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A phase 1, single-center, open-label, dose-rising clinical trial to evaluate the pharmacokinetics, safety and tolerability of Treprostinil Inhalation Powder (TreT) in healthy normal volunteers

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Background: United Therapeutics is developing a new drug-device product comprised of a dry powder formulation of treprostinil inhalation powder (TreT) and a small, portable, dry powder inhaler, to treat pulmonary arterial hypertension (PAH). The primary objective of this study was to evaluate the pharmacokinetics (PK), safety, and tolerability of TreT in healthy normal volunteers (HNVs).

Methods: This was an open-label, single ascending dose study in 36 HNVs that were sequentially assigned to 6 cohorts of ascending dose levels of TreT (30, 60, 90, 120, 150, and 180 Âµg). The safety and tolerability of TreT was evaluated in each sequential cohort prior to escalating the dose for the next cohort. Blood samples were obtained before TreT administration and at selected times through 480 minutes post dose. Blood samples were analyzed for treprostinil using a validated analytical method and PK parameters were calculated using noncompartmental methods.

Results: A total of 36 HNVs with a median age of 34 years (range: 22 to 51 years), majority female (n=20, 56%), and white (n=26, 72%) were randomized and dosed. There were no severe adverse events (AEs), serious AE, or deaths during this study. No AEs led to a subject's early termination. The most frequently reported AEs were cough (n=11, 30.6%) and headache (n=8, 22%). Bioanalysis data confirmed that the treprostinil plasma concentrations and exposure for TreT, achieved clinically relevant concentrations comparable to those observed in historical inhaled treprostinil (Tyvaso®) single-dose clinical studies. Cmax and AUC for treprostinil increased in a linear manner with increasing dose.

Conclusions: Overall, TreT was safe and well-tolerated and produced clinically relevant concentrations of treprostinil when inhaled as a dry powder.

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