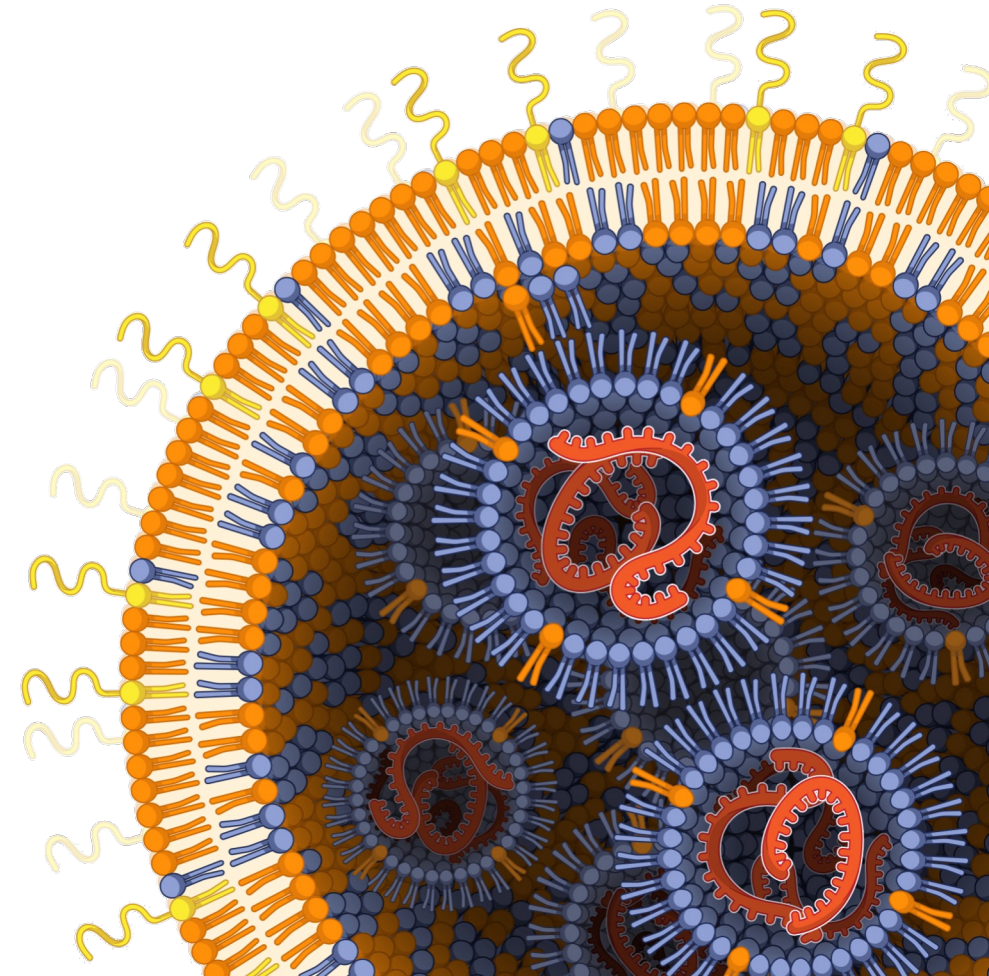


# Developing novel mRNA-based therapeutics

Non-confidential corporate presentation

October 2023



## PTXmRNA<sup>®</sup>

### Ensuring high target protein expression

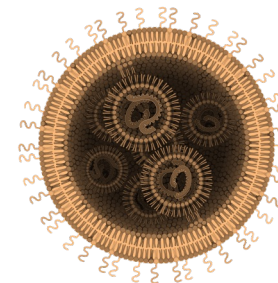
- Patented combination of proprietary potent short regulatory sequences for enhanced target protein expression
- High expression by state-of-the-art 5'-capping, uridine reduction and base modifications



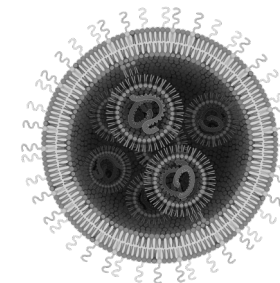
## PTXΔLNP<sup>®</sup>

### Lipid nanoparticles designed for selective organ targeting

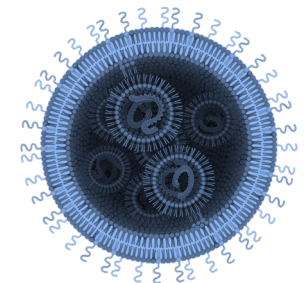
- Employing both ionizable and permanently charged lipids and their conjugated derivatives
- Proprietary lipid structures & compositions
- Covering LNPs for local and systemic mRNA administration
- LNPs with **cationic**, **neutral** or **anionic** surface charge



**PTXcLNP**

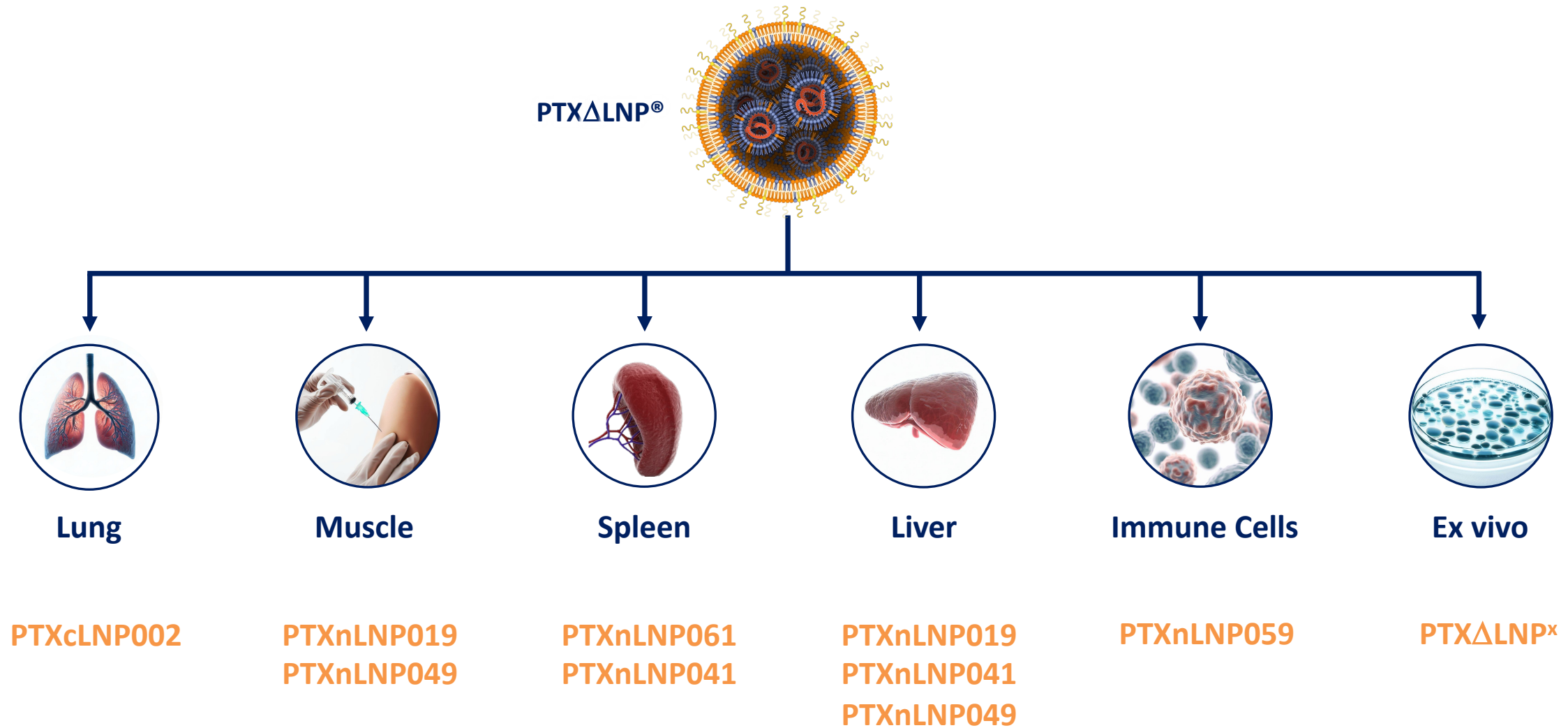


**PTXnLNP**



**PTXaLNP**

## Candidate formulations for mRNA expression in different tissues



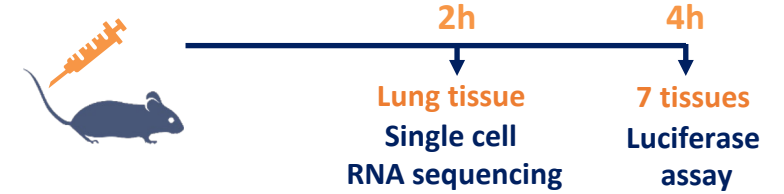
# Selective mRNA delivery to pulmonary endothelial capillary cells

## Study outline

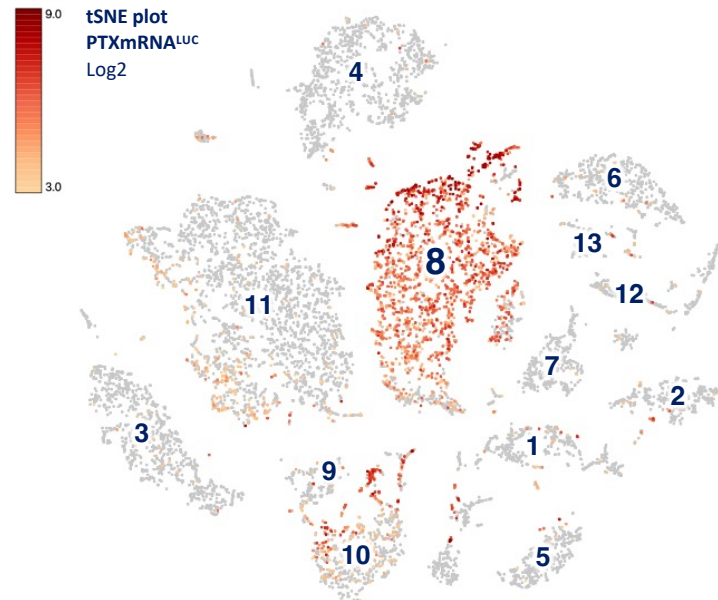
**Groups:**  
PTXmRNA<sup>LUC</sup>/cLNP002

**Group size:**  
n = 2-3  
C57BL/6 male mice

**Administration:**  
1.5 mg/kg  
Tail vein bolus injection  
(single i.v.)

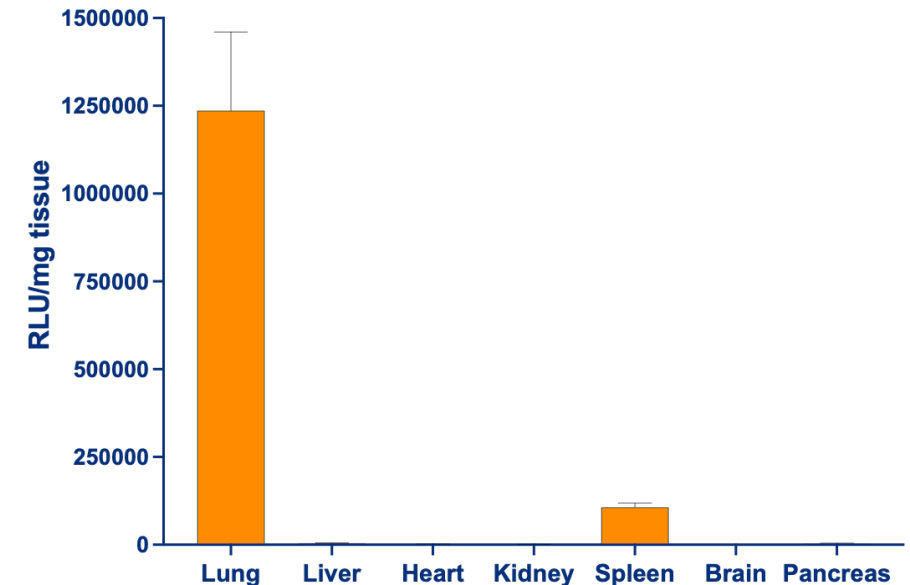


## Distribution of Luciferase-encoding PTXmRNA<sup>®</sup> in murine lung tissue (scRNA Seq)



1. Type 1 alveolar cells
2. Type 2 alveolar cells
3. B cells
4. T and NK cells
5. Alveolar macrophages
6. Fibroblasts (class 1)
7. Fibroblasts (class 2)
8. General capillary cells / Alveolar capillary cells
9. Interstitial macrophages
10. Monocytes
11. Neutrophils
12. Pericytes (class 1)
13. Pericytes (class 2)

## Luciferase activity in murine tissues





# Acute Respiratory Distress Syndrome (ARDS)



- Clinically defined syndrome with acute onset
- Respiratory failure caused by inflammatory response within the lung



- Pathophysiology is characterized by **early neutrophil infiltration** along with interstitial and intra-alveolar **lung edema**
- Current diagnosis based on clinical findings and radiological imaging
- Lack of pharmacological therapies



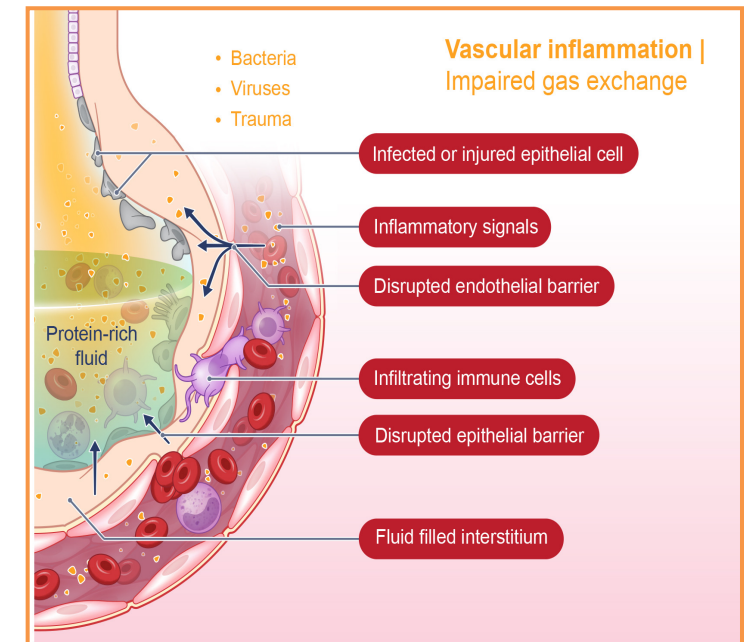
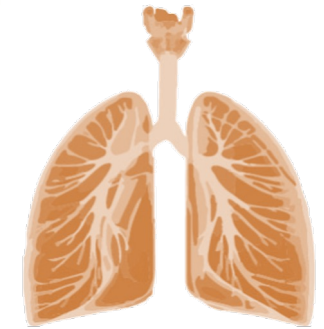
- Incidence range from 4-79 cases/100,000 persons/year
- Estimated total incident cases of > **1,000,000** in the 7MM\*
- Unmet medical need, lethality at 40-60%



- ARDS market size was USD 1,173.1 million in 2021\*

\* DelveInsight's 'Acute Respiratory Distress Syndrome-Market Insights, Epidemiology, and Market Forecast-2032'

## Pulmonary vascular inflammation & leakage

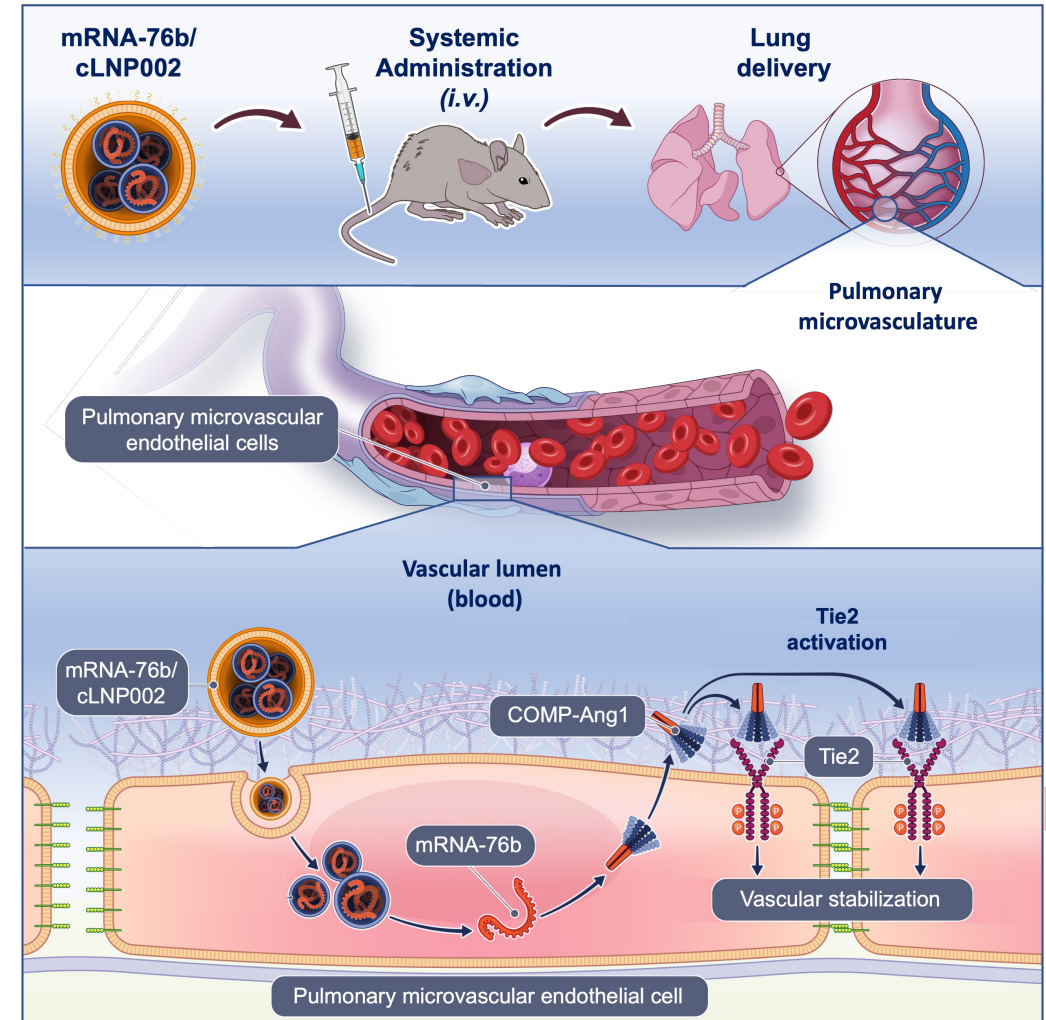
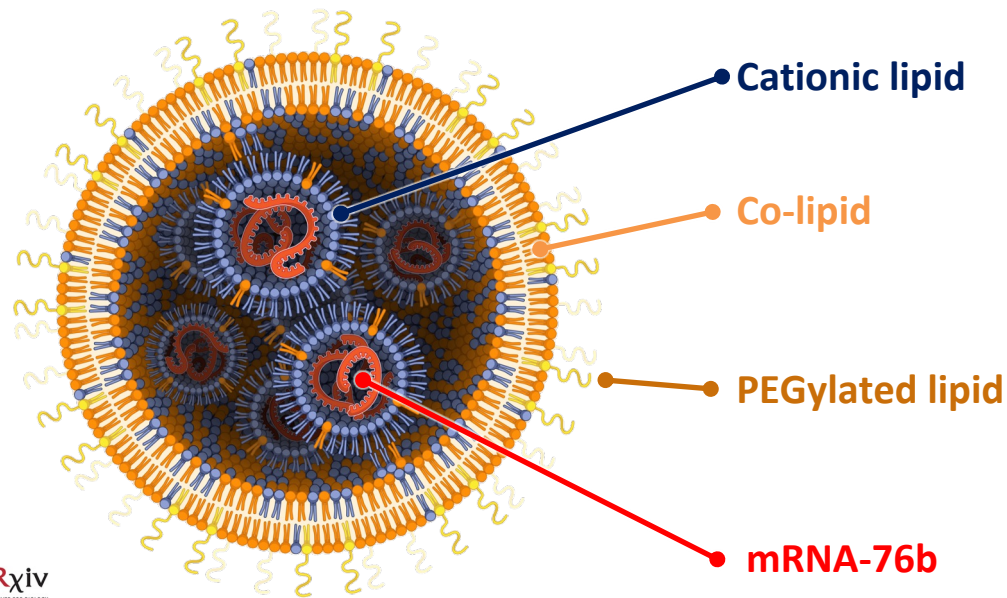


# A nucleoside-modified mRNA-LNP encoding COMP-Angiopoietin 1








## PAN004:

A systemically administered, first-in-class mRNA-LNP locally acting **therapeutic Tie2-agonist** for the prevention and early treatment of pulmonary edema in Acute Respiratory Distress Syndrome

**Drug product:** PAN004 (DS:EL at defined molar ratio)



# In-depth preclinical in vivo characterization of PAN004

Non clinical pharmacology (Non-GLP)		
Species	Study type	Objective/Findings
 <b>Mouse</b> (C57BL/6)	Pharmacodynamics: <b>COMP-Ang1 expression in vivo/ tissue specificity</b> ARDS	PoP: <b>COMP-Ang1 expression in vivo is restricted to the lung</b>
 <b>Mouse</b> (C57BL/6)	Pharmacodynamics: <b>mRNA-76 distribution in vivo</b>	PoP: <b>mRNA-76 localization in capillary endothelial cells of the lung</b>
 <b>Mouse</b> (C57BL/6)	Pharmacodynamics: <b>COMP-Ang1 expression in vivo: MoA analysis</b>	PoM: <b>COMP-Ang1 resulted in Tie2 activation in the lung</b>
 <b>Mouse</b> (C57BL/6)	Pharmacodynamics: <b>COMP-Ang1 expression in vivo.</b> <b>Formulation adjustments</b>	PoM: <b>COMP-Ang1 resulted in Tie2 pathway activation in the lung</b>
 <b>Mouse</b> (C57BL/6)	Pharmacodynamics: <b>Efficacy in Ex-vivo-isolated permeabilized mouse lung (IPML)</b>	PoC: <b>Prophylactic effect on lung edema development</b> Definition of effective doses
 <b>Mouse</b> (C57BL/6)	Pharmacodynamics: <b>Efficacy in an LPS-induced Neutrophilia Model</b>	PoC: <b>Therapeutic effect</b> on lung injury induced inflammation/ neutrophil influx
 <b>NHP</b>	Pharmakokinetics/Pharmacodynamics: <b>Dose escalation, single dose</b>	Non-clinical pharmacology: <b>Dose/Dosing determination</b> Establishment of dose dependent mRNA serum exposure

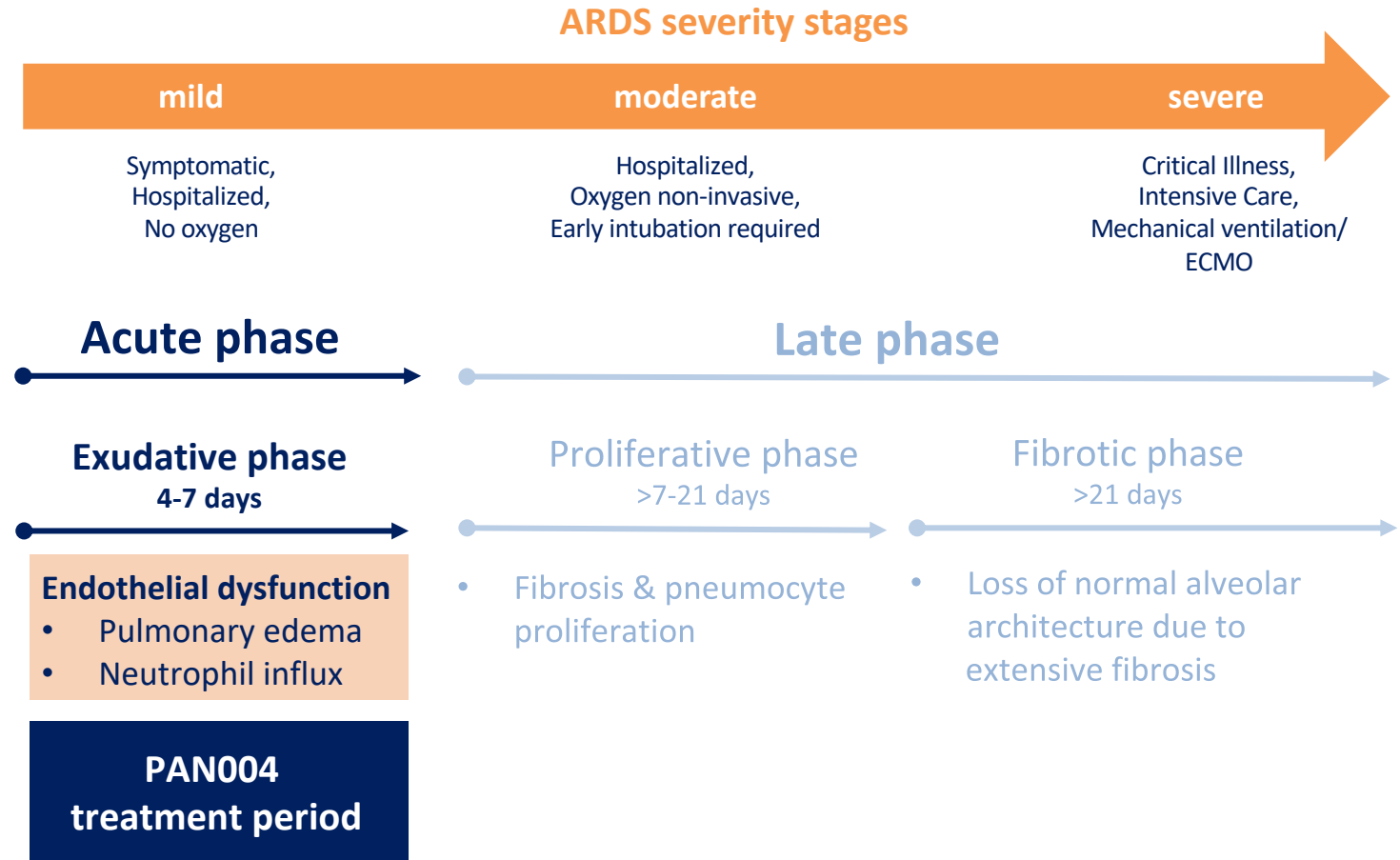
# Prevention of lung edema development during the acute phase of ARDS

## Initiating events:

- Sepsis
- Pneumonia
- Trauma/shock
- Aspiration
- Blood transfusion
- COVID-19



Acute Lung Injury







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