Preclinical and Phase 1 clinical characterization of LIQ861, a new dry powder formulation of treprostinil

Royal M1, Roscigno R1, Vaughn T1, Anderson S1, Wargin W. W2 Williams Jr, RL2, Forsythe C3, Hunt T3, Normand P4, Hantash M4, Dillberger J5.

1 Liquidia Technologies, RTP, NC, United States. 2 Nuventra, Inc., Durham, NC, United States 3 PPD Development, LLC Austin, TX, United States 4 ITR Laboratories, Montreal, Quebec, Canada. 5 J. Dillberger LLC, Nashville, IN, United States.

BACKGROUND

Inhalational drug delivery to treat pulmonary hypertension is attractive due to enhanced pulmonary specificity and reduced systemic adverse effects. Current approved agents require frequent administration and have tolerability issues. Liquidia is developing LIQ861, an inhaled dry powder formulation of Treprostinil (Tre) particles of precise size (2 µm) and trefoil shape using Liquidia’s PRINT® Technology (Particle Replication in Nonwetting Templates). LIQ861 is designed for inhalation using an approved handheld dry powder inhaler (DPI).

OBJECTIVES

To support clinical testing, single-dose pharmacokinetic (PK) studies in rats and dogs and 14-day and 26-week repeat-dose toxicity studies in rats were conducted. LIQ861 was also evaluated in a Phase 1 single ascending dose study to characterize safety, tolerability and PK.

METHODS

Anesthetized dogs administered single doses of LIQ861 or Tre solution via a cuffed endotracheal tube and controlled ventilation. Rats administered single doses of LIQ861 or Tre solution by nose-only inhalation. LIQ861 was evaluated clinically in a Phase I double-blind, placebo-controlled study at doses of 25-150µg. Assessments were performed through 8h post inhalation.

RESULTS

In dogs, LIQ861 and Tre solution produced similar PK profiles. In rats, PK profiles at the end of 14 days treatment were nearly identical. Following 26 weeks of daily dosing, Tre exposure was slightly higher in LIQ861-treated rats.

LIQ861 inhalation in healthy volunteers produced a dose proportional Tre PK profile similar to that reported for Tyvaso. LIQ861 was well-tolerated across the entire dose range with only mild (severity) adverse events (AEs) and no serious or unexpected AEs. The most commonly reported related AEs were cough, throat irritation, inspiratory tightness, lightheadedness, and headache.

CONCLUSIONS

Tre PK profiles were generally similar with LIQ861 dry powder inhalation or nebulized Tre solution. Treprostinil administered via the LIQ861 formulation is well-tolerated and has a PK profile that is similar to that reported for the Tyvaso formulation.