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Title: Dose escalation study in healthy male subjects to investigate safety, tolerability and systemic exposure of orally inhaled single-doses of AP301

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Body: Pulmonary edema is a major complication of Acute Lung Injury (ALI) and Acute Respiratory Distress Syndrome (ARDS) which is associated with higher mortality. AP301 is a synthetic peptide whose structure is based on the lectin-like domain of human Tumour Necrosis Factor alpha. The water soluble peptide can be administered into the lung by oral inhalation. AP301 was designed to activate the pulmonary epithelial sodium channel (ENaC) in type II alveolar cells to accelerate alveolar liquid clearance. We report the early clinical development of AP301: In the Phase I monocentric FiM trial “Dose escalation study in healthy male subjects to investigate safety, tolerability and systemic exposure of orally inhaled single-doses of AP301” the safety, tolerability and pharmacokinetic profile of AP301 was evaluated in a double-blind, randomized, placebo-controlled, parallel group study that started in April 2011 and was completed in October 2011 at the General Hospital in Vienna. 48 healthy young males received escalating doses of aerosolized AP301 in 6 dose groups between 0.07 mg/kg to 2 mg/kg AP301 per inhalation. Lung function parameters like FEV1 or PEF were not affected by AP301. Exhaled nitric oxide did not increase. Physical examinations showed no inhalation-related clinical signs or symptoms of paradoxical bronchospasm. No local reactions in the mouth like severe xerostomia or burning sensation were described. Vital signs, ECG and safety laboratory parameters showed no pathological findings. AP301 did not accumulate in plasma. This phase I trial demonstrated that orally inhaled AP301 was safe and well-tolerated by all study subjects.