**BACKGROUND**

- LIQ861 is an inhaled, dry-powder formulation of treprostinil produced using PRINT® (Particle Replication in Nonwetting Templates) technology, a proprietary process that allows the design and manufacture of highly uniform drug particles.
- The trefoil shape of particles in the LIQ861 formulation of treprostinil was selected based on its highly aerodynamic properties that support deep lung delivery.
- Enhanced lung deposition achieves higher tolerated dose levels than current inhaled therapies.
- Cmax, mean AUCinf, and the median time to Cmax (Tmax) of a single dose of 79.5 µg LIQ861 were 1.25 ng/ml, 0.101 ng·h/ml, and 0.17 hours, respectively.

**OBJECTIVES**

- The primary objective of the current study LT1-102 was to determine the comparative bioavailability of Liquidia Technologies inhaled treprostinil particles developed with their proprietary PRINT technology and delivered with the Plastiape RS00 Model 8 dry powder inhaler (DPI) device, comparing a 79.5-µg capsule dose of LIQ861 (approximate delivered dose 56.6 µg treprost inil) to 9 breaths of Tyvaso® (approximate delivered dose 54 µg treprostinil).
- A secondary objective was to evaluate the safety of LIQ861 in healthy male and female subjects.

**METHODS**

- This was an open-label, crossover study that enrolled healthy subjects 18 to 45 years of age inclusive.
- Subjects were randomized to 1 of 3 treatment sequences (LIQ861/LIQ861, Tyvaso®/LIQ861, and LIQ861/Tyvaso®) with each sequence consisting of 2 periods (Table 1).

**PHARMACOKINETIC RESULTS**

**SEQUENCE 1**

- During Sequence 1 (a 2-period replicate for LIQ861), the PK parameters between the 2 periods were nearly identical with low variability (Figure 2).

<table>
<thead>
<tr>
<th>Agent</th>
<th>Parameter</th>
<th>GMR</th>
<th>90% CI</th>
<th>Within Subject % CV</th>
</tr>
</thead>
<tbody>
<tr>
<td>LIQ861 79.5 µg vs Tyvaso® 54 µg</td>
<td>AUC&lt;sub&gt;0-12&lt;/sub&gt;</td>
<td>0.923</td>
<td>0.802, 1.064</td>
<td>14.6</td>
</tr>
<tr>
<td>LIQ861 79.5 µg vs Tyvaso® 54 µg</td>
<td>AUC&lt;sub&gt;last&lt;/sub&gt;</td>
<td>0.947</td>
<td>0.812, 1.103</td>
<td>15.8</td>
</tr>
<tr>
<td>LIQ861 79.5 µg vs Tyvaso® 54 µg</td>
<td>C&lt;sub&gt;max&lt;/sub&gt;</td>
<td>0.931</td>
<td>0.819, 1.059</td>
<td>13.3</td>
</tr>
</tbody>
</table>

- Cmax, mean AUC<sub>inf</sub>, and the median time to Cmax (Tmax) of a single dose of 79.5 µg LIQ861 were 1.25 ng/ml, 0.101 ng·h/ml, and 0.17 hours, respectively.

**SEQUENCES 2 and 3**

- In the crossover sequence 2 and 3, in the 8 patients receiving a single dose of each treatment, the absorption rate was comparable between LIQ861 and Tyvaso® with peak concentrations achieved at approximately 0.13 and 0.17 hours (median T<sub>max</sub>) post inhalation for LIQ861 and Tyvaso®, respectively.
- Following peak concentrations, mean plasma concentrations of treprostinil decreased in a monophasic manner with similar rate of elimination for both treatments (approximate mean half-life of 0.5 hours for 0.95 LIQ861 and 0.97 Tyvaso®) (Figure 3).

**COMPARATIVE BIOAVAILABILITY**

- During Sequences 2 and 3, LIQ861 and Tyvaso® crossover to determine the comparative bioavailability of treprostinil, the geometric mean ratios (LIQ861/Tyvaso®) were 0.923, 0.947, and 0.931 for AUC<sub>0-12</sub>, AUC<sub>last</sub>, and C<sub>max</sub>, respectively, and the 90% CIs for these ratios were within the acceptable equivalence limits of 0.80 to 1.26 (Table 3).

**SAFETY AND TOLERABILITY**

- Overall, administration of LIQ861 and Tyvaso® was well tolerated, with minimal differences between the 2 treatments.
- There were no deaths or SAEs and only one subject withdrawal from the study due to TEAEs.
- All TEAEs were expected based on the known safety profile of inhaled treprostinil.
- The most commonly reported were cough and nausea.

**CONCLUSIONS**

The assessment of the comparative bioavailability of LIQ861 and Tyvaso® demonstrated that treprostinil exposure from a single capsule dose of 79.5 µg LIQ861 (approximate delivered dose 56.6 µg treprostinil) was comparable to 9 breaths of Tyvaso® (approximately 54 µg dose). These results confirm that LIQ861 and Tyvaso® have comparable treprostinil systemic exposures. LIQ861 and Tyvaso® were generally well tolerated in this study, with no deaths, SAEs, or dose-limiting toxicities. All TEAEs associated with LIQ861 and Tyvaso® were mild and consistent with known prostanoid effects.