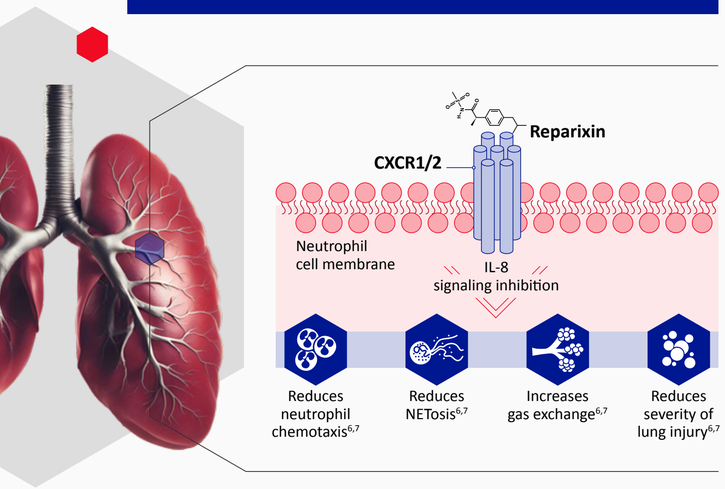
Reparixin Clinical Trial Overview in ARDS and CAP: RESPIRATIO and REPAVID-22

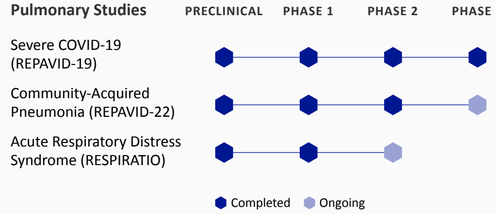
Reparixin: An Investigational Therapy to Reduce IL-8-Mediated Hyperinflammation

- Reparixin is an investigational, potent, noncompetitive allosteric inhibitor of the IL-8 receptors CXCR1 and CXCR2, and is being evaluated for treatment of ARDS and CAP[1–4]
- IL-8 binding to CXCR1 and CXCR2 leads to inflammatory responses, including chemotaxis, degranulation, and neutrophil extracellular trap (NET) formation[2,5]
- Modulating IL-8 activity through these receptors may therefore reduce neutrophil recruitment and inflammation and the subsequent tissue damage seen in severe CAP, ARDS, and associated complications[6,7]



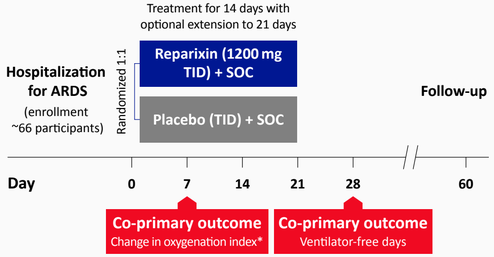
Dompé's Pulmonary Platform

Two clinical trials are ongoing to assess reparixin in ARDS and CAP: RESPIRATIO (NCT05496868)[3] and REPAVID-22 (NCT05254990)[4]



RESPIRATIO Study in ARDS[3]

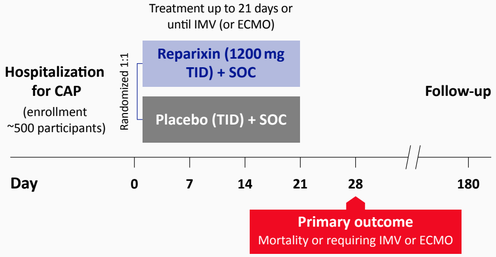
Phase 2, multinational, randomized, double-blind trial is ongoing to evaluate the efficacy and safety of oral reparixin as add-on therapy to SOC in moderate-to-severe ARDS



TARGET POPULATION	ADDITIONAL KEY END POINTS
• Hospitalized adults (aged ≥18 years) • Mechanically ventilated patients with PaO_2/FiO_2 ≤200 mmHg (in the presence of PEEP ≥5 cm H_2O) • ≤48 hours from fulfilling ARDS diagnosis (plus 12 hours if the patient is transferred from another institution) • Not pregnant or planning to become pregnant within 30 days after the study ends	**Secondary** • Acute lung injury score† • Ventilatory ratio‡ • Sequential organ failure assessment score • Incidence of ECMO • ICU-free and hospital-free days • All-cause mortality • Use of vasoactive medications **Pharmacokinetic** • Plasma levels of reparixin and relevant metabolites **Safety** • Incidence of TEAEs and SAEs • Incidence of secondary infections • Measurement of hematology and biochemistry values • 12-lead ECG and rhythm analysis

REPAVID-22 Study in CAP[4]

Phase 3, multinational, randomized, double-blind, placebo-controlled trial is ongoing to evaluate the efficacy and safety of oral reparixin as add-on therapy to SOC in limiting disease progression of CAP



TARGET POPULATION	ADDITIONAL KEY END POINTS
• Hospitalized adults (aged ≥18 years) • Clinically suspected viral or bacterial CAP within 72 hours of hospital admission • Need for noninvasive supplemental oxygen • Not pregnant or planning to become pregnant within 30 days after the study ends	**Secondary** • All-cause mortality at Day 180 • Alive and discharged at Day 28 • Ventilator-free days at Day 28 • Need for IMV or ECMO by Day 28 • Length of hospital stay **Pharmacokinetic** • Serum concentration of reparixin (bound and free) collected immediately before and 1 hour after dosing **Safety** • Incidence of TEAEs and SAEs, biochemistry changes, and ECG analysis • Incidence of fungal lung infections by Day 28

*Oxygenation index is defined as percent mean airway pressure × PaO_2/FiO_2. †Composite of PaO_2/FiO_2 ratio, PEEP, lung compliance (plateau airway pressure minus PEEP/tidal volume), and extent of pulmonary infiltrates. ‡Defined as the product of minute ventilation and $PaCO_2$.

Abbreviations: ARDS, acute respiratory distress syndrome; CAP, community-acquired pneumonia; COVID-19, coronavirus disease-2019; CXCR, CX chemokine receptor; ECG, electrocardiogram; ECMO, extracorporeal membrane oxygenation; FiO2, fraction of inspired oxygen; ICU, intensive care unit; IL, interleukin; IMV, invasive mechanical ventilation; PaCO2, partial pressure of carbon dioxide; PaO2, partial pressure of oxygen; PEEP, positive end-expiratory pressure; SAE, serious adverse event; SOC, standard of care; TEAE, treatment-emergent adverse event; TID, three times a day.

References: 1. Bertini R, Allegretti M, Bizzarri C, et al. Noncompetitive allosteric inhibitors of the inflammatory chemokine receptors CXCR1 and CXCR2: prevention of reperfusion injury. *Proc Natl Acad Sci*. 2004;101:11791–11796. **2.** Ha H, Debnath B, Neamati N. Role of the CXCL8-CXCR1/2 axis in cancer and inflammatory diseases. *Theranostics*. 2017;7:1543–1588. **3.** ClinicalTrials.gov. NCT05496868. Accessed April 1, 2024. www.clinicaltrials.gov/study/NCT05496868. **4.** ClinicalTrials.gov. NCT05254990. Accessed April 1, 2024. www.clinicaltrials.gov/study/NCT05254990. **5.** Pease JE, Sabroe I. The role of interleukin-8 and its receptors in inflammatory lung disease: implications for therapy. *Am J Respir Med*. 2002;1:19–25. **6.** Alsabani M, Abrams ST, Cheng Z, et al. Reduction of NETosis by targeting CXCR1/2 reduces thrombosis, lung injury, and mortality in experimental human and murine sepsis. *Br J Anaesth*. 2022;128:283–293. **7.** Zarbock A, Allegretti M, Ley K. Therapeutic inhibition of CXCR2 by reparixin attenuates acute lung injury in mice. *Br J Pharmacol*. 2008;155:357-364.

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For more information, contact Dompé at usmedinfo@dompe.com

Dompé

Reparixin is under investigation in clinical trials and is not FDA approved.

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