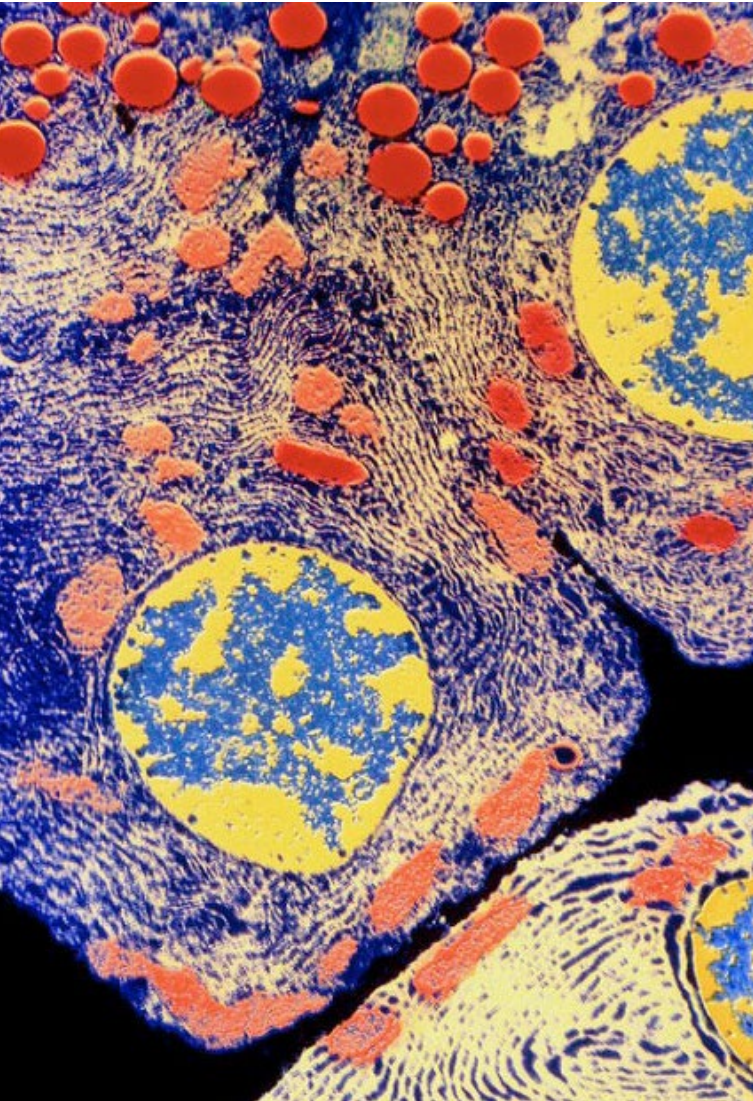




*CalciMedica*



## Developing Novel Therapies for Acute Inflammatory and Immunologic Diseases






December 2024

# Forward-Looking Statements

This presentation contains forward-looking statements which include, but are not limited to, statements regarding CalciMedica's business strategy and clinical development plans; the design and potential benefits of CalciMedica's product candidates; CalciMedica's ongoing and planned clinical trials; expected IP protections; the timing for CalciMedica's receipt and announcement of data from its clinical trials and other clinical milestones; the estimated patient populations and addressable market for CalciMedica's product candidates; and expectations regarding CalciMedica's cash runway. These forward-looking statements are subject to the safe harbor provisions under the Private Securities Litigation Reform Act of 1995. CalciMedica's expectations and beliefs regarding these matters may not materialize. Actual outcomes and results may differ materially from those contemplated by these forward-looking statements as a result of uncertainties, risks, and changes in circumstances, including but not limited to risks and uncertainties related to: the impact of fluctuations in global financial markets on CalciMedica's business and the actions it may take in response thereto; CalciMedica's ability to execute its plans and strategies; the ability to obtain and maintain regulatory approval for CalciMedica's product candidates; results from clinical trials may not be indicative of results that may be observed in the future; potential safety and other complications from CalciMedica's product candidates; economic, business, competitive, and/or regulatory factors affecting the business of CalciMedica generally; CalciMedica's ability to protect its intellectual property position; expected length of IP protection for CalciMedica's product candidates; the impact of government laws and regulations; and CalciMedica's cash runway and need for additional capital. Additional risks and uncertainties that could cause actual outcomes and results to differ materially from those contemplated by the forward-looking statements are included under the caption "Risk Factors" in CalciMedica's most recently filed periodic report, and subsequent periodic reports filed by CalciMedica, under the Securities Exchange Act of 1934, as amended, from time to time and available at [www.sec.gov](http://www.sec.gov). These documents can be accessed on CalciMedica's web page at [calcimedica.com](http://calcimedica.com).

These forward-looking statements are based on information available to, and expectations of, CalciMedica of the date of this presentation. CalciMedica disclaims any obligation to update these forward-looking statements, except as may be required by law.




# CalciMedica: The Calcium Release-Activated Calcium (CRAC) channel company

	Proprietary Technology	CRAC channel inhibitors for life-threatening inflammatory diseases with high unmet need
	Compelling Clinical Data	Consistent positive clinical activity and good tolerability in multiple Phase 2 clinical trials in acute critical illnesses
	Substantial Market Opportunity	~1 million target AKI population and ~100 thousand target AP population represent \$multi-billion U.S. market opportunities with no approved therapies
	Strong IP	Composition of matter (2036), formulation (2038), and methods of use (2036-2041+) worldwide patent protection
	Cash to Fund Clinical Programs	Current cash runway into 1H26 expected to fund current operations and completion of the ongoing KOURAGE Phase 2 trial in AKI patients

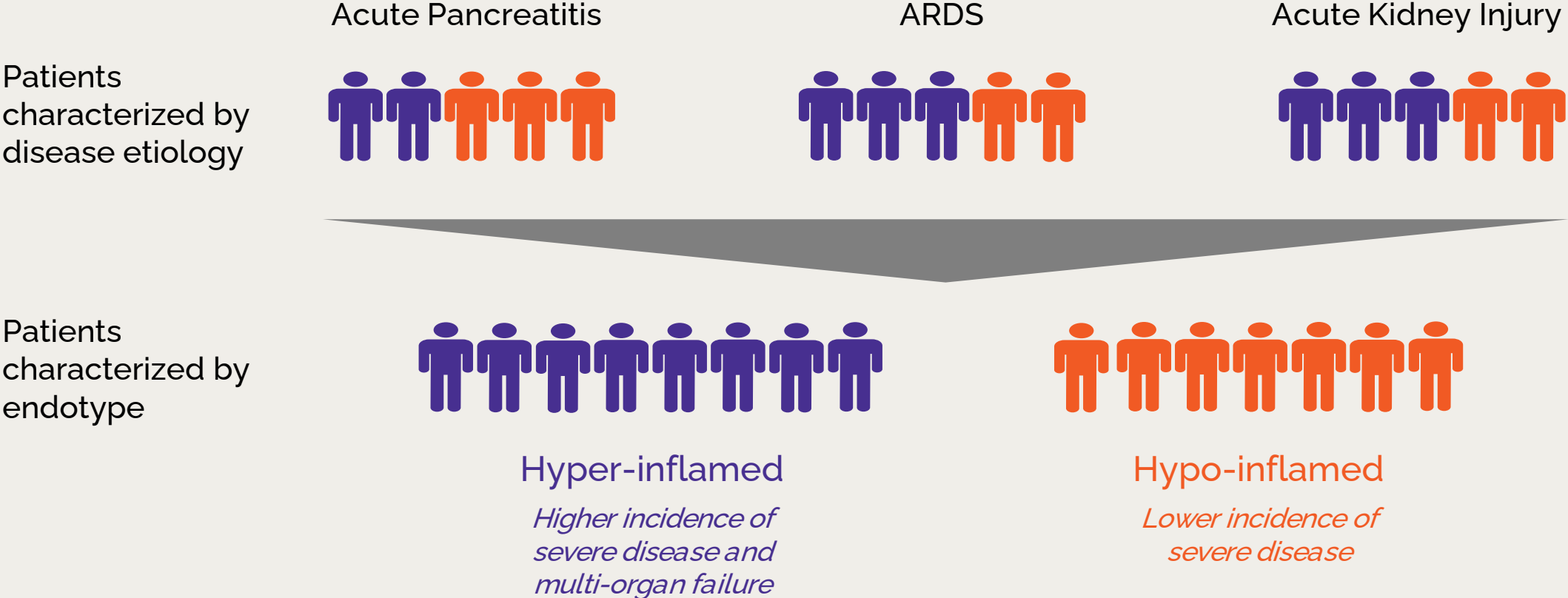
# Advanced pipeline in acute illnesses, with potential future expansion to chronic illness

Program	Indication	Phase of Development				Anticipated Milestones
		Preclinical	Phase 1	Phase 2	Phase 3	
<b>Acute Disease (IV)</b>						
Auxora	Acute Pancreatitis	████████	████████	████████▶	██████	CARPO Phase 2b trial completed and positive data announced; Next step: End-of-Phase 2 Meeting with FDA
Auxora	Acute Kidney Injury	████████	████████	████████▶	██████	KOURAGE Phase 2 trial ongoing; Data expected in 2025
Auxora	Asparaginase-Induced Pancreatic Toxicity in Pediatric Patients	████████	████████	████████▶	██████	CRSPA Phase 1/2 trial ongoing; Data expected in 2025
<b>Chronic Disease (Oral)</b>						
CM6336	Chronic Pancreatitis	████████▶	██████	██████	██████	Potential IND submission in 2025
CM6336	Rheumatoid Arthritis	████████▶	██████	██████	██████	Potential IND submission in 2025

# Targeting acute inflammatory illnesses that are large and underserved markets

AP with SIRS <sup>1</sup>	AKI Stages 2 & 3	AIPT
 <p>100K US Patients/yr<sup>2</sup></p>	 <p>1.1M US Patients/yr<sup>2</sup></p>	 <p>300 US Patients/yr<sup>2</sup></p>
<ul style="list-style-type: none"> <li>• <u>No approved therapies</u></li> <li>• SOC<sup>3</sup> primarily supportive care</li> <li>• Disease progression:               <ul style="list-style-type: none"> <li>➤ Pancreatic necrosis</li> <li>➤ Organ failure</li> <li>➤ Mortality</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• <u>No approved therapies</u></li> <li>• SOC primarily supportive care</li> <li>• Disease progression:               <ul style="list-style-type: none"> <li>➤ Chronic kidney disease</li> <li>➤ End stage renal disease</li> <li>➤ Mortality</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• <u>No approved therapies</u></li> <li>• Ultra-orphan pediatric indication</li> <li>• Accelerated approval opportunity</li> <li>• Disease progression:               <ul style="list-style-type: none"> <li>➤ Pancreatic necrosis in 50%</li> </ul> </li> </ul>

# Across acute illnesses, hyper-inflamed patients are at higher risk of severe disease and multi-organ failure



A therapeutic that can treat hyper-inflamed patients can potentially treat multiple forms of acute illness

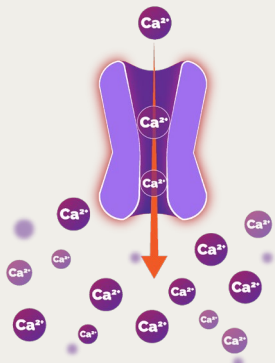


# CRAC channel inhibitors are mechanistically well suited to treat acute illnesses

## What are CRAC Channels?

CRAC channels are specialized ion channels found in the plasma membrane of certain cells that play a key role in signaling or regulating  $\text{Ca}^{2+}$  homeostasis in those cells

Found on many cells, including immune, endothelial, lung, pancreas, kidney and neuronal cells



## Potential features of CRAC Channel inhibition as a therapeutic target

1

Powerful and broad immunomodulation

- CRAC channels highly expressed on immune cells
- Activation upstream of multiple pro-inflammatory pathways
- Inhibition → down-regulation of multiple cytokines and immune activation
  - Reductions in  $\text{TNF-}\alpha$ ,  $\text{INF-}\gamma$ , IL-6, IL-17, neutrophil infiltration, T-lymphocyte and macrophage activation

2

Organ tissue protection

- CRAC channels in certain organ tissues (e.g. endothelial cells and pancreatic acinar cells) can become over-activated causing tissue damage
- Lungs: Reduced endothelial damage → improved oxygenation
- Pancreas: Reduced death of acinar cells → reduced autodigestion & necrosis
- Kidney: Reduced endothelial damage → recovery/preservation of GFR

3

Safety profile

- 350+ critically ill patients have received Auxora → well tolerated with no SUSARs (Sudden Unexpected Serious Adverse Reactions) to-date
- Other broad immunomodulators – corticosteroids and JAK inhibitors – with challenging side effects - insomnia and mood swings, GI upset, hyperglycemia, fluid retention and a black box warning (MIs, strokes, blood clots), respectively

# Our lead candidate, Auxora, has shown consistent reduction and prevention of acute respiratory failure and mortality

Trial	Acute Pancreatitis Phase 2a	COVID-19 Pneumonia Phase 2a	CARDEA: COVID-19 Pneumonia Phase 2	CARPO: Acute Pancreatitis Phase 2b	KOURAGE: Acute Kidney Injury Phase 2
Year	2019 →	2020 →	2021 →	2024 →	Expected 2025
Number of Patients	21	30	284	216	150
Hypoxemia at Enrollment	P/F<360	P/F<300	P/F<200	Not required	P/F<300
Expected Mortality	<10%	15-25%	15-25%	<5%	~50%
Auxora Results					
Respiratory Failure	↓ Ventilator use	↓ Ventilator use	↓ 33% Ventilator use	↓ 100%* New onset severe respiratory failure	Primary Endpoint Days ALIVE, not on a VENTILATOR and not on DIALYSIS
Severe Organ Failure	Too few events	Too few events	↓ 40% New onset AKI	↓ ~60%* Severe organ failure (respiratory, renal and cardio)	
Mortality	Too few events	↓ 50%	↓ 56%	Too few events	

Notes: For illustrative purposes only. Not a head-to-head comparison. Differences exist between clinical trial design and patient populations, and caution should be excised when comparing data across trials.

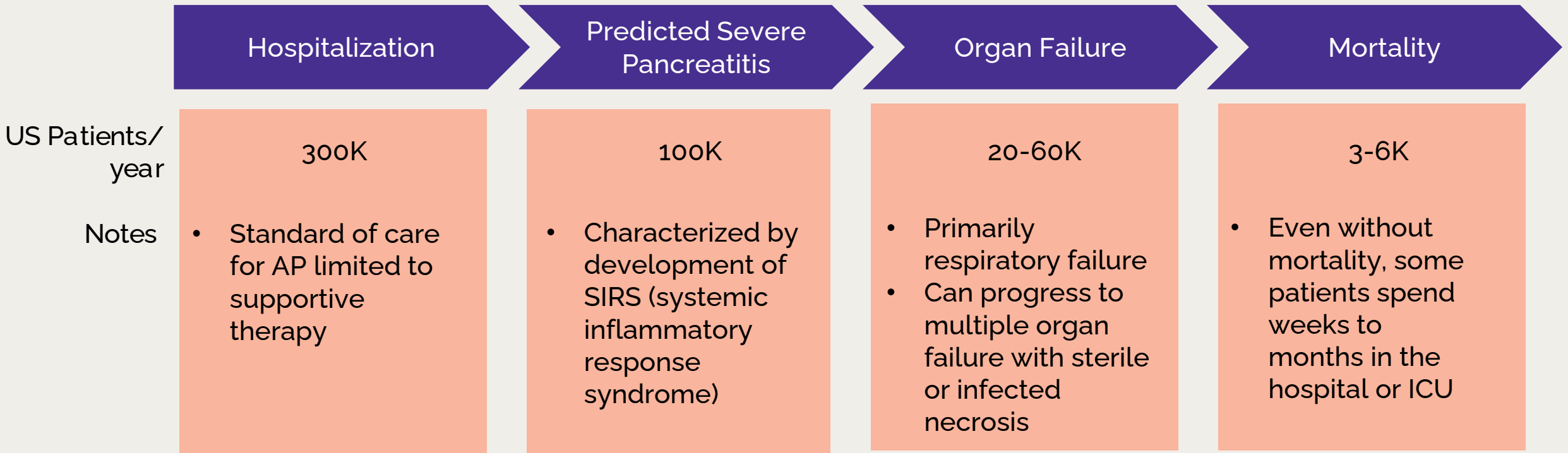
\* The high and medium dose patients showed a reduction in respiratory failure and severe organ failure compared to both the placebo and low dose patients



# Auxora for Acute Pancreatitis (AP)

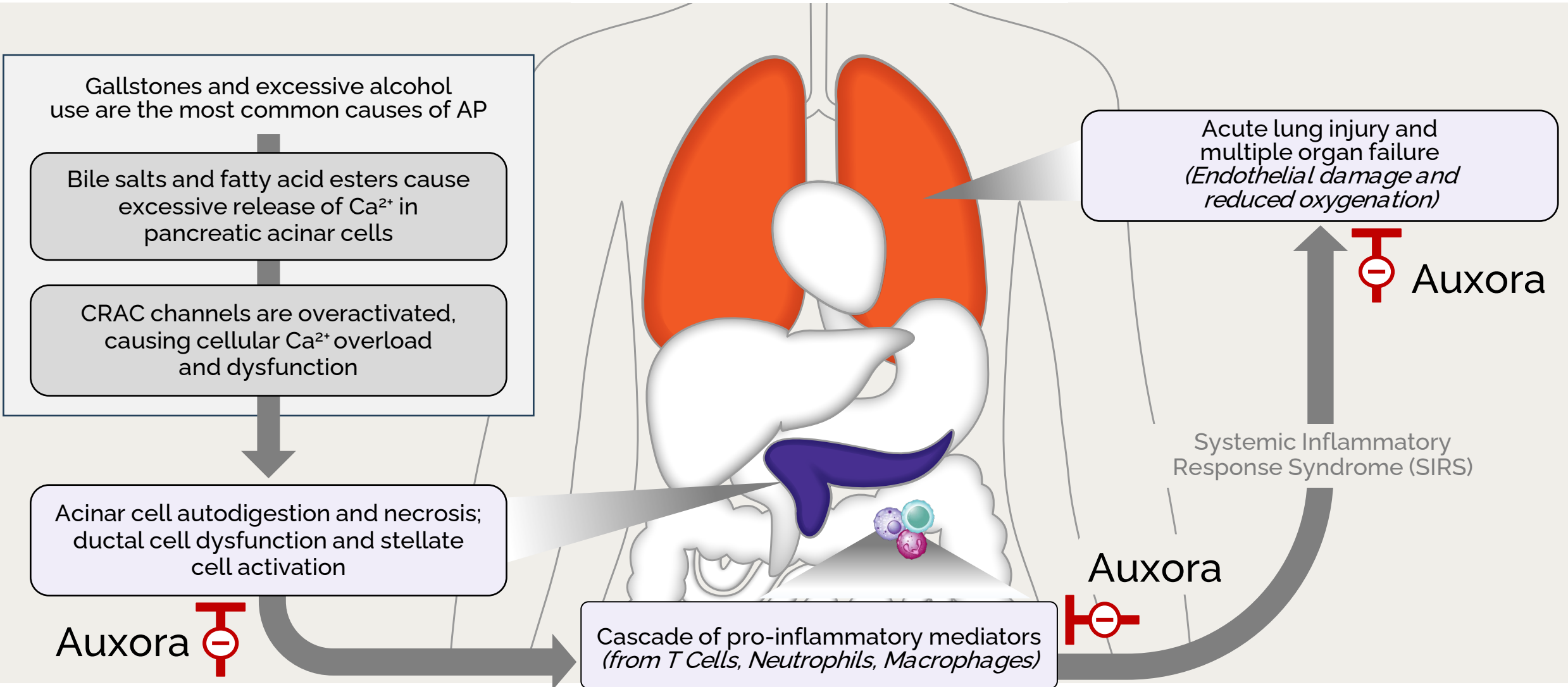
# AP carries a significant disease burden

## Disease Progression in Acute Pancreatitis



Additionally, a major economic burden: >1M+ patient days in hospital per year and >\$3B cost per year

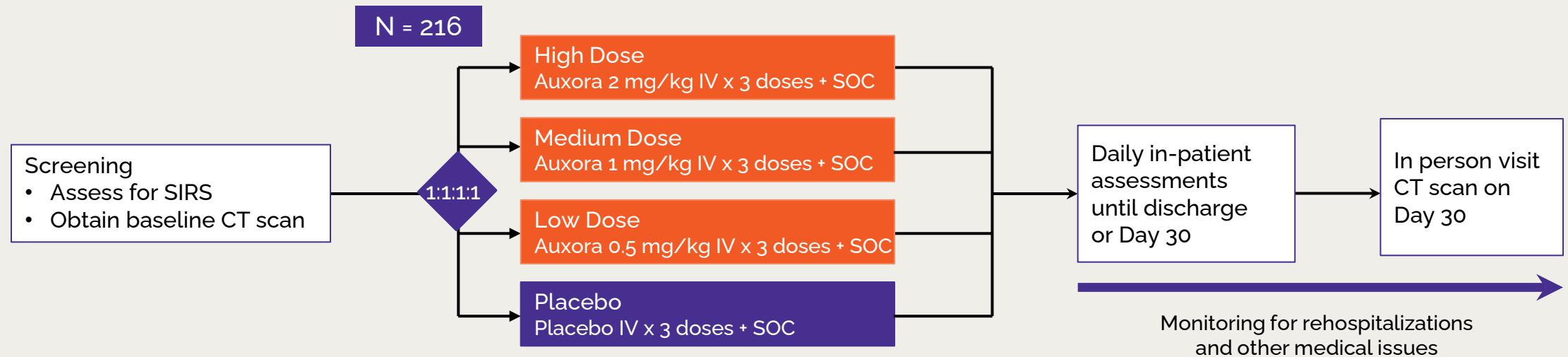
# Auxora targets multiple injury pathways activated in AP and respiratory failure



# CARPO Phase 2b clinical trial in AP

## Endpoints

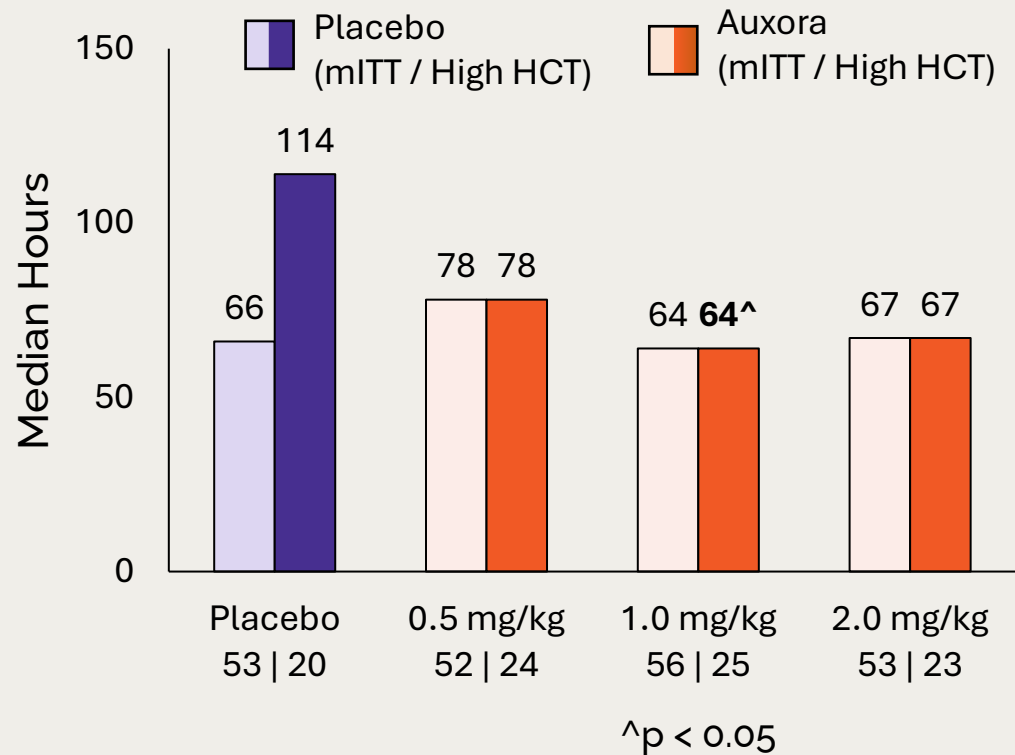
- Time to solid food tolerance (primary endpoint)
- Severe organ failure
- Respiratory failure
- Length of hospital stay
- Time to medically indicated discharge
- Necrosis as determined by CT



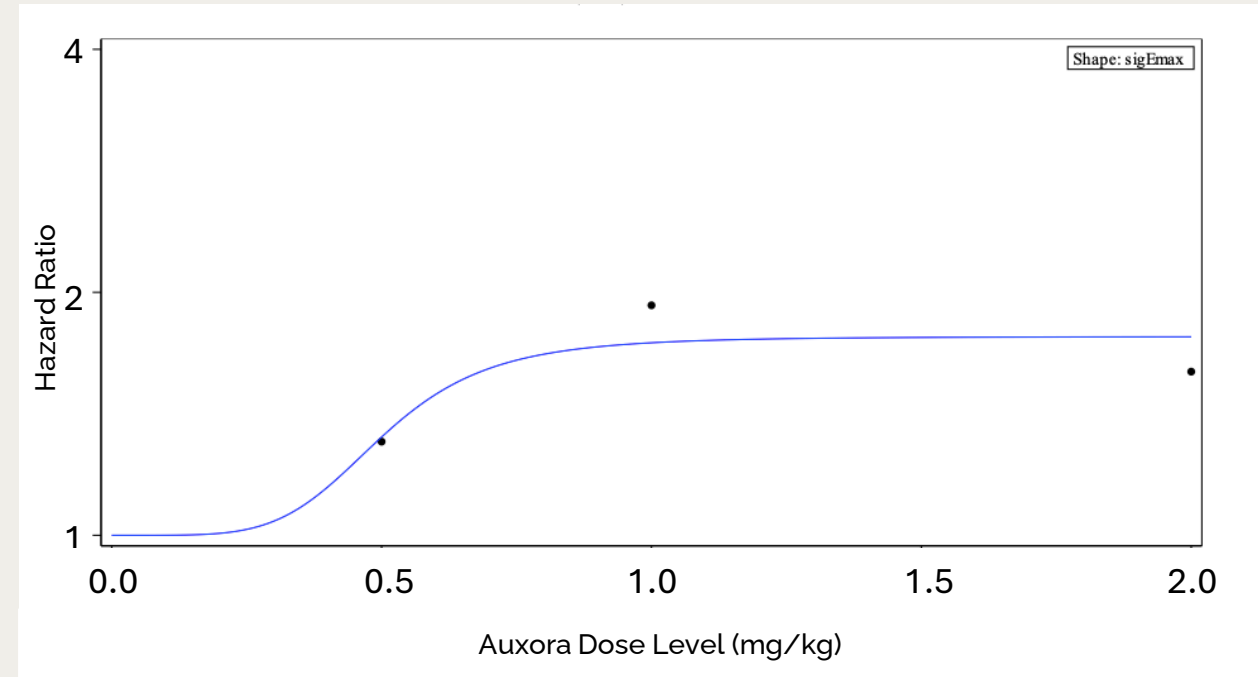
Primary Objective: Dose Response on Primary and Secondary Endpoints

# Dose response observed on the Primary Endpoint (Time to Solid Food Tolerance) in High Hematocrit subgroup

Time to Solid Food Tolerance  
mITT Population and Pre-Defined High Hematocrit (HCT) Sub-Group



gMCP-Mod Analysis  
Time to Solid Food Tolerance  
in the High Hematocrit Group



p-value of 0.057 | (The pre-defined  $\alpha$  was 0.15)

# Auxora High and Medium Doses reduced all types of Severe Organ Failure and prevented New Onset Severe Respiratory Failure

## Reduced Severe Organ Failure

	Placebo	0.5 mg/kg	1.0 mg/kg	2.0 mg/kg
Respiratory	4/53 (7.5%)	5/52 (9.6%)	2/56 (3.6%)	2/53 (3.8%)
Renal	1/53 (1.9%)	2/52 (3.8%)	1/56 (1.8%)	0/53 (0.0%)
Cardiovascular	1/53 (1.9%)	3/52 (5.8%)	1/56 (1.8%)	1/53 (1.9%)
Any Severe Organ Failure	5/53 (9.4%)	5/52 (9.6%)	2/56 (3.6%)	2/53 (3.8%)

## Prevented New Onset Severe Respiratory Failure

	Placebo	0.5 mg/kg	1.0 mg/kg	2.0 mg/kg
New Onset Severe Respiratory Failure	4/47 (8.5%)	4/48 (8.3%)	0/52 (0%)	0/50 (0%)

	Placebo + 0.5 mg/kg	1.0 mg/kg + 2.0 mg/kg
New Onset Severe Respiratory Failure	8/95 (8.4%)	0/102 (0%)
Difference		-8.4 %
Relative Reduction		100%
p-value		0.0027

Severe Respiratory Failure: Receiving invasive mechanical ventilation (IMV) OR use of either high flow nasal cannula (HFNC) or non-invasive mechanical ventilation (NIMV) for ≥ 48 hours

Severe Renal Failure: Initiation of renal replacement therapy

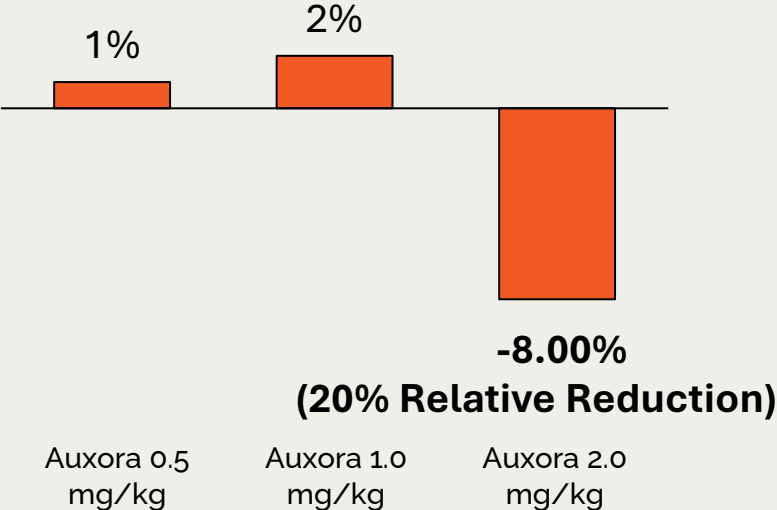
Severe Cardiovascular Failure: Use of vasopressor or inotropic support for ≥48 hours



# Auxora High-Dose demonstrated improvements in additional Key Secondary Endpoints

## New Onset Necrotizing Pancreatitis (NP)

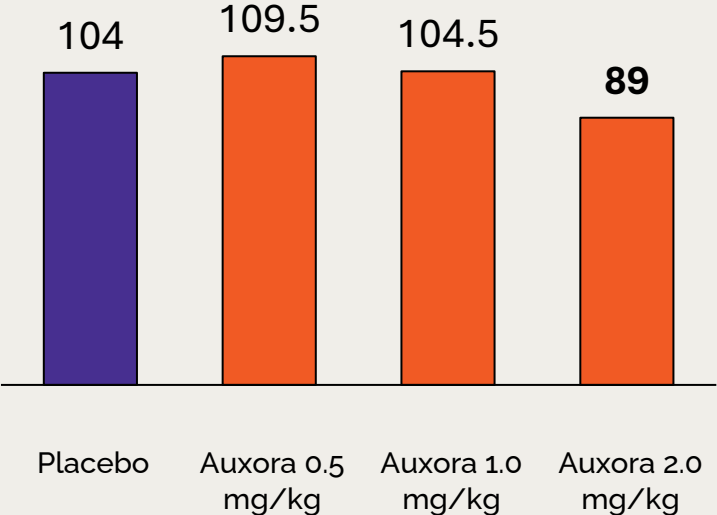
Absolute Percentage Pt. Difference vs. Placebo<sup>1</sup>



Percentage is based on the number of subjects without Necrotizing Pancreatitis at Screening and non-missing Day 30 Visit or post-treatment unscheduled visit CECT reading results

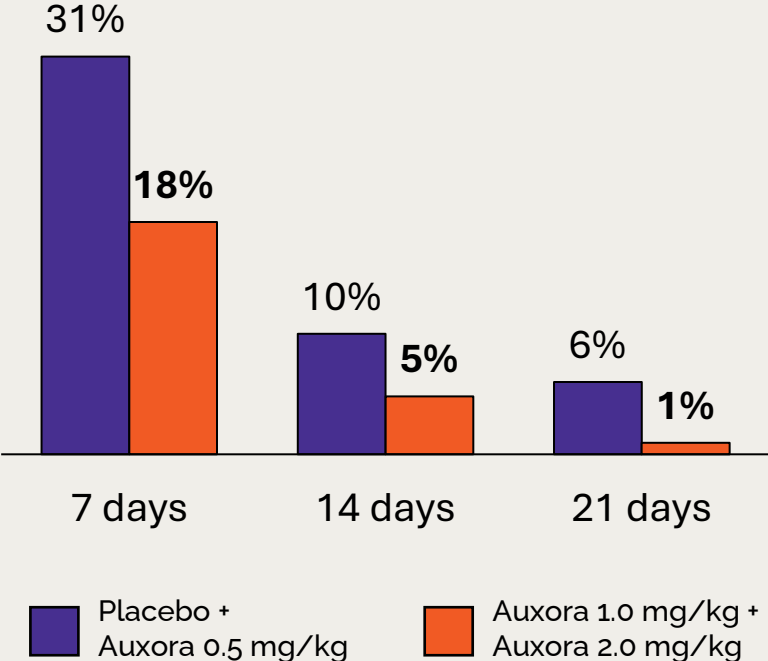
## Time to Medically Indicated Discharge (TMID)

TMID Median Hours



TMID defined as: 1) No clinical evidence of infection necessitating continued hospitalization; 2) Solid food tolerance; 3) Abdominal pain has resolved or controlled with medications (non-opiate)

## Proportion of Patients Remaining in the Hospital



1. Cochran-Mantel-Haenszel test stratified by CRF recorded gender (male or female) and the risk for HCT (higher or lower) based on CRF data; If the Day 30 visit data was missing, the last available unscheduled post-treatment data was used for Day 30 analysis based on the LOCF method.

# Integration of key endpoints into Win Ratio demonstrates potential benefits of Auxora High-Dose compared to Placebo

Win Ratio	All-cause Mortality	New Onset Severe Respiratory Failure	Necrotizing Pancreatitis	Time to Medically Indicated Discharge	Total Wins
Placebo wins	0	0	374	546	920
Auxora 2.0 mg/kg dose wins	0	208	615	730	1553

Stratified Win Ratio: 1.640 | p-value: 0.0372 | 95% CI: 1.030 – 2.612

The win ratio approach provides a comprehensive evaluation of Auxora for AP

Reduction in respiratory failure will reduce mortality

Reduction in necrotizing pancreatitis will reduce morbidity

Reduction in hospital stays will reduce economic burden

# Auxora for Acute Kidney Injury (AKI)

# High unmet need in AKI - particularly with concurrent respiratory failure

~3.7M AKI hospitalizations annually (U.S.)

SOC is supportive therapy

Stage 1  
↑ sCr<sup>2</sup> 1.5x

71%

Stage 2  
↑ sCr 2x

17%

Stage 3  
↑ sCr 3x

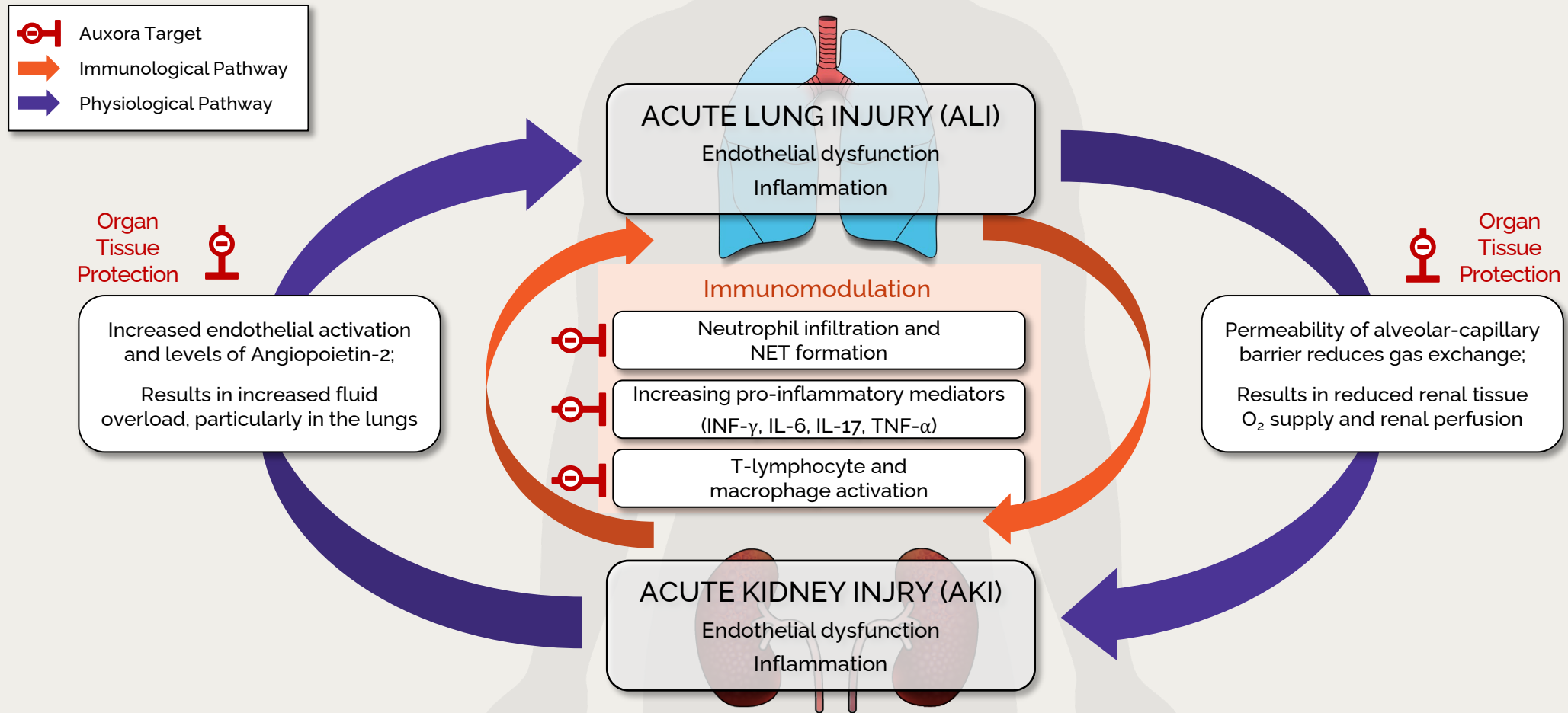
12%

- Fluid resuscitation
- Diuretics
- Nutrition
- Correction of underlying cause

Auxora Target Market:  
1.1M<sup>1</sup> Patients

Over half of these patients have respiratory failure with 90-day mortality 50% or greater

# Auxora targets multiple injury pathways activated in AKI and ALI

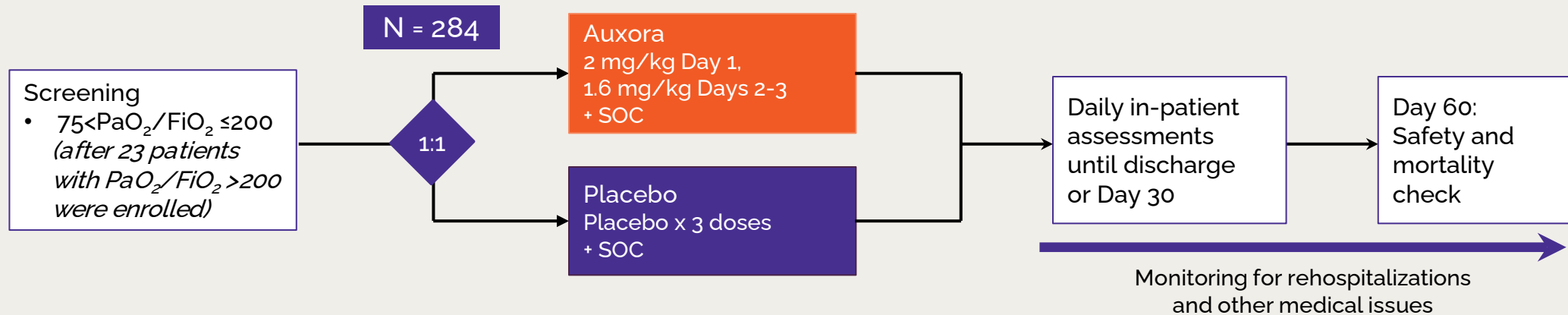


# Prior Ph2 study in Severe and Critical COVID-19 Pneumonia (CARDEA) studied Auxora in a population with relevance to our AKI program

## CARDEA: Ph2 in Severe and Critical COVID-19 Pneumonia Patients

### Endpoints

- Days to Recovery
- Mortality
- Ventilation use
- Days in the hospital



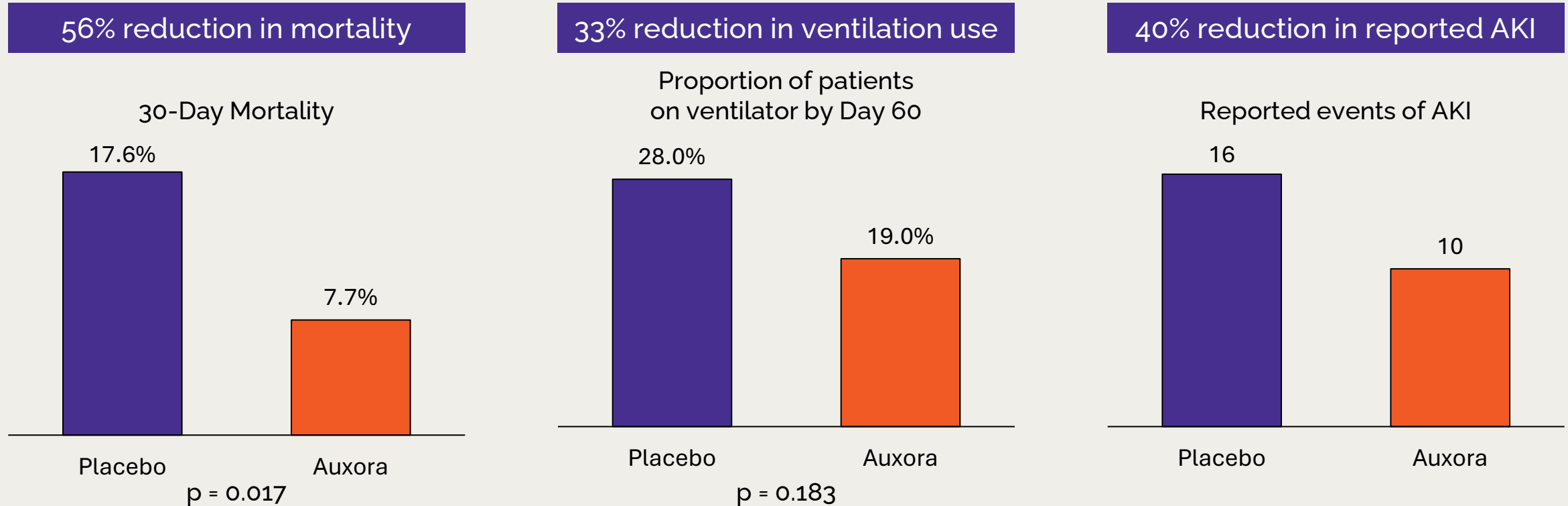
### Relevance to Auxora in AKI

- Study population was severely sick, hospitalized, and with lung injury / hypoxemic
- 37 patients had acute kidney injury at time of enrollment
- 190 patients had daily blood samples taken over first four days, providing biomarker data



# Results from CARDEA reinforce Auxora's potential impact on key endpoints in patients with impaired respiratory and kidney function

CARDEA: Ph2 in Severe and Critical COVID-19 Pneumonia Patients

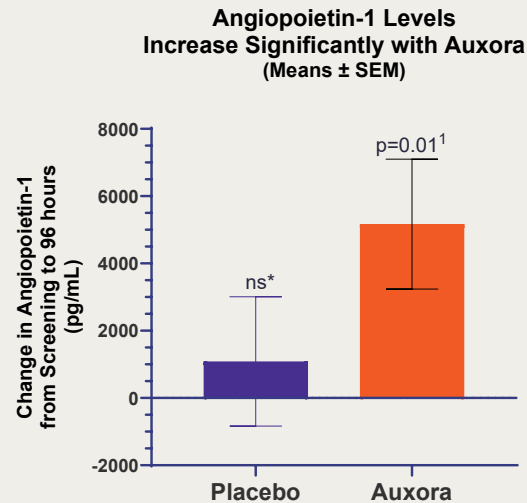


Additionally, even greater mortality benefit observed in patients with compromised kidney function (low GFR) at time of enrollment (details pending publication)

# In CARDEA, Auxora demonstrated positive effects on Ang-1/Ang-2, which help control vascular integrity and lung function

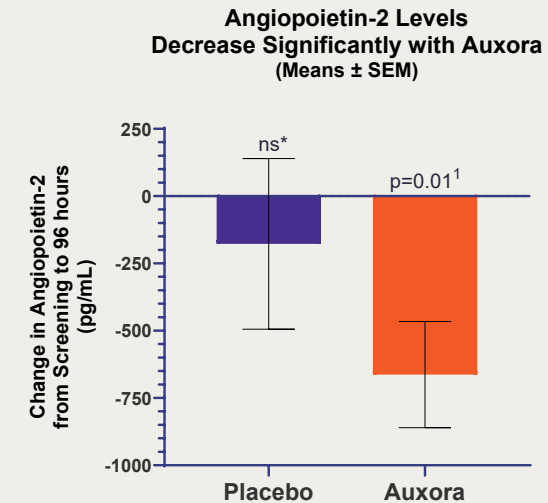
Biomarker Data from Ph2 in Severe and Critical COVID-19 Pneumonia Patients (N = 190)

Ang-1/Tie2 signaling maintains vascular integrity



- Increased Ang-1 correlated with:
- Improved Recovery at 1 week (p<0.05)

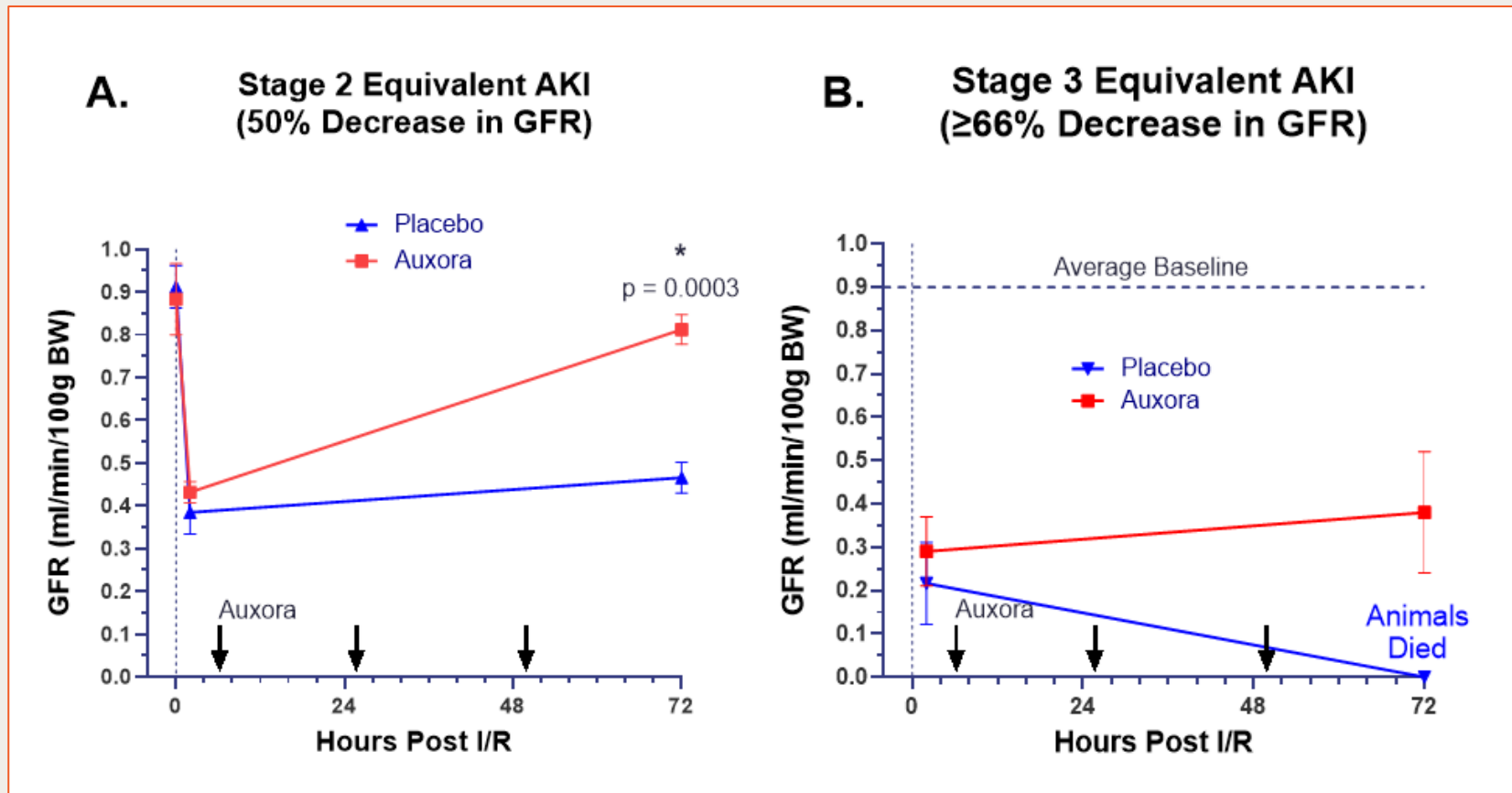
Ang-2/Tie2 results in endothelial inflammation with increased endothelial permeability



- Decreased Ang-2 correlated with:
- Decreased d-dimer at 72 hours (p<0.01)  $\rightarrow$  reduced hypercoagulability
  - Decreased sCD25 at 96 hours (p<0.01)  $\rightarrow$  reduced inflammation
  - Improved Recovery at 1 week (p<0.05)

# Auxora improved kidney recovery and survival in Severe AKI rat models

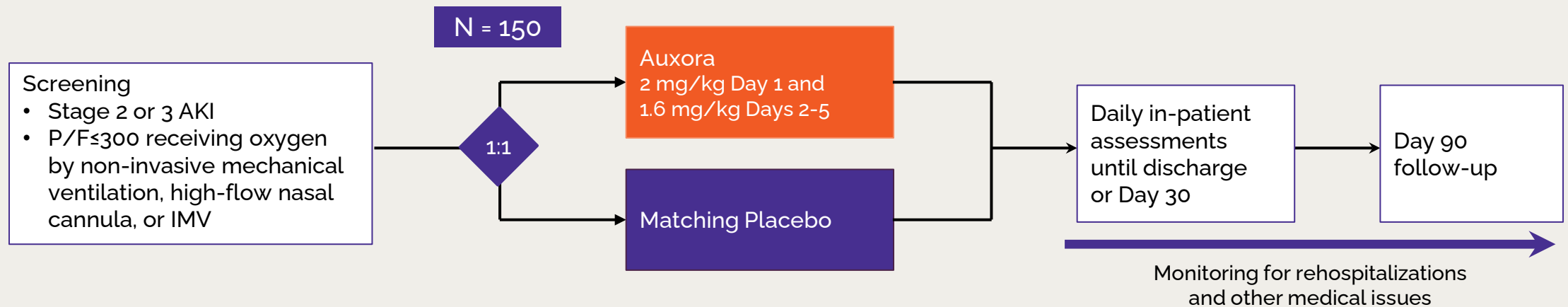
Three doses of Auxora or placebo were administered daily starting 6 hours after ischemia/reperfusion injury



# KOURAGE: AKI with Associated Acute Hypoxemic Respiratory Failure Phase 2 trial design

## Endpoints

- Days alive, ventilator-free and dialysis-free through Day 30 (primary)
- Morality
- Need for ventilator
- Need for dialysis
- GFR status at day D0
- MAKE (Major Adverse Kidney Events) at Day 90



# Platform Application for CRAC Channel Inhibition

# Preclinical results support development in other I&I indications

Indication	Intended Formulation	Preclinical Observations	Potential Next Steps
Chronic Pancreatitis (CP)	Oral	In vivo efficacy in a mouse model of CP using CM5480 (Szabo et al, 2023)	Confirm with lead oral candidate
Acute Ulcerative Colitis	IV	In vivo efficacy of zegocractin in a mouse model of inflammatory bowel disease (Letizia et al., 2022)	Ongoing discussions with investigators about potential clinical trials
Allergic Asthma	IV or Inhaled	In vivo efficacy of zegocractin in a mouse model of allergic asthma (Kahlfuss et al., 2022)	Pursue strategic partnership
Traumatic Brain Injury (TBI)	IV or Oral	In vivo efficacy of CM5480 in a mouse model of TBI (Mizuma et al., 2018)	Confirm results with lead oral compound or Auxora
Rheumatoid Arthritis (RA)	Oral	In vivo efficacy of zegocractin and CM5480 in rat RA models (CalciMedica unpublished data)	Confirm results with lead oral candidate



# Anticipated Milestones

# Anticipated milestones

AP	CARPO Phase 2b Trial Completed and Positive Data Announced Next Step: End-of-Phase 2 Meeting with FDA
AKI	KOURAGE Trial Enrolling Data Expected in 2025
AIPT	CRSPA Initial First Cohort Data Released at ASH 2023 Trial Expansion Underway; Data Expected in 2025
Cash Runway	Current Cash Runway into 1H26 Expected to Fund Current Operations and Completion of KOURAGE Phase 2 Trial