**Comparative Pharmacokinetics Between Tyvaso® and L606, Extended-Release Formulation of Treprostinil for Inhalation Therapy**

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**RATIONALE:** For treatment of pulmonary hypertension (PH), inhalation therapy features a target delivery, low systemic side-effect and ventilation/perfusion match over oral and injection administration. However, the short half-life of prostacyclin restricted the dosing schedule in practical use. A novel combination of liposome formulation and mesh-vibrating nebulizer offers a simple, convenient and extended release treatment regimen. **METHODS:** A single-dose, open-label, randomized, 2-period, 2-sequence crossover comparative bioavailability (BA) study was conducted in 12 healthy adult subjects. In this study, we compared the systemic exposure (Cmax and AUC) following oral inhalation of a single dose (51 µg) of L606 and a single dose (54 µg) of Tyvaso. Blood sampling for PK analysis for treprostinil occurred at pre pre-dose, 15, and 30 minutes and 1, 1.5, 2, 4, 6, 8, 10, 12, 14, 16, and 24 hours post-dose (L606); or at pre pre-dose, and at 5, 10, 15, 30 minutes and 1, 2, 4, 6, 8, and 12 hours post post-dose (Tyvaso).

**RESULTS & DISCUSSIONS:** No serious AEs were observed following L606 or Tyvaso administration. All AEs resolved within 24 hours of dosing. Cmax of treprostinil following L606 administration was 0.140 ng/mL (24 %CV), substantially lower than the Cmax after Tyvaso administration [1.09 ng/mL (38.4 %CV)]. The area under the curve from 0 to infinity (AUC_{0-∞}) was similar between two products, 1.03 ng•hr/mL (16.6 %CV) and 1.04 ng•hr/mL (27.8 %CV) for L606 and Tyvaso, respectively. Administration of L606 also resulted in a delayed Tmax and increased t_{1/2}, resulting in prolonged and stable systemic exposure to treprostinil versus administration of Tyvaso. **CONCLUSIONS:** The pharmacokinetics of L606 showed an extend release for 10-12 hour. It is able to reduce the dosing frequency to twice a day (every 10-12 hours) covering sleeping time. The phase 3 study is planned to evaluate the safety profile upon transition from Tyvaso® QID to L660 BID in PAH patients.

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