Acceleron 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

This presentation is for investor relations purposes only – Not for product promotional purposes.
Our Vision for Sotatercept in Pulmonary Arterial Hypertension (PAH)

BACKBONE THERAPY IN PAH
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

Sotatercept is an investigational therapy that is not approved for any use in any country.
ATS 2021 Presentation Highlights

- 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-011\(^1\) 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-011\(^1\) 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.

This presentation is for investor relations purposes only – Not for product promotional purposes.
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, Mardi Gomberg-Maitland³, Marius M. Hoeper⁴, Vallerie McLaughlin⁵, Ioana R. Preston⁶, Rogerio Souza⁷, Aaron Waxman⁸, Solaiappan Manimaran⁹, Jennifer Barnes⁹*, Janethe de Oliveira Pena⁹ and Marc Humbert¹⁰

¹University of Colorado, Aurora, CO, USA; ²National Heart & Lung Institute, Imperial College London, London, England; ³George Washington University, Washington, DC, USA; 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; ⁹Acceleron 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 dysfunction.

- 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 pathology.

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.

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

**Primary endpoint**
Change from baseline to week 24 in PVR

**Select secondary endpoints**
Change from baseline to week 24 in 6MWD, NT-proBNP, and WHO FC

---


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

### 6MWD (m)

<table>
<thead>
<tr>
<th>Group</th>
<th>Week 24 (receiving placebo during placebo-controlled period)</th>
<th>Week 24 (receiving sotatercept during placebo-controlled period)</th>
<th>Week 48</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo + SOC / 0.3 mg/kg + SOC</td>
<td>43.0 ± 22.1</td>
<td>365.8 ± 211.4</td>
<td>13 ± 8.8</td>
</tr>
<tr>
<td>Placebo + SOC / 0.7 mg/kg + SOC</td>
<td>24.3 ± 11.8</td>
<td>13.9 ± 157.1</td>
<td>13 ± 8.8</td>
</tr>
<tr>
<td>Continuing 0.3 mg/kg + SOC</td>
<td>57.4 ± 6.7</td>
<td>-246.2 ± 163.9</td>
<td>31 ± 8.2</td>
</tr>
<tr>
<td>Continuing 0.7 mg/kg + SOC</td>
<td>53.9 ± 8.7</td>
<td>-24.3 ± 11.8</td>
<td>38 ± 8.6</td>
</tr>
</tbody>
</table>

### NT-proBNP (pg/mL)

<table>
<thead>
<tr>
<th>Group</th>
<th>Week 24 (receiving placebo during placebo-controlled period)</th>
<th>Week 24 (receiving sotatercept during placebo-controlled period)</th>
<th>Week 48</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo + SOC / 0.3 mg/kg + SOC</td>
<td>57.4 ± 6.7</td>
<td>-689.2 ± 169.9</td>
<td>17 ± 5.8</td>
</tr>
<tr>
<td>Placebo + SOC / 0.7 mg/kg + SOC</td>
<td>66.5 ± 12.5</td>
<td>-555.5 ± 198.7</td>
<td>33 ± 7.4</td>
</tr>
<tr>
<td>Continuing 0.3 mg/kg + SOC</td>
<td>57.4 ± 6.7</td>
<td>-246.2 ± 163.9</td>
<td>31 ± 8.2</td>
</tr>
<tr>
<td>Continuing 0.7 mg/kg + SOC</td>
<td>66.5 ± 12.5</td>
<td>-555.5 ± 198.7</td>
<td>33 ± 7.4</td>
</tr>
</tbody>
</table>

### WHO FC improvement (%)

<table>
<thead>
<tr>
<th>Group</th>
<th>Week 24 (receiving placebo during placebo-controlled period)</th>
<th>Week 24 (receiving sotatercept during placebo-controlled period)</th>
<th>Week 48</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo + SOC / 0.3 mg/kg + SOC</td>
<td>24.3 ± 11.8</td>
<td>13.9 ± 157.1</td>
<td>53 ± 12.9</td>
</tr>
<tr>
<td>Placebo + SOC / 0.7 mg/kg + SOC</td>
<td>53.6 ± 22.8</td>
<td>-782.1 ± 417.3</td>
<td>13 ± 8.8</td>
</tr>
<tr>
<td>Continuing 0.3 mg/kg + SOC</td>
<td>67.7 ± 17.7</td>
<td>-433.3 ± 124.7</td>
<td>31 ± 8.2</td>
</tr>
<tr>
<td>Continuing 0.7 mg/kg + SOC</td>
<td>67.7 ± 17.7</td>
<td>-433.3 ± 124.7</td>
<td>31 ± 8.2</td>
</tr>
</tbody>
</table>

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.

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.

### PULSAR: Overall safety experience including open-label extension

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

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.
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 program\textsuperscript{1–3}
  
  – 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.

Acknowledgments

- We thank all the patients, their families, and all the PULSAR study investigators and coordinators who participated in the trial

- The study was sponsored by Acceleron Pharma, Cambridge, MA, USA

- The authors received editorial assistance from InterComm International Ltd., supported by Acceleron Pharma
Aaron Waxman, MD, PhD
Director, Pulmonary Vascular Disease Program, Brigham and Women’s Hospital; Associate Professor of Medicine, Harvard Medical School

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

This presentation is for investor relations purposes only – Not for product promotional purposes.
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)

Aaron B. Waxman¹, Michael Risbano², Robert Frantz³, Solaiappan Manimaran⁴, Jonathan Lu⁴, and Franz Rischard⁵

¹Brigham and Women’s Hospital, Boston, MA; ²University of Pittsburgh Medical Center, Pittsburgh, PA; ³Mayo Clinic, Rochester, NY; ⁴Acceleron 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
Inclusion criteria
• WHO PH Group I (PAH)
• WHO Functional Class III
• Right heart catheterization with PVR ≥4 Wood units
• 6-minute walk distance (6MWD) 100–550 m
• Stable combination PAH therapy

Open-label treatment period (24 weeks)
Cycle 1:
Sotatercept 0.3 mg/kg + SOC (n=21)

Cycle 2 onward:
Sotatercept 0.7 mg/kg + SOC (n=21)

Extension period* (18 months)
Sotatercept 0.7 mg/kg + SOC

Primary endpoint
• Change from baseline to week 24 in peak oxygen uptake (VO2 max)

Select secondary endpoints
• Change from baseline to week 24 in exercise measures, including:
  • $V_{E}/V_{CO2}$ slope, Ca-vO2, workload, mPAP, mRAP, PAWP, and cardiac output
• Change from baseline to week 24 in 6MWD

iCPET baseline
iCPET primary endpoint (n=10 as of this data cut)
iCPET 48 weeks


*Extension period followed by 8-week post-treatment follow-up.
6MWD: 6-minute walk distance; Ca-vO2: arteriovenous O2 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; $V_{E}/V_{CO2}$: ventilatory efficiency; VO2: peak oxygen uptake; WHO: World Health Organization.
**SPECTRA: Baseline characteristics**

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

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

*Interim analysis data cut-off date: 25 February 2021.
6MWD: 6-minute walk distance; EOT: end of treatment; PAH: pulmonary arterial hypertension.
At rest, reductions were seen in mean change from baseline to week 24 in PVR and mPAP.

<table>
<thead>
<tr>
<th></th>
<th>Baseline n=10</th>
<th>Week 24 n=10</th>
<th>Mean change at week 24 n=10</th>
</tr>
</thead>
<tbody>
<tr>
<td>PVR, dynes-sec/cm$^5$</td>
<td>576.4 (139.2)</td>
<td>369.2 (121.1)</td>
<td>-207.3 (146.4)</td>
</tr>
<tr>
<td>mPAP, mmHg</td>
<td>43.4 (9.7)</td>
<td>30.6 (9.7)</td>
<td>-12.8 (7.1)</td>
</tr>
<tr>
<td>PAWP, mmHg</td>
<td>10.0 (4.0)</td>
<td>9.1 (4.8)</td>
<td>-0.9 (3.4)</td>
</tr>
<tr>
<td>Cardiac output, L/min</td>
<td>4.7 (0.7)</td>
<td>4.8 (1.4)</td>
<td>0.1 (1.4)</td>
</tr>
</tbody>
</table>
SPECTRA study: iCPET assessments

- **Primary endpoint:** Change from baseline in peak oxygen uptake ($\text{VO}_2\text{ max}$) at 24 weeks

- **Secondary endpoints from iCPET measured as change from baseline at 24 weeks:**
  - Ventilatory efficiency ($\text{VE/VO}_2\text{ slope}$)
  - Cardiac index ($\text{L/min/m}^2$)
  - Mean pulmonary artery pressure (mPAP, mmHg)
  - Arteriovenous $\text{O}_2$ content difference ($\text{Ca-vO}_2$)
  - VD/VT
  - $\text{VO}_2$ at AT ($\text{O}_2$ 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?

- VO₂ and VCO₂
- CaO₂: Arterial oxygen content
- CvO₂: Venous oxygen content

Procedure:
- Incremental exercise to peak
- 2-min recovery
- 1-hour post peak

2-min unloaded cycling

Brigham Health
Brigham and Women's Hospital
Harvard Medical School
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.

<table>
<thead>
<tr>
<th>Resting supine hemodynamics</th>
<th>Baseline</th>
<th>Week 24</th>
<th>Week 48</th>
</tr>
</thead>
<tbody>
<tr>
<td>mPAP, mmHg</td>
<td>39</td>
<td>13</td>
<td>11</td>
</tr>
<tr>
<td>mRAP, mmHg</td>
<td>8</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>PAWP, mmHg</td>
<td>8</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>CO, L/min</td>
<td>3.73</td>
<td>4.24</td>
<td>3.42</td>
</tr>
<tr>
<td>DPG, mmHg</td>
<td>20</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>PVR, dynes-sec/cm²</td>
<td>665</td>
<td>170</td>
<td>187</td>
</tr>
</tbody>
</table>

- 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)

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 24</th>
<th>Week 48</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Work, W</strong></td>
<td>39</td>
<td>66</td>
<td>85</td>
</tr>
<tr>
<td><strong>mPAP, mmHg</strong></td>
<td>41</td>
<td>27</td>
<td>23</td>
</tr>
<tr>
<td><strong>TPG, mmHg</strong></td>
<td>37</td>
<td>25</td>
<td>22</td>
</tr>
<tr>
<td><strong>PAWP, mmHg</strong></td>
<td>4</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td><strong>CO₂ L/min</strong></td>
<td>7.0</td>
<td>7.84</td>
<td>7.4</td>
</tr>
<tr>
<td><strong>PVR, dynes-sec/cm⁵</strong></td>
<td>423</td>
<td>255</td>
<td>237</td>
</tr>
<tr>
<td><strong>Pulmonary artery compliance, mL/mmHg</strong></td>
<td>2.2</td>
<td>3.9</td>
<td>2.3</td>
</tr>
<tr>
<td><strong>VO₂ max, mL/kg/min</strong></td>
<td>10.7</td>
<td>17.7</td>
<td>20</td>
</tr>
<tr>
<td><strong>VO₂ max, % predicted</strong></td>
<td>33%</td>
<td>54%</td>
<td>62%</td>
</tr>
<tr>
<td><strong>Ca-vO₂, mL/dL</strong></td>
<td>9</td>
<td>10.4</td>
<td>15.3</td>
</tr>
<tr>
<td><strong>V₉/VCO₂ slope</strong></td>
<td>55</td>
<td>27</td>
<td>30</td>
</tr>
</tbody>
</table>

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; V₉/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

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 24</th>
<th>Mean change at week 24</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=10</td>
<td>n=10</td>
<td></td>
</tr>
<tr>
<td>VO₂ max, mL/min/kg</td>
<td>12.7 (3.5)</td>
<td>14.0 (4.4)</td>
<td>1.27 (2.6)</td>
</tr>
<tr>
<td>Vₑ/VCO₂ slope</td>
<td>50.7 (25.8)</td>
<td>41.2 (13.1)</td>
<td>-9.5 (15.7)</td>
</tr>
<tr>
<td>Ca-vO₂, mL/100 mL</td>
<td>9.7 (2.1) *</td>
<td>11.5 (3.2) *</td>
<td>1.4 (2.1) †</td>
</tr>
<tr>
<td>Workload, W</td>
<td>72.3 (34.0)</td>
<td>88.5 (37.6)</td>
<td>16.2 (13.0)</td>
</tr>
<tr>
<td>mPAP, mmHg</td>
<td>66.8 (14.3)</td>
<td>55.2 (14.1)</td>
<td>-11.6 (9.4)</td>
</tr>
<tr>
<td>mRAP, mmHg</td>
<td>10.9 (9.8)</td>
<td>4.7 (4.7)</td>
<td>-6.2 (8.4)</td>
</tr>
<tr>
<td>PAWP, mmHg</td>
<td>18.1 (23.2) ^</td>
<td>10.7 (5.6) ^</td>
<td>-9.7 (21.6) #</td>
</tr>
<tr>
<td>Cardiac output, L/min</td>
<td>9.7 (3.1) *</td>
<td>9.1 (2.2)</td>
<td>-0.5 (2.3) †</td>
</tr>
</tbody>
</table>

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; Vₑ/VCO₂: ventilatory efficiency.

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

### Table: Treatment Emergent Adverse Events

<table>
<thead>
<tr>
<th>Category</th>
<th>n (%)</th>
<th>n=21</th>
</tr>
</thead>
<tbody>
<tr>
<td>TEAEs</td>
<td>16 (76)</td>
<td></td>
</tr>
<tr>
<td>Serious TEAEs</td>
<td>3 (14)</td>
<td></td>
</tr>
<tr>
<td>Serious related TEAEs</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>TEAEs of special interest*</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>TEAEs leading to treatment discontinuation</td>
<td>1 (5)*</td>
<td></td>
</tr>
<tr>
<td>TEAEs leading to death</td>
<td>0 (0)</td>
<td></td>
</tr>
</tbody>
</table>

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.
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 program\(^1-3\)
  
  - 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.

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
This presentation is for investor relations purposes only – Not for product promotional purposes.
ATS 2021 Key Takeaways

- 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

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

Sotatercept is an investigational therapy that is not approved for any use in any country.
STELLAR Phase 3 Trial Design Schema

**Randomization**
1:1 Stratified by WHO FC and Background therapy

**N=284**

**Screening (up to 4 weeks)**

**Double-Blind Primary treatment period (24 weeks)**
- Placebo + background PAH therapy (mono, double, or triple)
  - N = 142

- Sotatercept 0.3 mg/kg first dose to 0.7 mg/kg Q21 days + background PAH therapy (mono, double, or triple)
  - N = 142

**Long-term Double-Blind treatment period (up to 72 weeks)**

**24-Week Endpoint Analysis**
- 1° EP: Change from baseline in 6MWD
- Key 2° EP: Proportion of participants achieving the multicomponent improvement endpoint

This presentation is for investor relations purposes only – Not for product promotional purposes. Sotatercept is an investigational therapy that is not approved for any use in any country.
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

**SOTATERCEPT VISION**

**BACKBONE THERAPY IN PAH**

---

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

This presentation is for investor relations purposes only – Not for product promotional purposes.
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

Sotatercept and ACE-1334 are investigational therapies that are not approved for any use in any country.