**Introduction**

Treprostinil (Tre), a synthetic prostacyclin analogue, is currently approved for inhalation administration to patients with pulmonary arterial hypertension (PAH) via nebulized Tyvaso® Inhalation Solution (Tre Solution) administered four times per day. A convenient, dry powder inhalation formulation of Tre offers a simple, portable treatment regimen that is a meaningful improvement over the current nebulized therapy.

Liquidia is developing LIQ861, a dry powder formulation of treprostinil, specifically designed to improve deep lung delivery and the safety profile of the inhaled route. Using our proprietary PRINT® technology, LIQ861 particles are a precise, uniform size (1µm) and retold pollen-like shape. We conducted single-dose pharmacokinetic (PK) studies in rats and dogs and repeat-dose toxicity studies in rats.

LIQ861 was evaluated in a Phase 1 safety, tolerability and PK single ascending dose study in healthy adult subjects who received 25 mcg to 150 mcg in two inhalations per capsule.

**Particle Characterization**

**Dry Powder Inhaler**

**Animal Pharmacokinetic Data**

**Similar Treprostinil Exposure with LIQ861 or Simulated Tre Solution**

**Conclusions**

1. Systemic treprostinil exposures (C_{Tre,a}, AUC_{Tre,a} and AUC_{Tre,c}) were similar when administered as LIQ861 Dry Powder or Simulated Tre Solution.

2. No evidence of treprostinil accumulation with repeated exposure of LIQ861 or Simulated Tre Solution.

**LIQ861 Summary: No SAEs; only mild TEAEs**

<table>
<thead>
<tr>
<th>Reported Adverse Events (AEs) by Relatedness and Treatment</th>
<th>No (%) of Subjects</th>
<th>No. of Events</th>
<th>No (%) of Subjects</th>
<th>No. of Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Related to treatment</td>
<td>29 (27.4%)</td>
<td>60</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Cough</td>
<td>11 (25.6%)</td>
<td>11</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Throat irritation</td>
<td>9 (20.9%)</td>
<td>9</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Headache</td>
<td>4 (9.1%)</td>
<td>4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Nausea</td>
<td>2 (4.5%)</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Dizziness</td>
<td>1 (2.3%)</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Hot Flush</td>
<td>1 (2.3%)</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Venipuncture site pain</td>
<td>1 (2.3%)</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

**Acknowledgements**

We thank Dr. Nicholas Hill and Dr. Michele Stone for their valuable contributions.


**LIQ861 PK Results**

**Phase I Ascending Single Dose Escalation Study**

**Trial Design**

**Animal Study Designs**

**Single Administration PK Study in Anesthetized Male Beagle Dogs:**

- Administered via endotracheal tube and controlled ventilation ( inspiratory: 30%, expiratory: 70%)
- Tre Solution (Simulated) – Par LLC Plus Jet Nebulizer
- LIQ861 – Lineair Powder Feeder
- Lung Deposition ≠ 70%

**Repeat Dose Toxicity Study (14 Days & 26 weeks):**

- Administered via five-peak nose-only inhalation exposure system
- Tre Solution – clinical inhaler (Solodose®)
- LIQ861 – PrinTech Rotating Brush Generator
- Lung Deposition ≥ 70%