Tenax Strategic Update

Specialty pharmaceutical company focused on search, development, and commercialization of drugs that address diseases with high unmet medical need

• Shift levosimendan development focus to pulmonary hypertension
  • WHO Group 2- pulmonary hypertension associated with heart failure with preserved ejection fraction (PH-HFpEF)
• Continue ongoing search for assets and collaborations that will build shareholder value
Shift Levosimendan Development Focus to Pulmonary Hypertension, WHO-Group 2

• Leverage positive levosimendan clinical study data
  • Positive levosimendan Phase 2 pulmonary hypertension study data
  • Positive levosimendan right heart failure data

• **Focus development in PH-HFpEF** — (Pulmonary Hypertension in patients with Heart Failure and Preserved Ejection Fraction)
  • High unmet medical need
  • Large patient population with no approved drugs

• **Capitalize on PH-HFpEF advisors expertise and advocacy**
  • Validate clinical development strategy with PH-HFpEF experts
PH-HFpEF Development Strategy Validated by World Recognized Experts in Pulmonary Hypertension and HFpEF

• Lead Scientific Advisor – Stuart Rich, MD

Stuart Rich, M.D.
Professor of Medicine
Northwestern University Feinberg School of Medicine
Director, Pulmonary Vascular Disease Program:
Bluhm Cardiovascular Institute;
Previous FDA Cardio-Renal Advisory Committee Member;
Recognized Global Pulmonary Hypertension Expert
Rationale for Development of Levosimendan in PH-HFpEF

• PH-HFpEF is an area of high unmet medical need
  • High mortality (up to 50% at 5 years)
  • Poor quality of life (poor exercise capacity)
  • No approved therapies in PH-HFpEF

• Commercially attractive market
  • Large potential market - Estimated PH-HFpEF prevalence in the US >1,500,000
  • High value chronic therapy that addresses a large unmet need

• Mechanistic rationale for Levosimendan in PH-HFpEF
  • Including mechanisms directed at right heart failure

• Existing preliminary positive Phase 2 clinical data in Pulmonary Hypertension

• Efficient and timely Phase 2 trial is planned

• IV Levosimendan exclusivity as NCE
Global Pulmonary Hypertension Pharmaceutical Market
> $5 Billion in 2016

Based on publicly reported sales from company annual reports
**Pulmonary Hypertension WHO Classification**

**Levosimendan Development Focused on Group 2**


Global Pulmonary Hypertension Product Sales - 2016
Allocated by WHO Group Approved Indication

Excludes potential off-label uses
PH-HFpEF Unmet Need
Approved WHO Group 1 Drugs are **not Approved or Effective in** Group 2 Patients

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Pulmonary Hypertension WHO Group 1 (PAH)</th>
<th>Pulmonary Hypertension WHO Group 2 (HFpEF)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PDE5 Inhibitors</td>
<td>FDA Approved</td>
<td>Efficacy not established</td>
</tr>
<tr>
<td>Endothelin Receptor Antagonists</td>
<td>FDA Approved</td>
<td>Efficacy not established</td>
</tr>
<tr>
<td>Soluble Guanylate Cyclase Stimulators</td>
<td>FDA Approved</td>
<td>Efficacy not established</td>
</tr>
<tr>
<td>Prostacyclins (IV/SC/Inhaled/Oral)</td>
<td>FDA Approved</td>
<td>Efficacy not established</td>
</tr>
</tbody>
</table>
PH-HFpEF Patients have Poor Outcomes
PH-HFpEF + RV Dysfunction is Associated with Highest Mortality

PH-HFpEF with Right Heart Dysfunction (RHD): Large Target Market with Very High Needs

US PH-HFpEF Patients
~1,500,000-2,000,000

US HFpEF Patients
>3,000,000

RHD
~500,000 - 700,000

Estimates based on
Mechanistic Rationale for Levosimendan in PH-HFpEF – More than just a Vasodilator

Problem

Right Heart → Pulmonary Vasculature → Left Heart

- RV Failure
- Increased Pulmonary Congestion & Pressure
- Poor LV Relaxation and Reduced Cardiac Output

Levosimendan MOA

- Ca Sensitizer
- K-ATP Channel
- Ca Sensitizer

Potential Benefits

- Inotropic & Lusitropic Effects to Improve RV Function
- Pulmonary Vasodilation to Reduce PA Pressure/RV Afterload
- Inotropic & Lusitropic Effects to Improve LV Function
Increasing Number of Scientific Publications on Levosimendan in Pulmonary Hypertension

• Clinical Studies

• Preclinical Studies
Results from a Multicenter, Randomized, Placebo Controlled, Pilot Study of Levosimendan in Pulmonary Hypertension Patients

Kleber et al Patient Demographics

<table>
<thead>
<tr>
<th></th>
<th>Levosimendan (n = 18)</th>
<th>Placebo (n = 10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>62 ± 11</td>
<td>58 ± 12</td>
</tr>
<tr>
<td>Sex, M/F</td>
<td>9/9</td>
<td>8/2</td>
</tr>
<tr>
<td>Etiology of pulmonary hypertension</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonary arterial hypertension</td>
<td>7 (39)</td>
<td>4 (40)</td>
</tr>
<tr>
<td>Idiopathic</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Portal hypertension</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Congenital systemic to pulmonary shunts</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Pulmonary venous hypertension due to left-sided heart disease</td>
<td>10 (56)</td>
<td>4 (40)</td>
</tr>
<tr>
<td>Pulmonary hypertension due to chronic thrombotic and/or embolic disease</td>
<td>1 (5)</td>
<td>2 (20)</td>
</tr>
<tr>
<td>Signs of right heart failure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jugular venous distension</td>
<td>12 (67)</td>
<td>7 (70)</td>
</tr>
<tr>
<td>Peripheral edema</td>
<td>14 (78)</td>
<td>8 (80)</td>
</tr>
<tr>
<td>Known response to vasodilator testing</td>
<td>18 (100)</td>
<td>10 (100)</td>
</tr>
<tr>
<td>Systemic hemodynamics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>121 ± 23</td>
<td>116 ± 15</td>
</tr>
<tr>
<td>Diastolic blood pressure</td>
<td>72 ± 10</td>
<td>75 ± 12</td>
</tr>
<tr>
<td>Heart rate</td>
<td>75 ± 18</td>
<td>70 ± 13</td>
</tr>
<tr>
<td>New York Heart Association class</td>
<td></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>15 (83)</td>
<td>9 (90)</td>
</tr>
<tr>
<td>IV</td>
<td>3 (17)</td>
<td>1 (10)</td>
</tr>
<tr>
<td>mRAP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>12 ± 5.9 (n = 15)</td>
<td>14 ± 4.9 (n = 9)</td>
</tr>
<tr>
<td>Range</td>
<td>5-29</td>
<td>7-24</td>
</tr>
<tr>
<td>Use of vasoactive medication</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diuretics</td>
<td>15 (83)</td>
<td>8 (80)</td>
</tr>
<tr>
<td>Angiotensin-converting enzyme inhibitor/AT2-blocker</td>
<td>14 (78)</td>
<td>6 (60)</td>
</tr>
<tr>
<td>β-Blocker</td>
<td>10 (56)</td>
<td>7 (70)</td>
</tr>
<tr>
<td>Calcium channel blocker</td>
<td>6 (33)</td>
<td>4 (40)</td>
</tr>
<tr>
<td>Bosentan</td>
<td>3 (17)</td>
<td>2 (20)</td>
</tr>
</tbody>
</table>

Values are mean ± SD or n (%). Medication is expressed as the number of patients taking the drug (%). a. According to the Ventic classification. 24
Change in PVR (mean ± SEM) during 24-hour infusion and 6-hour infusion at week 8

*Primary Endpoint - Change in PVR at the end of the Initial 24-hour infusion

Baseline
Levosimendan n=15
Placebo n=9

Day 0

Time
Week 8
Levosimendan n=13
Placebo n=7

P= 0.009*
P= 0.253
Change in mPAP (mean ± SEM) during 24-hour infusion and 6-hour infusion at week 8

<table>
<thead>
<tr>
<th>Time</th>
<th>Levosimendan n=18</th>
<th>Placebo n=10</th>
<th>Levosimendan n=16</th>
<th>Placebo n=8</th>
</tr>
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<tbody>
<tr>
<td>Baseline</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 8</td>
<td></td>
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</table>

P = 0.056

P = 0.172
Levosimendan in Pulmonary Hypertension
The Clinical Respiratory Journal (September 2017)

Primary endpoint-Change in WHO Functional Class

A. Change in WHO-FC after infusion of levosimendan from basement to post-treatment. World Health Organization Function Class: WHO-FC.

Primary Endpoint- Change in Dyspnea Scores

B. Change in Borg dyspnoea scores from basement to post-treatment

Phase 2 Study Design

• Double-blind study of PH-HFpEF Patients
  • PAP ≥35, PCWP ≥20, CI ≤2.2, NYHA Class III/IV, LVEF ≥40%
• Targets: 50 patients; 20 sites; 14-18 months
• Primary Endpoint:
  • hemodynamic effect (with exercise) at 6 weeks compared to the baseline measurements manifested by:
    • ↓5mmHg in pulmonary capillary wedge pressure (PCWP), and/or
    • ↑10% in cardiac index (CI)
• 90% power; assuming responses of 67% (levosimendan) and 13% (placebo)
• Secondary Endpoints:
  • Change in resting PCWP and CI
  • Change in PVR effect at rest and with exercise
  • Change in PCWP when supine, legs elevated, and at max exercise
  • Patient global assessment (based on a 7-point Likert scale) at Wk 6
  • Exercise duration at Wk 6
Summary
The Opportunity for Levosimendan in PH-HFpEF

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