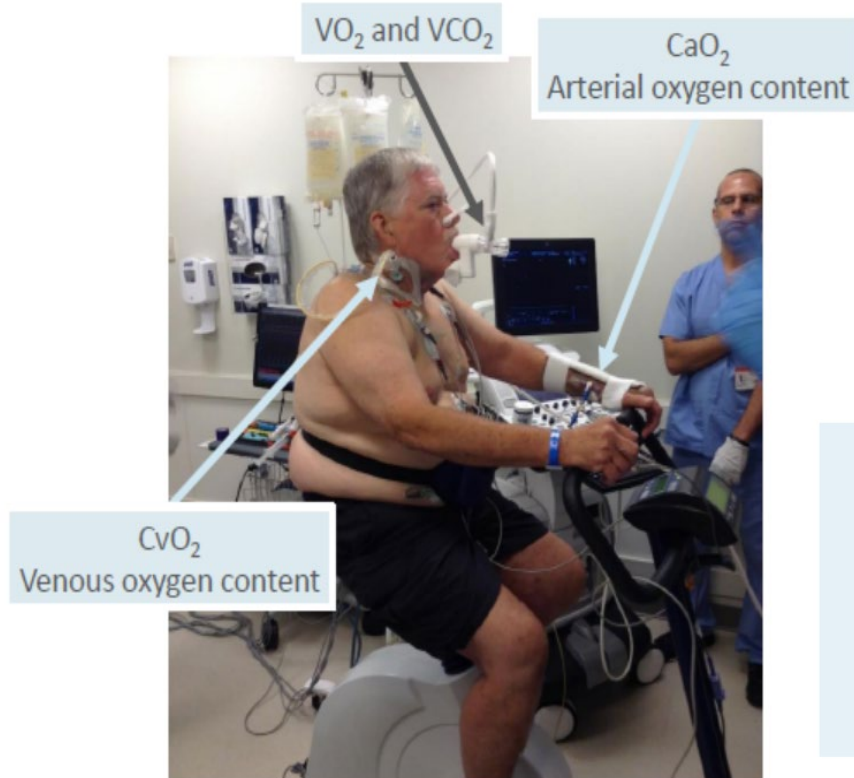
SPECTRA study: iCPET assessments

- Primary endpoint: Change from baseline in peak oxygen uptake (VO_2 max) at 24 weeks
- Secondary endpoints from iCPET measured as change from baseline at 24 weeks:
 - Ventilatory efficiency (VE/VCO_2 slope)
 - Cardiac index ($\text{L}/\text{min}/\text{m}^2$)
 - Mean pulmonary artery pressure (mPAP, mmHg)
 - Arteriovenous O_2 content difference ($\text{Ca}-\text{vO}_2$)
 - VD/VT
 - VO_2 at AT (O_2 consumption at anaerobic threshold)

Why iCPET?

- Affords the dynamic and simultaneous assessment of cardiovascular, respiratory, and metabolic function during exercise
- iCPET informs clinicians regarding the pathophysiologic basis of dyspnea to provide a definitive diagnosis, even in patients with comorbid cardiovascular and pulmonary disease
- iCPET has evolved as the preferred diagnostic strategy for patients in whom the predominate mechanism of dyspnea is unresolved

How Do We Perform iCPET?



SPECTRA Study:

Case Report of First Patient (1/2)

- 25-year-old female, idiopathic PAH for 4.7 years, receiving tadalafil and ambrisentan for the treatment of PAH. At baseline, subject was classified as WHO FC III and 6MWD was 285.5 m.
- The subject's medical history includes gastroesophageal reflux disease, sleep disorder, depression, endometriosis, restless leg syndrome and dust allergy.

Resting supine hemodynamics	Baseline	Week 24	Week 48
mPAP, mmHg	39	13	11
mRAP, mmHg	8	2	2
PAWP, mmHg	8	4	3
CO, L/min	3.73	4.24	3.42
DPG, mmHg	20	3	5
PVR, dynes-sec/cm ⁵	665	170	187

- **At 24 weeks**, subject was classified as WHO FC I and 6MWD was 468.7 m (183.2 m increase from baseline).
- **At 48 weeks**, subject remained WHO FC I and 6MWD was 443.7 (158.2 m increase from baseline).

Data cut-off date 21 Sept 2020

6MWD: 6-minute-walk distance; CO: cardiac output; DPG: diastolic pressure gradient; FC: functional class; mPAP: mean pulmonary arterial pressure; mRAP: mean right arterial pressure; PAH: pulmonary arterial hypertension; PAWP: pulmonary arterial wedge pressure; PVR: pulmonary vascular resistance; WHO: World Health Organization

SPECTRA Study

Case Report of First Patient (2/2) Peak Exercise Hemodynamics (iCPET)

	Baseline	Week 24	Week 48
Work, W	39	66	85
mPAP, mmHg	41	27	23
TPG, mmHg	37	25	22
PAWP, mmHg	4	2	1
CO, L/min	7.0	7.84	7.4
PVR, dynes-sec/cm⁵	423	255	237
Pulmonary artery compliance, mL/mmHg	2.2	3.9	2.3
VO₂ max, mL/kg/min	10.7	17.7	20
VO₂ max, % predicted	33%	54%	62%
Ca-vO₂, mL/dL	9	10.4	15.3
V_E/VCO₂ slope	55	27	30

Data cut-off date 21 Sept 2020

Ca-vO₂: arteriovenous O₂ content difference; CO: cardiac output; iCPET: invasive cardiopulmonary exercise testing; mPAP: mean pulmonary arterial pressure; PAWP: pulmonary arterial wedge pressure; PVR: pulmonary vascular resistance; TPG: transpulmonary pressure gradient; VO₂: oxygen consumption; V_E/VCO₂: ventilatory efficiency

SPECTRA: Peak exercise measures and 6-minute walk distance

- Improvements in mean change from baseline to week 24 were observed for peak oxygen uptake, ventilatory efficiency, total workload, and arteriovenous O₂ content difference
- Improvements were seen in mean change from baseline to week 24 in key peak exercise hemodynamics

	Peak exercise		
	Baseline n=10	Week 24 n=10	Mean change at week 24 n=10
VO ₂ max, mL/min/kg	12.7 (3.5)	14.0 (4.4)	1.27 (2.6)
V _E /VCO ₂ slope	50.7 (25.8)	41.2 (13.1)	-9.5 (15.7)
Ca-vO ₂ , mL/100 mL	9.7 (2.1)*	11.5 (3.2)*	1.4 (2.1) [†]
Workload, W	72.3 (34.0)	88.5 (37.6)	16.2 (13.0)
mPAP, mmHg	66.8 (14.3)	55.2 (14.1)	-11.6 (9.4)
mRAP, mmHg	10.9 (9.8)	4.7 (4.7)	-6.2 (8.4)
PAWP, mmHg	18.1 (23.2) [^]	10.7 (5.6) [^]	-9.7 (21.6) [#]
Cardiac output, L/min	9.7 (3.1)*	9.1 (2.2)	-0.5 (2.3)*

- In nine patients with available data, 6MWD improved by an average of 72.4 m (SD 87.7) from baseline to week 24

Interim analysis data cut-off date: 25 February 2021.

Data presented as mean (SD); *n=9, †n=8, ^n=7, #n=6.

6MWD: 6-minute walk distance; Ca-vO₂: arteriovenous O₂ content difference; mPAP: mean pulmonary arterial pressure; mRAP: mean right arterial pressure; O₂: oxygen; PAWP: pulmonary arterial wedge pressure; SD: standard deviation; VO₂: oxygen consumption; V_E/VCO₂: ventilatory efficiency.



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SPECTRA: Safety

- As of the interim data cut, with a median follow up of 5.5 months (with up to 22 months), 16/21 (76%) patients reported treatment-emergent adverse events (TEAEs)
- Three serious TEAEs were reported (hematochezia, complication associated with central line, and fluid overload), but none were considered related to study drug and no dose interruption or reduction was required
- Sotatercept was generally well tolerated, consistent with the safety profile in other PAH studies

n (%)	n=21
TEAEs	16 (76)
Serious TEAEs	3 (14)
Serious related TEAEs	0 (0)
TEAEs of special interest*	0 (0)
TEAEs leading to treatment discontinuation	1 (5)^
TEAEs leading to death	0 (0)

Interim analysis data cut-off date: 25 February 2021.

*TEAEs of special interest defined as any adverse event of fertility disorders with a focus on suppression of FSH, hepatic toxicity, cardiac events and embolic and thrombotic events, thrombocytopenia, leukopenia, and neutropenia.

^Patient discontinued due to worsening pain at Remodulin® site injection.

FSH: follicle-stimulating hormone; PAH: pulmonary arterial hypertension; TEAE: treatment emergent adverse event.



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Conclusions

- In this preliminary analysis of patients in the ongoing SPECTRA study, encouraging results in hemodynamics, iCPET, and 6MWD were seen
- Safety findings were consistent with previous reports in PAH and in other patient populations
- These interim results further highlight the clinical efficacy of sotatercept and its potential as a new treatment option for patients with PAH
- The SPECTRA study is ongoing with further analyses planned; sotatercept will be further evaluated in a Phase 3 program¹⁻³
 - The randomized, double-blind, placebo-controlled STELLAR study is currently recruiting (NCT04576988) and the HYPERION study in newly diagnosed intermediate- and high-risk patients with PAH is now active (NCT04811092)

6MWD: 6-minute walk distance; iCPET: invasive cardiopulmonary exercise testing; PAH: pulmonary arterial hypertension.

1. ClinicalTrials.gov. A study of sotatercept for the treatment of pulmonary arterial hypertension (STELLAR). <https://clinicaltrials.gov/ct2/show/NCT04576988> [Accessed 24 March 2021]; 2. ClinicalTrials.gov. A long-term follow-up study of sotatercept for PAH treatment (SOTERIA). <https://clinicaltrials.gov/ct2/show/NCT04796337> [Accessed 24 March 2021]; 3. ClinicalTrials.gov. Study of sotatercept in newly diagnosed intermediate- and high-risk PAH patients (HYPERION). <https://clinicaltrials.gov/ct2/show/NCT04811092> [Accessed 24 March 2021].



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Acknowledgments

- We thank all the patients, their families, and all the SPECTRA study investigators and coordinators who participated in the trial
 - SPECTRA study investigators: Aaron B. Waxman, MD, PhD, Franz Rischard, MD, Michael Risbano, MD, and Robert Frantz, MD
- The study was sponsored by Acceleron Pharma, Cambridge, MA, USA
- The authors received editorial assistance from InterComm International Ltd., supported by Acceleron Pharma





JAY BACKSTROM, MD, MPH
**HEAD OF RESEARCH &
DEVELOPMENT**

- Week 48 PULSAR data reinforces the efficacy of sotatercept across multiple endpoints
 - Sustained and further improvement in **6MWD** with consistent and reproducible improvement of ≥50-meter mean change from baseline in all cohorts including the placebo cross over patients
 - Continued improvement in **WHO functional class** with 36% at week 48 compared to 23% at week 24
 - Further reductions in **NT-proBNP** at week 48 (change from baseline)
 - 55% reduction in the patients who continued sotatercept (both doses combined)
 - 42% reduction in the placebo cross over patients (both doses combined)
- SPECTRA:
 - Improvement in exercise hemodynamics an indicator of functional improvement
- Sotatercept was generally well tolerated
- Non-clinical data provide additional scientific rationale for moving into Group 2



A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study to Compare the Efficacy and Safety of Sotatercept Versus Placebo When Added to Background Pulmonary Arterial Hypertension (PAH) Therapy for the Treatment of PAH

Key Inclusion Criteria for PULSAR Relative to STELLAR Phase 3 Trial



Key Inclusion criteria

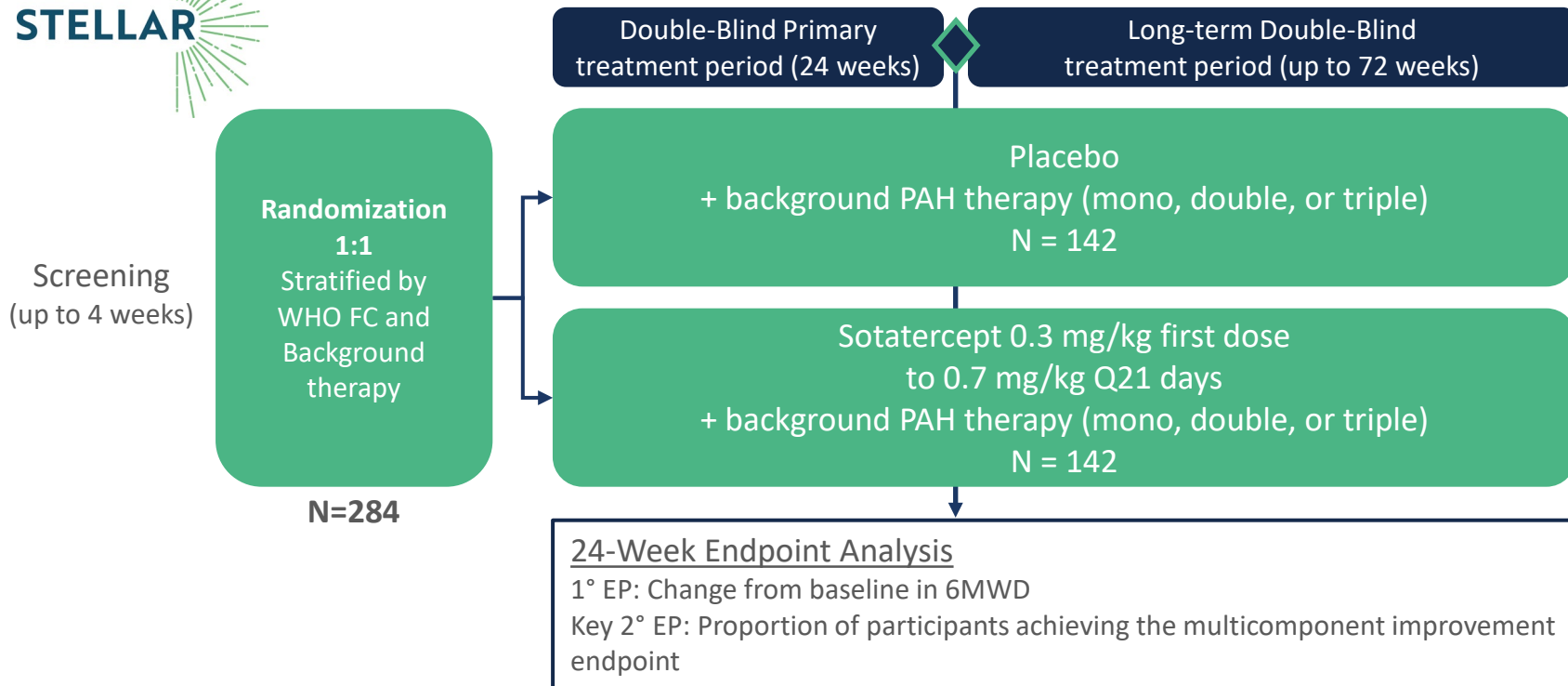
- Adults ≥ 18 years old
- WHO Group 1 PAH
- WHO Functional Class II or III
- Baseline RHC with PVR ≥ 5 Wood units
- Baseline 6-minute walk distance 150-550 m
- Stable treatment with SOC therapies, including mono, double, and triple therapies
 - An endothelin-receptor antagonist, a phosphodiesterase 5 inhibitor, a soluble guanylate cyclase stimulator, and/or a prostacyclin (including IV)

Key Inclusion criteria

- Adults ≥ 18 years old
- WHO Group 1 PAH
- WHO Functional Class II or III
- Baseline RHC with PVR ≥ 5 Wood units
- Baseline 6-minute walk distance 150-500 m
- Stable treatment with SOC therapies, including mono, double, and triple therapies
 - An endothelin-receptor antagonist, a phosphodiesterase 5 inhibitor, a soluble guanylate cyclase stimulator, and/or a prostacyclin (including IV)

WHO: World Health Organization; RHC: right heart catheterization; PVR: Pulmonary vascular resistance.

STELLAR Phase 3 Trial Design Schema



Sotatercept Phase 3 Clinical Development Plan and Vision



REGISTRATIONAL

STELLAR

Main Phase 3 Study



LABEL EXPANSION

HYPERION

Phase 3 Newly Diagnosed Intermediate
and High-Risk Patient Study

ZENITH

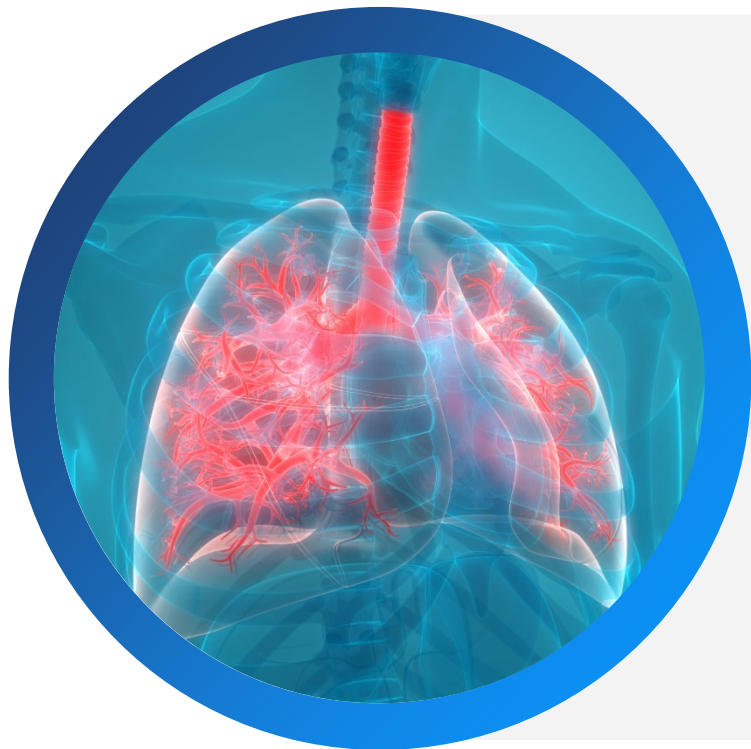
Phase 3 WHO Functional Class III/IV at
High Risk of Mortality Study

Planned

SOTATERCEPT VISION

**BACKBONE
THERAPY IN PAH**





SAVE THE DATE **R&D Day 2021**



June 22nd, 2021



HABIB DABLE

Chief Executive Officer



JANETHE PENA, MD, PHD

Head of Pulmonary
Medical Research



JAY T. BACKSTROM, MD, MPH

Head of Research & Development



TODD JAMES

SVP, Corporate Affairs and
Investor Relations



Sujay Kango

Chief Commercial Officer



AARON WAXMAN, MD, PHD

*Principal investigator in the
SPECTRA trial and a paid consultant
to Accelaron*





APPENDIX



Upcoming and Ongoing Corporate Priorities for Pulmonary Programs



■ Sotatercept

- STELLAR Phase 3 trial enrollment and execution
- HYPERION Phase 3 trial planned start by **2H:2021**
- ZENITH Phase 3 trial expected initiation by **2H:2021**
- PULSAR open-label extension trial completion
- SPECTRA Phase 2 trial completion
- Initiate Phase 2 trial in PH WHO Group 2 planned in **2021**

■ ACE-1334

- Initiate Phase 1b/Phase 2 trial in SSc-ILD expected in **2021**