

Once Daily Oral Dosing of Rodatristat Ethyl (RVT-1201) Achieves Reductions in Serotonin Biosynthesis Comparable to Those Associated with Reversal of Vascular Remodeling in PAH Animal Models

Carpenter D., Keller L.*, Palacios M., Rurka J., Crizer K., Pack T., Snyder M. and Wring S.

Altavant Sciences, 6501 Weston Parkway #330, Cary, NC, USA * Presenting author

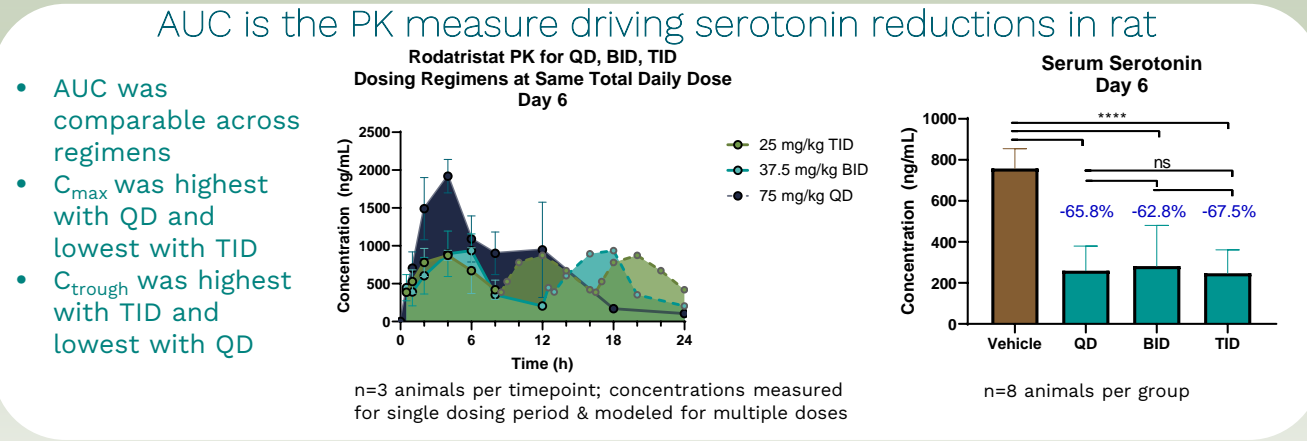
BACKGROUND

- **Rodatristat ethyl (RE)** currently is in Phase 2 clinical development (**ELEVATE 1 study**) for pulmonary arterial hypertension (**PAH**)
- RE is an orally bioavailable pro-drug for the tryptophan hydroxylase (**TPH**) inhibitor **rodatristat**
- **TPH1** is the rate-limiting enzyme for **peripheral biosynthesis of serotonin (5-HT)** and is **up-regulated in PAH**
- **5-HT** plays a causative role in the development and progression of **PAH**

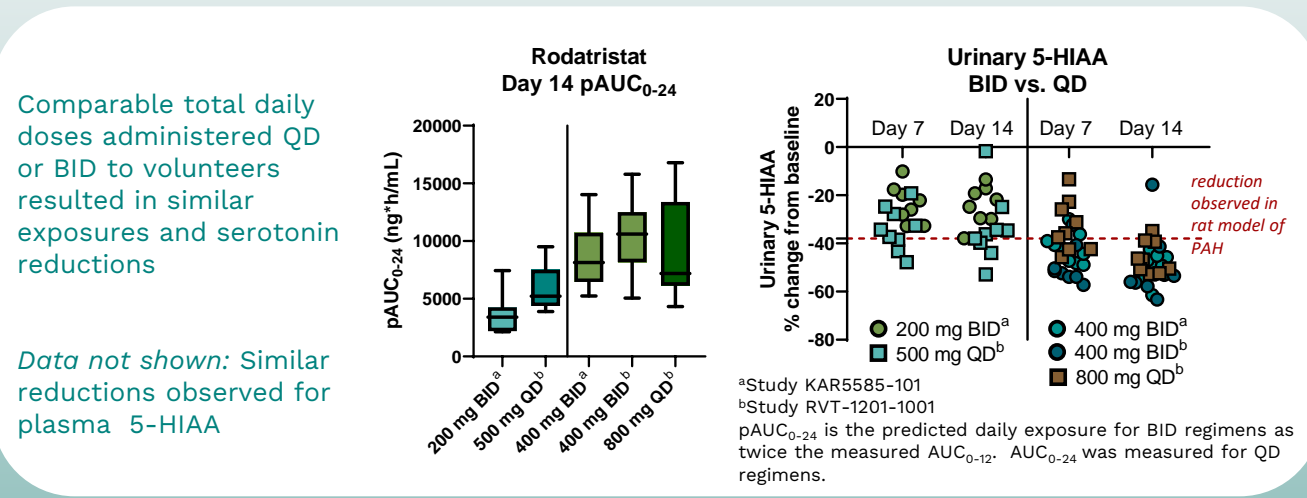
METHODS

- **Healthy rats** were administered the same total daily dose of RE divided once- (QD), twice- (BID), or three-times daily (TID) by oral gavage for 6 days; vehicle=QD
- **Healthy subjects** received daily oral doses of RVT-1201 or placebo (PBO), either as single (QD) or divided (BID) doses for 14 days across two Phase I studies (KAR5585-101, RVT-1201-1001)
 - 200 mg BID, 400 mg BID
 - 500 mg QD, 800 mg QD
 - 9 active, 3 placebo per cohort

These studies were conducted to identify the PK parameter that correlates with 5-HT lowering and to assess the potential for once-daily dosing to lower circulating 5-HT



Once daily dosing of *rodatristat ethyl* can achieve potentially therapeutically *meaningful reductions in serotonin biosynthesis*



CONCLUSIONS

In rats and healthy human subjects, **AUC drove reductions in serotonin biosynthesis**

In healthy subjects, administration of once or twice daily rodatristat was associated with similar lowering of serotonin biosynthesis indicating potential for once daily dosing in PAH

Scan for our white paper discussing the role of 5-HT in PAH

