# European Respiratory Society
# Annual Congress 2013

**Abstract Number:** 3924

**Publication Number:** P488

**Abstract Group:** 4.3. Pulmonary Circulation and Pulmonary Vascular Disease

**Keyword 1:** Pulmonary hypertension **Keyword 2:** Inflammation **Keyword 3:** Animal models

**Title:** Human apyrase (APT102) treatment attenuates the development of severe pulmonary arterial hypertension (PAH)

Maike 24337 Leberl Maike.Leberl@ucdenver.edu [1], Ridong 24338 Chen rchen@apt-therapeutics.com [2], Zakaria 24339 Moumen Zakaria.Moumen@ucdenver.edu [1], Martin 24340 Zamora Marty.Zamora@ucdenver.edu MD [1] and Laima 24341 Taraseviciene-Stewart Laima.Taraseviciene@ucdenver.edu [1]. [1] Medicine, University of Colorado, Aurora, CO, United States, 80045 and [2] Drug Development, APT-Therapeutics, St. Louis, MO, United States, 63108 .

**Body:** Introduction: The apyrase CD39 is expressed on the surface of immune and endothelial cells, where it hydrolyzes adenosine triphosphate (ATP) to adenosine bi- (ADP) and monophosphate (AMP). This function is especially important during hypoxia and lung injury, when ATP is released from vascular and blood cells. Objective: We hypothesize that excessive extracellular ATP contributes to pathological vascular remodeling and right ventricular hypertrophy in the pathogenesis PAH. Methods: Sprague Dawley rats (n=3/per group) were treated with a single injection of vascular endothelial growth factor receptor (VEGFR) blocker SU5416 and exposed to hypoxia (Hx) for 2 weeks, and then treated with APT102, an optimized human apyrase for another 3 weeks. The enzymatic activity of CD39 in lung CD4+ T and other cells; right ventricular systolic pressure (RVSP) and right ventricle over left ventricle plus septum (RV/LV+S) weight ratios were assessed. Results from APT102-treated rats were compared to those from Hx control and Hx/SU5416 treated rats. Results: Animals treated with endogenous APT102 had reduced RV/LV+S ratio (0.44±0.06) compared to Hx/SU5416 rats (0.57±0.09, $p<0.04$)), but higher than Hx controls (0.33±0.03). When compared to Hx/SU5416-treated rats, apyrase treatment reduced RVSP, close to the levels of Hx exposed controls. The APT102-treated rats had an increase in ADP hydrolysis in both cell types as compared to Hx-exposed controls. Conclusions: The treatment with APT102 attenuated the development of experimental PAH, suggesting that APT102 might be beneficial to treat human condition. Funded by AHA 0735388N, 11GRNT7520020, FAMRI CIA 072053 and Emphysema Research Fund.