PBI-4050 is Safe and Well Tolerated and Shows Evidence of Benefit in Idiopathic Pulmonary Fibrosis

Phase 2, Open-label, Single Arm, Exploratory, Observational Study to Evaluate the Safety and Tolerability of PBI-4050 in Patients with Idiopathic Pulmonary Fibrosis (IPF)

J. Parker¹, R. Sawtell², L. Gagnon², A. Hagerimana², P. Laurin², M. Kolb³, A. Cantin⁴ and J. Moran²

¹ ProMetic BioTherapeutics Inc, Rockville, MD
² ProMetic BioSciences Inc, Laval, QC/CA
³ McMaster University – Hamilton, ON/CA
⁴ Centre de recherche du Centre Hospitalier Universitaire de Sherbrooke (CHUS-CRC) – QC/CA
PBI-4050 IPF Phase 2 Investigators

- Andre Cantin, MD; University of Sherbrooke, Sherbrooke, QC, Canada
- Shane Shapera, MD; University Health Network, Toronto General Hospital, Toronto, ON, Canada
- Nasreen Khalil, MD; The Lung Centre, Vancouver General Hospital, Vancouver, BC, Canada
- Chris Ryerson, MD; Pacific Lung Health Centre, St. Paul's Hospital, Vancouver, BC, Canada
- Helene Manganas, MD; Notre Dame Hospital of the CHUM, Montreal, QC, Canada
- Paul Hernandez, MD; Queen Elizabeth II HSC, Halifax, NS, Canada
PBI-4050 Targets Multiple Pathways Involved in Pulmonary Fibrosis

Study Design

Primary Endpoints: Safety & Tolerability; vital signs; biochemistry; ECG

Secondary Endpoints: Change in pulmonary function (FVC)

Key Inclusion/Exclusion Criteria:
- Diagnosis of IPF per ATS/ERS guidelines (2011) per investigator
- 40 years old or older
- No emphysema > fibrosis on HRCT
- Active smoker (within 3 months of screening)

Background therapy: Pirfenidone and nintedanib therapy were allowed but not required

Data analysis: Data analyzed by presence/absence of concurrent IPF therapy

Treatment Period

Screening -28 to 0 W1 W2 W6 W12/EOT W16 FUP

PBI-4050, 800 mg once daily (soft gel capsules)
### Results: Baseline Characteristics

41 subjects enrolled
- 40 subjects completed treatment
- 1 subject on PBI-4050 and pirfenidone withdrew due to an IPF exacerbation after 2 weeks on the study and was not included in the analysis

<table>
<thead>
<tr>
<th>Baseline</th>
<th>PBI-4050 alone (N=9)</th>
<th>PBI-4050 + N (N=16)</th>
<th>PBI-4050 + P (N=15)</th>
<th>Total (N=40)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs,SD)</td>
<td>71.6 (5.9)</td>
<td>69.4 (8.3)</td>
<td>66.1 (5.5)</td>
<td>68.6 (7.2)</td>
</tr>
<tr>
<td>Male Gender (%)</td>
<td>66.7</td>
<td>75.0</td>
<td>80.0</td>
<td>75.0</td>
</tr>
<tr>
<td>FVC % Predicted Normal (% ,SD)</td>
<td>83.1 (16.4)</td>
<td>71.5 (16.3)</td>
<td>70.8 (14.3)</td>
<td>73.9 (16.4)</td>
</tr>
<tr>
<td>FVC (L)</td>
<td>2.88 (0.72)</td>
<td>2.76 (0.51)</td>
<td>2.85 (0.72)</td>
<td>2.82 (0.66)</td>
</tr>
<tr>
<td>DLCO % Predicted Normal (% , SD)</td>
<td>47.2 (11.0)</td>
<td>50.8 (14.3)</td>
<td>49.1 (15.8)</td>
<td>48.9 (14.4)</td>
</tr>
<tr>
<td>Duration of IPF (yrs)</td>
<td></td>
<td></td>
<td></td>
<td>1.82 (1.2)</td>
</tr>
</tbody>
</table>

N = nintedanib; P = pirfenidone
Baseline Characteristics: Comparison with Recent Studies

<table>
<thead>
<tr>
<th>Baseline</th>
<th>PBI-4050</th>
<th>INPULSIS (nintedanib)</th>
<th>ASCEND (pirfenidone)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>68.6</td>
<td>66.7</td>
<td>68.4</td>
</tr>
<tr>
<td>Male Gender (%)</td>
<td>75.0</td>
<td>79.5</td>
<td>79.9</td>
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<td>73.9</td>
<td>79.3</td>
<td>67.8</td>
</tr>
<tr>
<td>DLCO % Predicted Normal (%)</td>
<td>48.9</td>
<td>47.4</td>
<td>43.7</td>
</tr>
</tbody>
</table>
Subject Disposition

52 subjects screened

41 subjects enrolled

40 subjects completed
12 W treatment

1 subject withdrawn by Investigator at 2 weeks (too ill to continue)
# Results: Lung Function

## Mean Change from Baseline

<table>
<thead>
<tr>
<th>Measure</th>
<th>PBI-4050 alone (N=9)</th>
<th>PBI-4050 + N (N=16)</th>
<th>PBI-4050 + P (N=15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC % Predicted Normal (%) (95% CI)</td>
<td>-1.1 ((-4.0, 1.8))</td>
<td>+0.1 ((-1.9, 2.0))</td>
<td>-2.7 ((-4.8, -0.6))</td>
</tr>
<tr>
<td>FVC (mL) (95% CI)</td>
<td>-12* ((-102, +77))</td>
<td>+2** ((-61, +64))</td>
<td>-102 ((-172, -32))</td>
</tr>
</tbody>
</table>

* P = 0.14 vs. PBI-4050 + P  
** P < 0.04 vs PBI-4050 + P

N = nintedanib; P = pirfenidone
PBI-4050 PK Profiles by Concomitant Medication

- PBI-4050 pharmacokinetics for IPF subjects were similar to healthy volunteers for PBI-4050 and PBI-4050 + nintedanib.
- PBI-4050 PK is significantly reduced with PBI-4050 + pirfenidone combination, suggesting a drug-drug interaction.
Results: Safety

Summary
- No deaths; 1 SAE of pneumonia; no TEAEs requiring study drug discontinuation.
- Most frequent TEAE was diarrhea, with the lowest frequency in the PBI-4050 alone group

Related TEAEs by Frequency (≥ 2)

<table>
<thead>
<tr>
<th>Preferred Term</th>
<th>PBI-4050 alone (N=9)</th>
<th>PBI-4050 + N (N=16)</th>
<th>PBI-4050 + P (N=16)</th>
<th>Total (N=41)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea</td>
<td>1</td>
<td>6</td>
<td>4</td>
<td>11</td>
</tr>
<tr>
<td>Dizziness</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Somnolence</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Fatigue</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

N = nintedanib; P = pirfenidone
PBI-4050 Phase 2 Study Confirms Safety & Early Evidence of Efficacy in IPF

➢ Provides valuable information for the design of 2 phase 2/3 trials

* INPULSIS-2 - Richeldi & al., New England Journal of Medicine, 270;29, May 29 2014, page 2076
ASCEND - King & al., New England Journal of Medicine, 270;29, May 29 2014, page 2088
Conclusions

- PBI-4050 was well tolerated and demonstrated a good safety profile in IPF subjects when given alone or in combination with nintedanib/pirfenidone
- PBI-4050 alone and in combination with nintedanib demonstrated promise in slowing or stopping the decline in lung function
- PBI-4050 in combination with pirfenidone demonstrated a greater decline in lung function
- Pharmacokinetics of PBI-4050 in subjects with IPF were similar to healthy volunteers for PBI-4050 alone or in combination with nintedanib; however, PBI-4050 levels were reduced in combination with pirfenidone suggesting a possible drug-drug interaction
- Additional study of PBI-4050 alone or in combination with nintedanib is warranted:
  - Planning underway for a phase 2/3 study with PBI-4050 as an add-on to nintedanib
  - Planning underway for a phase 2/3 study with PBI-4050 for patients unable to tolerate or fail SOC