

RLS-0071, A Novel Dual-targeting, Anti-inflammatory Agent Demonstrates Proof of Mechanism in a Phase 1b Inhaled LPS Study, Significantly Reducing Lung Neutrophils

J.M. Hohlfeld¹, O. Holz², M. Müller², S. Carstensen², L. Dell³, J. Goss³, P. Hair³, P. Badorrek², K. Cunnion³, U. Thienel³

¹Fraunhofer Institute for Toxicology and Experimental Medicine ITEM, German Center for Lung Research (DZL), Hannover Medical School, Hannover, Germany; ²Fraunhofer Institute for Toxicology and Experimental Medicine ITEM, German Center for Lung Research (DZL), Hannover, Germany ³ReAlta Life Sciences, Norfolk, VA

INTRODUCTION

- RLS-0071 is a first in class 15 amino acid peptide that both inhibits humoral inflammation by blocking classical pathway complement activation and cellular inflammation by blocking the neutrophil effectors myeloperoxidase (MPO) and neutrophil extracellular traps
- RLS-0071 has previously been shown to inhibit neutrophil-mediated lung disease in animal models of ARDS as well as neutrophilic asthma

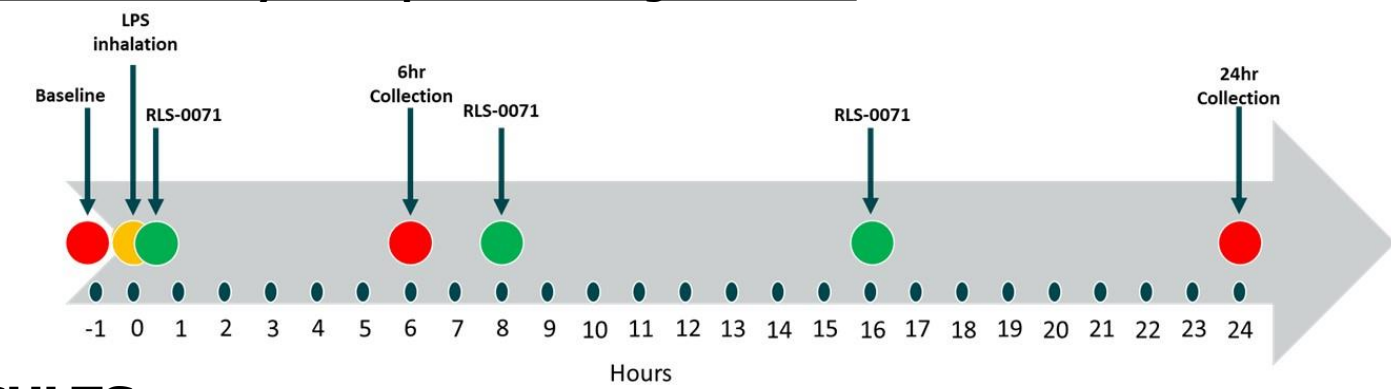
OBJECTIVE

- RLS-0071 was studied in a Phase 1b Proof-of-Mechanism clinical trial to evaluate the translatability of mechanisms of action from animal disease models to humans. ClinicalTrials.gov Identifier: NCT05351671

METHODS

- Randomized double-blind clinical trial with 3 arms: placebo, low-dose, high-dose (10 subjects per arm, 30 subjects total)
- Healthy Volunteers: 18 male, 12 female; age 20-55 years; 90% white
- Low-dose = 10 mg/kg IV Q8hr; High dose 120 mg/kg, 40 mg/kg, 40 mg/kg starting post LPS inhalation² (2µg) as therapeutic regimen

Inhaled LPS Study Therapeutic Dosing Schedule

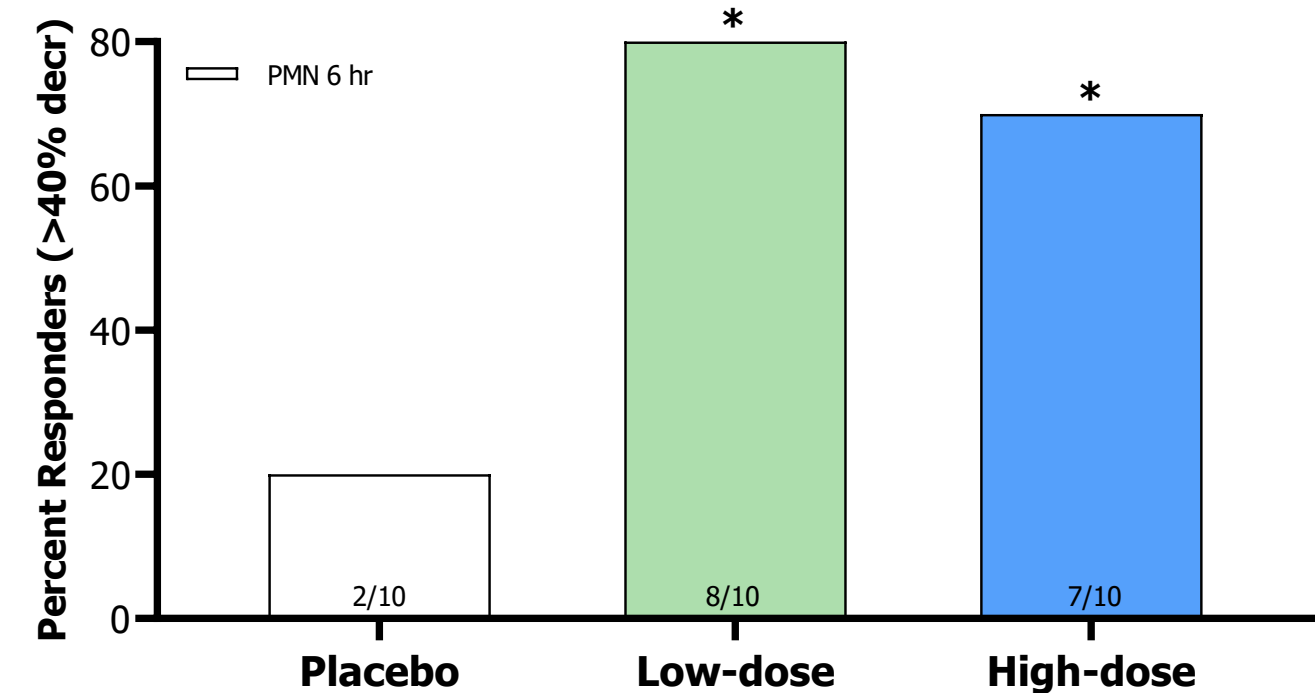


RESULTS

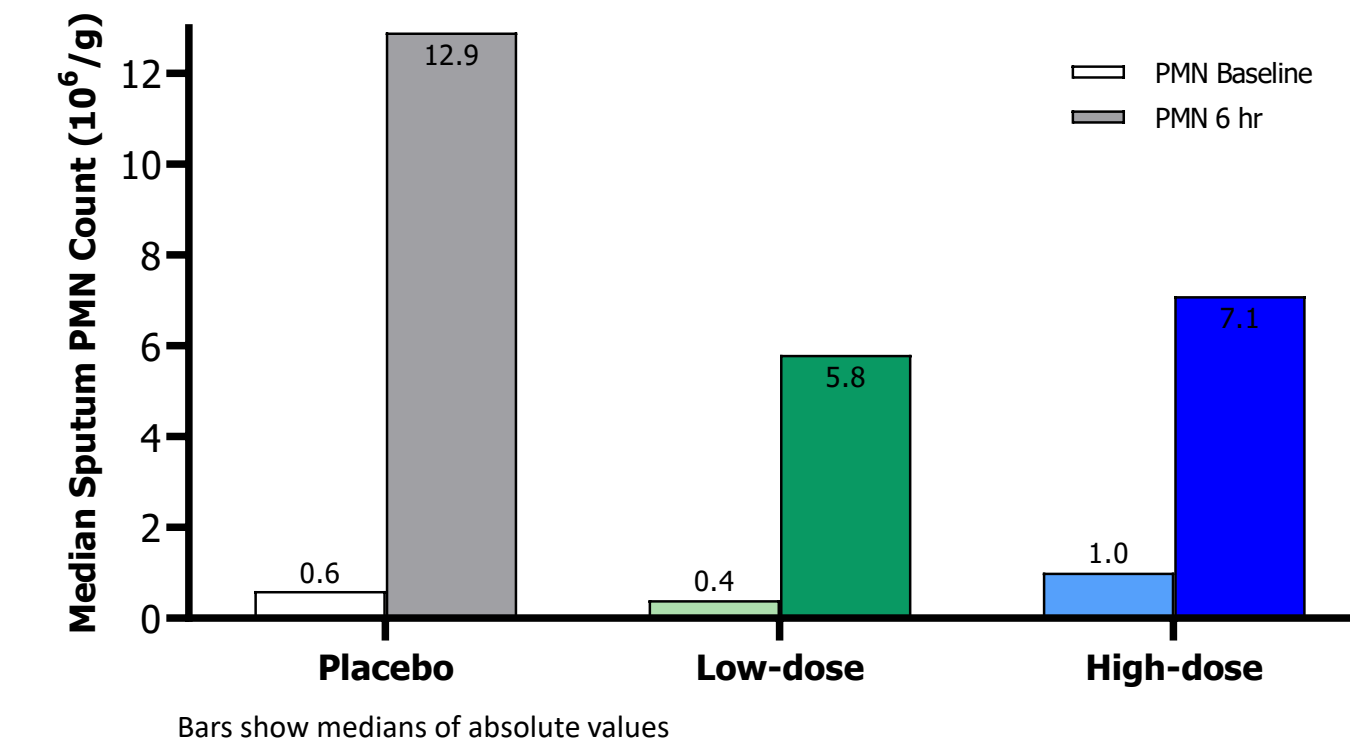
SAFETY:

- No SAEs or serious TEAEs occurred during the study
- No TEAEs led to death or withdrawal from the study
- No AESIs (ie, infusion reactions or bacterial infections) were reported
- No clinically significant changes in laboratory values or other safety evaluations were observed.

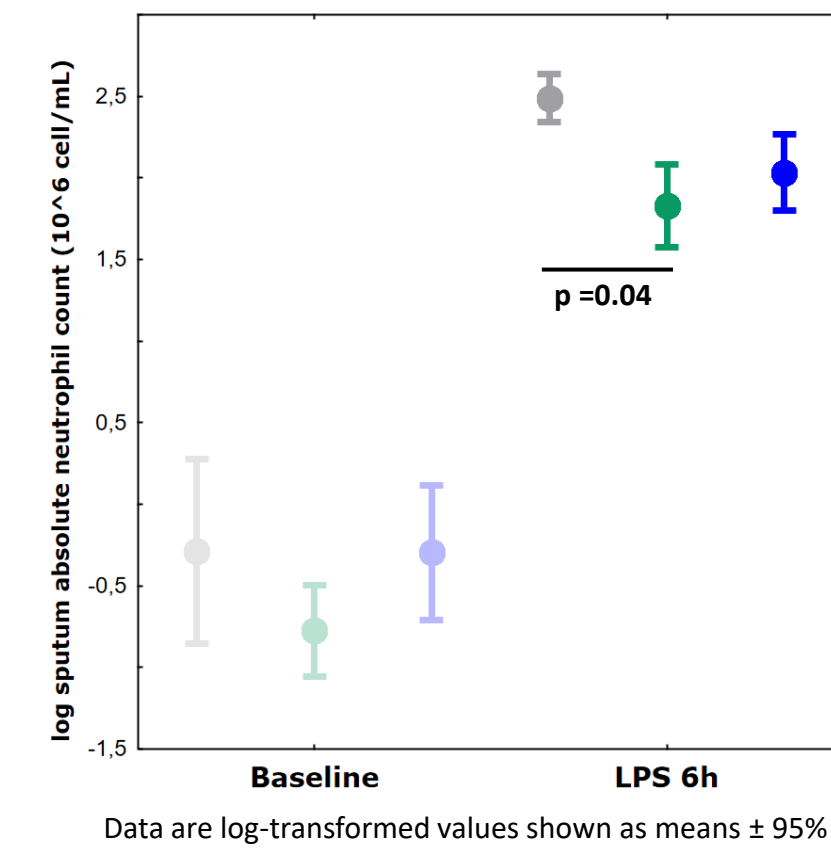
Responder Analysis: RLS-0071 showed in 70 – 80% of treated subjects >40% reduction in sputum neutrophils



Median sputum neutrophil counts reduced ~50% for RLS-0071 at 6 hours

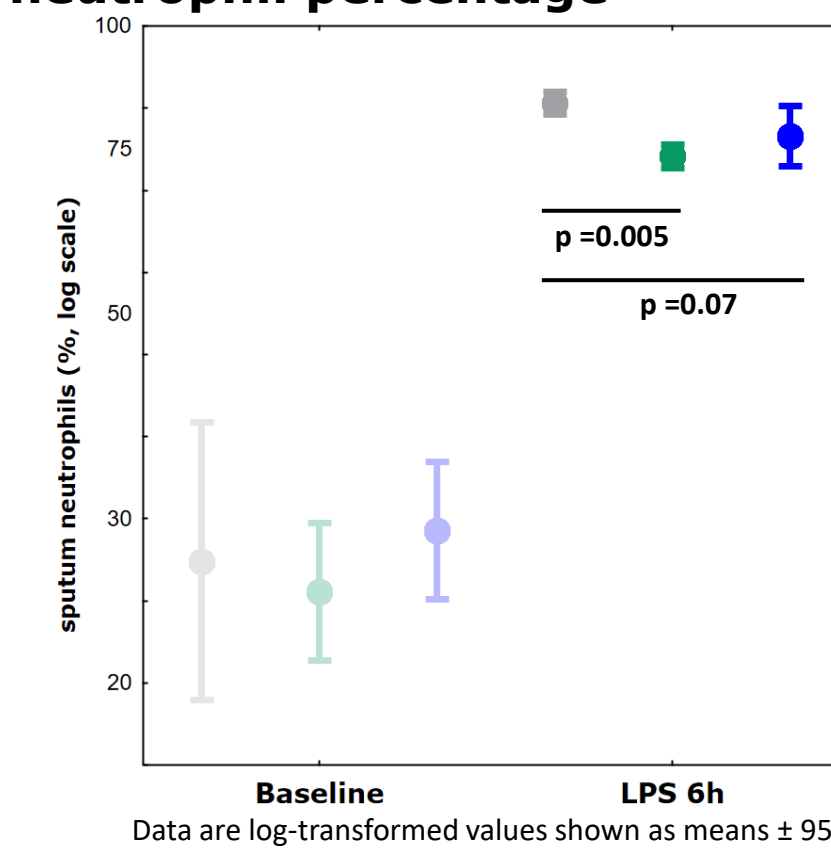


Low-dose RLS-0071 showed statistically significant reduction in log-transformed sputum neutrophil counts

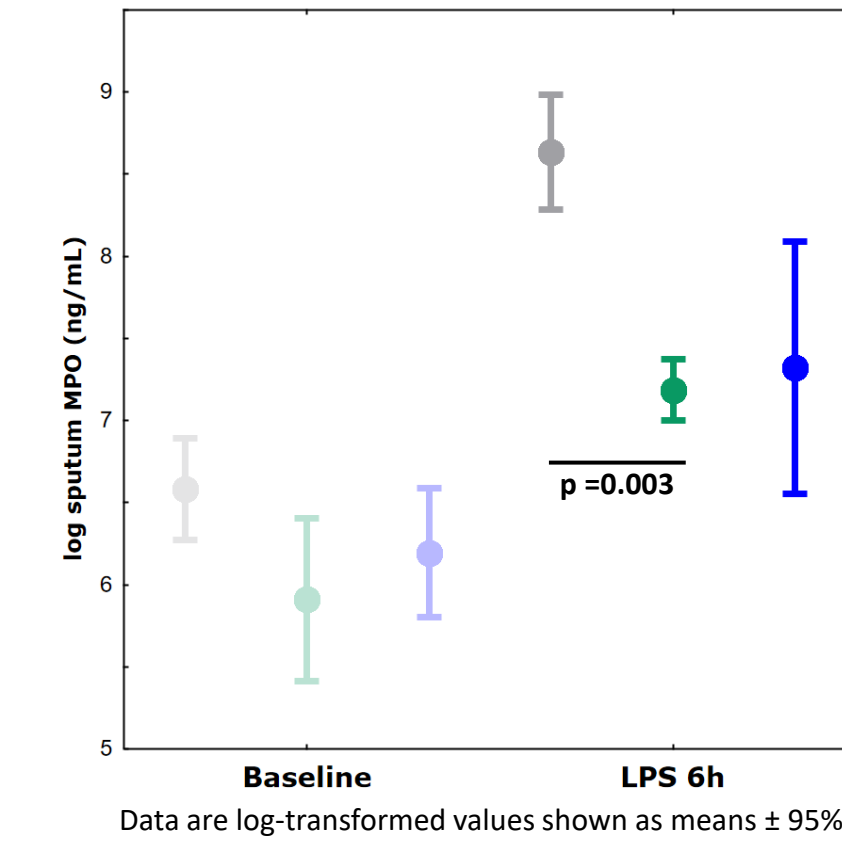


● placebo
● low dose
● high dose

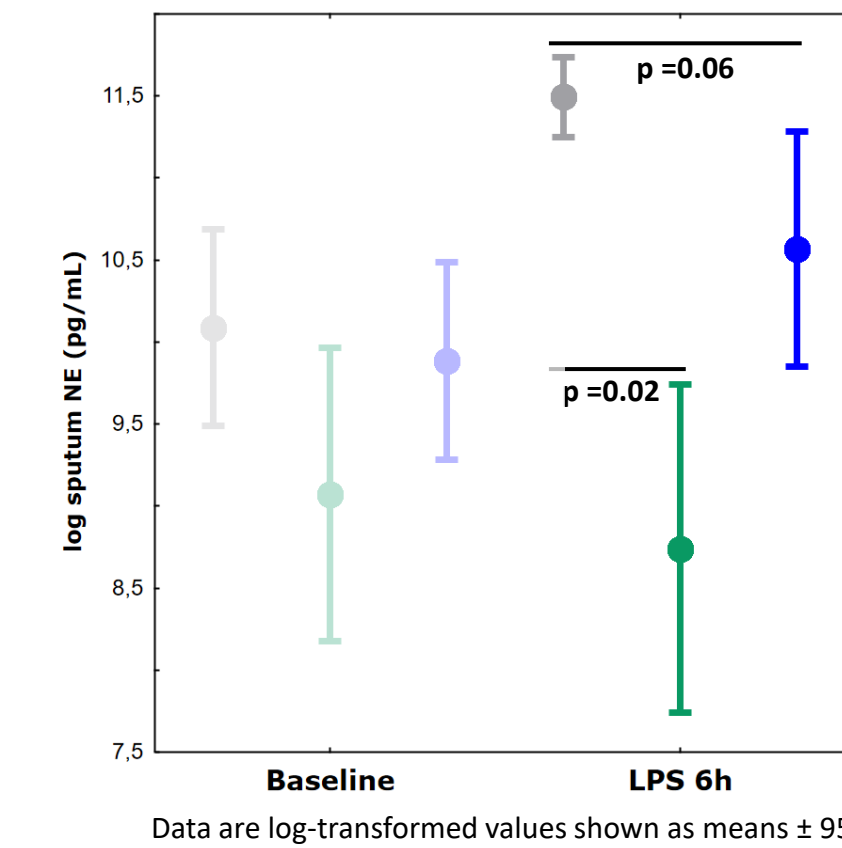
RLS-0071 showed statistically significant reduction in sputum neutrophil percentage



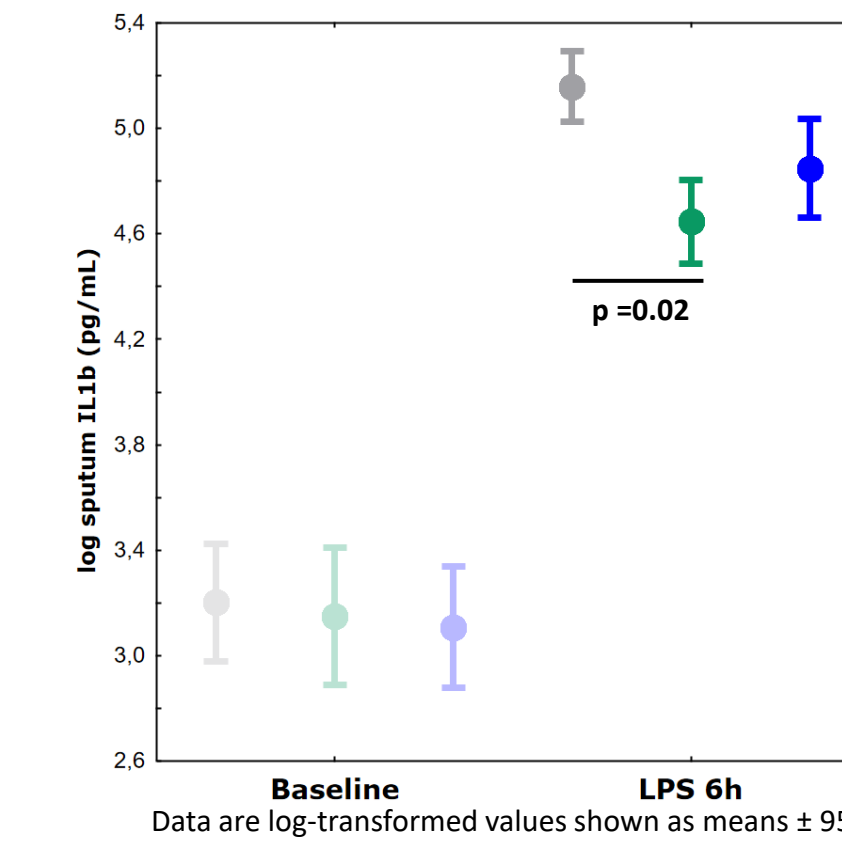
RLS-0071 showed a statistically significant decrease in log-transformed sputum MPO levels



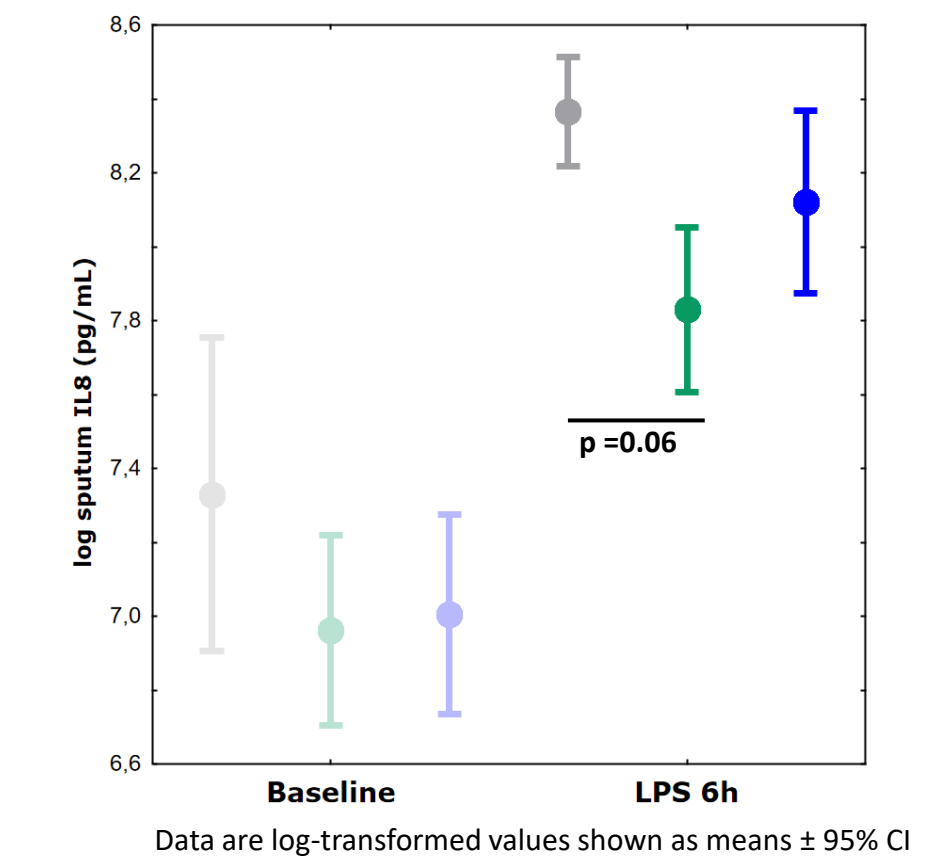
RLS-0071 showed a statistically significant decrease in log-transformed sputum neutrophil elastase (NE) levels



Low-dose RLS-0071 showed a statistically significant decrease in log-transformed sputum IL-1β levels



RLS-0071 showed a trend decrease in log-transformed sputum IL-8 levels



CONCLUSIONS

- RLS-0071 was safe and well-tolerated
- RLS-0071 strongly inhibited neutrophil migration into the lungs ~50%
- RLS-0071 decreased pro-inflammatory cytokines IL-1β and IL-8
- RLS-0071 consistently decreased neutrophil effectors myeloperoxidase and neutrophil elastase

Summary:

RLS-0071 demonstrated Proof-of-Mechanism inhibiting neutrophil infiltration, neutrophil effectors and key pro-inflammatory cytokines in this human model of LPS-initiated acute lung disease

References

1. Sampson et al. Peptide inhibition of acute lung injury in a novel two-hit rat model. PLoS One. 2021 Oct 28;16(10):e0259133. doi: 10.1371/journal.pone.0259133.
2. Janssen et al. Low-dose endotoxin inhalation in healthy volunteers--a challenge model for early clinical drug development. BMC Pulm Med. 2013 Mar 28;13:19. doi: 10.1186/1471-2466-13-19.

Disclosures

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