

Developing Novel Therapies for Acute Inflammatory and Immunologic Diseases






October 2024

Forward-Looking Statements

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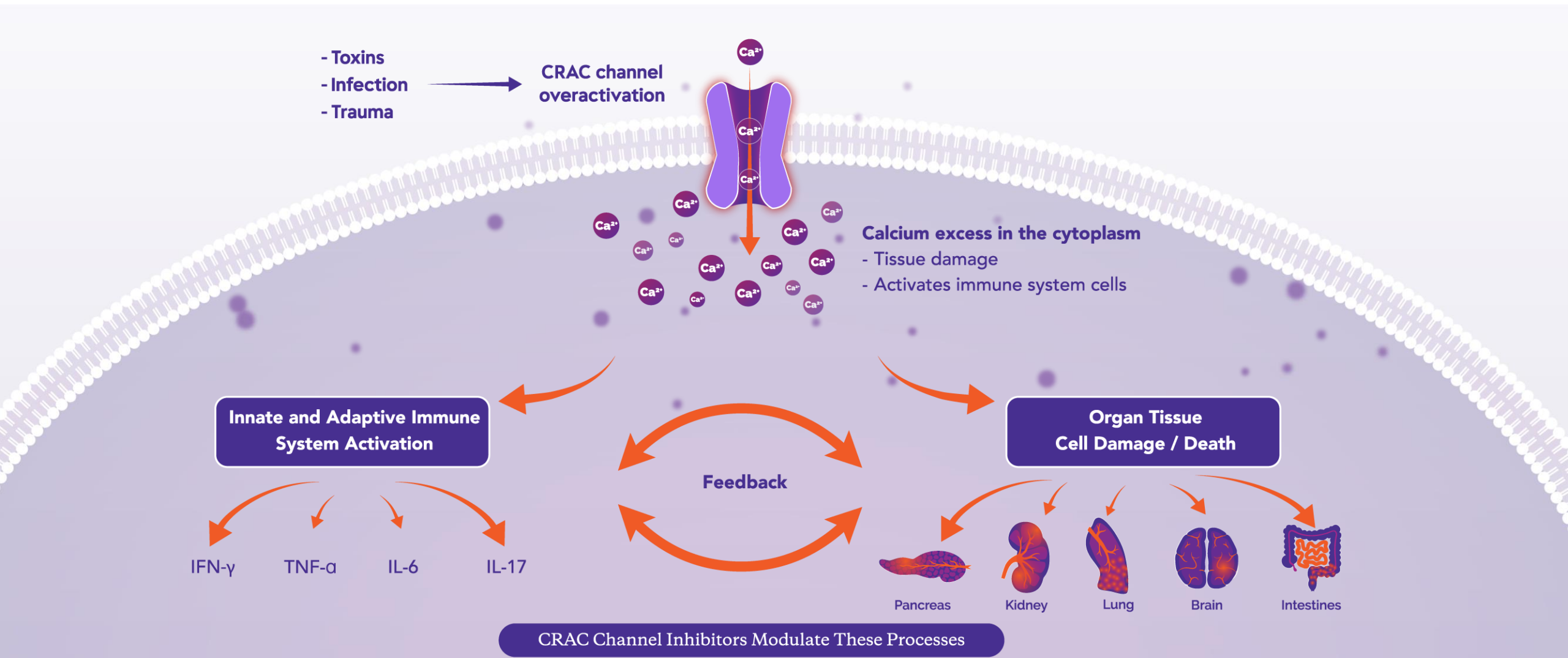
Investment Highlights

	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 six phase 2 trials in acute critical illnesses
	Substantial Market Opportunity	~1 million U.S. target AKI population and ~100 thousand U.S. target AP population representing \$ multi-billion opportunities in diseases with no approved therapies
	Strong IP	Composition of matter (2036), formulation (2038), and methods of use (2036-2041+) worldwide patent protection
	Recent PIPE Financing	Completed 1Q24 private placement expected to fund operations and completion of the ongoing KOURAGE Phase 2 trial in AKI patients into 2H25

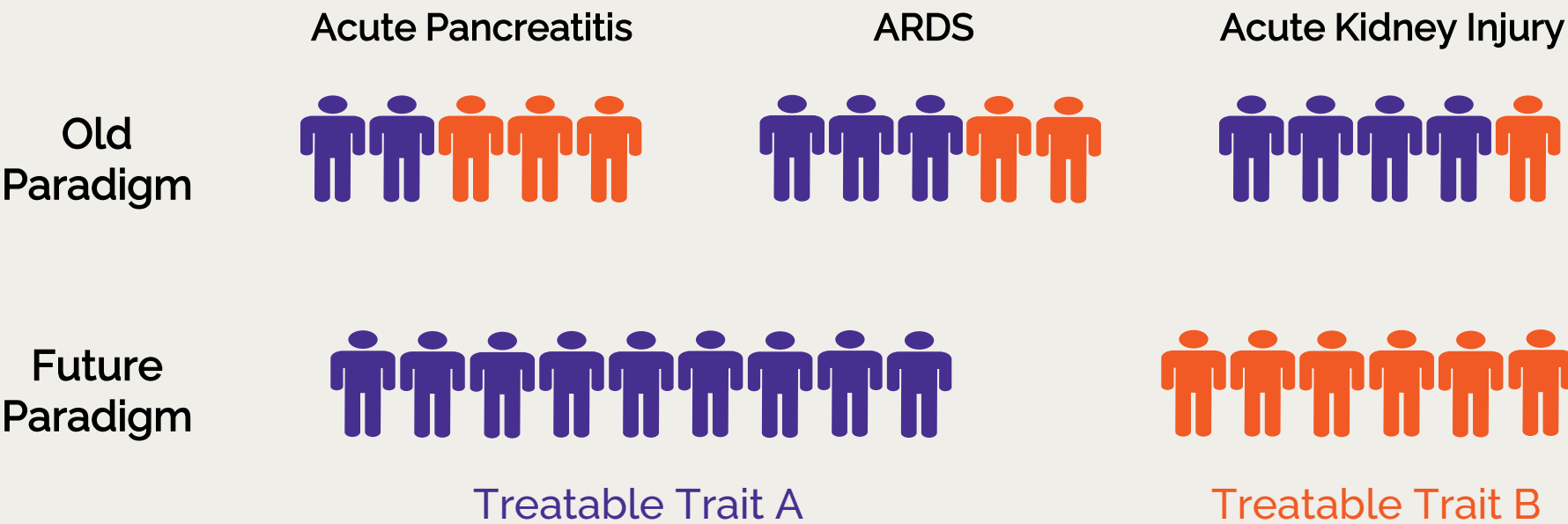
Differentiated Pipeline in Acute and Chronic Inflammatory and Immunologic Diseases

Program ¹	Indication	Phase of Development				Anticipated Milestones
		Preclinical	Phase 1	Phase 2	Phase 3	
Acute Disease (IV)						
Auxora	Acute Pancreatitis	<div></div>	<div></div>	<div></div>	<div></div>	CARPO Phase 2b trial positive topline data released; Final data expected in 2H2024
Auxora	Asparaginase-Induced Pancreatic Toxicity in Pediatric Patients	<div></div>	<div></div>	<div></div>	<div></div>	CRSPA Phase 1/2 trial ongoing; Data expected in 2025
Auxora	Acute Kidney Injury	<div></div>	<div></div>	<div></div>	<div></div>	KOURAGE Phase 2 trial ongoing; Data expected in 2025
Chronic Disease (Oral)						
CM6336	Chronic Pancreatitis	<div></div>	<div></div>	<div></div>	<div></div>	Potential IND submission in 2025
CM6336	Rheumatoid Arthritis	<div></div>	<div></div>	<div></div>	<div></div>	Potential IND submission in 2025

Overactivation of CRAC Channels: Immune System Activation and Tissue Cell Injury



Acute Inflammation: Underlying Cause Across Many Diseases



Auxora has demonstrated positive clinical results in all 3 of these large, underserved patient populations

1) Sources: Reddy, Kiran, Carolyn S. Calfee, and Danny F. McAuley. "Acute respiratory distress syndrome subphenotypes beyond the syndrome: a step toward treatable traits?." American Journal of Respiratory and Critical Care Medicine 203.12 (2021): 1449-1451.

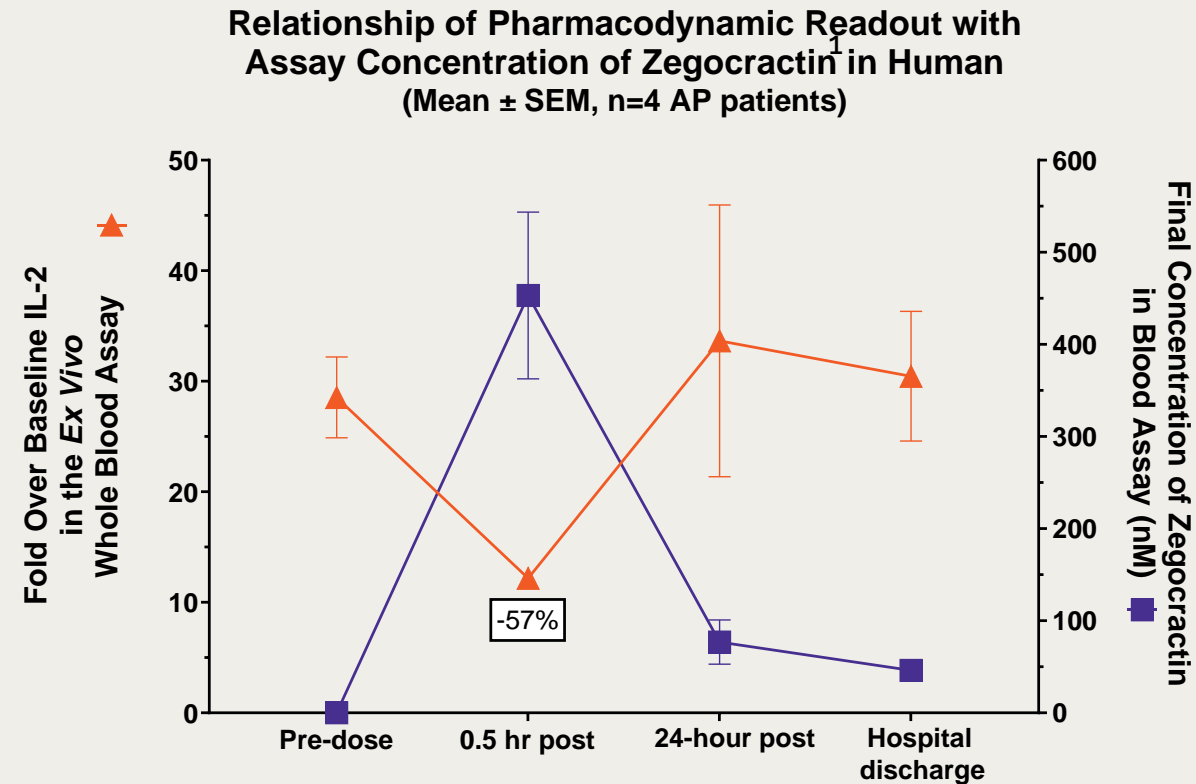
Auxora Clinically Active and Well-Tolerated in Multiple Phase 2 Trials

Population	Phase	Size	Results	Publication
CARPO: Acute Pancreatitis With SIRS	2b	N=216	<ul style="list-style-type: none"> • Severe organ failure reduction of ~60% in high and medium dose patients • Respiratory failure reduced considerably in high and medium dose patients • Time to solid food tolerance dose response and improvement up to 2.1 days • Length of hospital stay improvement of up to 1.9 days 	TBD
CARDEA: COVID-19 with Respiratory Failure On LFO ₂ ¹ or HFNC ²	2	N=284	<ul style="list-style-type: none"> • Mortality at day 30 reduction of 56% • Respiratory failure requiring ventilation reduction of 33% • Severe organ failure reduction with reduction in new onset AKI of ~40% • Length of hospital stay improvement of >2 days 	Critical Care (2022)
Acute Pancreatitis Accompanied by SIRS and Hypoxemia	2a	N=21	<ul style="list-style-type: none"> • Time to solid food tolerance reduction • Respiratory failure requiring ventilation reduction of >50% • Length of hospital stay improvement of 2 days 	Pancreas (2021)
COVID-19 with Respiratory Failure On LFO ₂ ¹ or HFNC ²	2a	N=30	<ul style="list-style-type: none"> • Mortality at day 30 reduction of 50% • Respiratory failure requiring ventilation reduction of >50% • Time to recovery improved by >2 days 	Critical Care (2020)
CRSPA: Asparaginase-Induced Pancreatic Toxicity	1b/2a	N=9³	<ul style="list-style-type: none"> • Pancreatic necrosis of >30% eliminated • Total parental nutrition requirement eliminated 	ASH 2023
COVID-19 with Respiratory Failure On IMV ⁴	1b/2a	N=9	<ul style="list-style-type: none"> • Macrophage and neutrophils levels reduced • Inflammatory cytokine gene expression reduced • Functional protein gene expression unaffected 	TBD

1) LFO₂: Low Flow Oxygen; 2) HFNC: High-Flow Nasal Cannula; 3) Represents first cohort of patients; 4) IMV: Invasive Mechanical Ventilation

IV Formulation Provides Ideal Benefits for Acute Inflammation

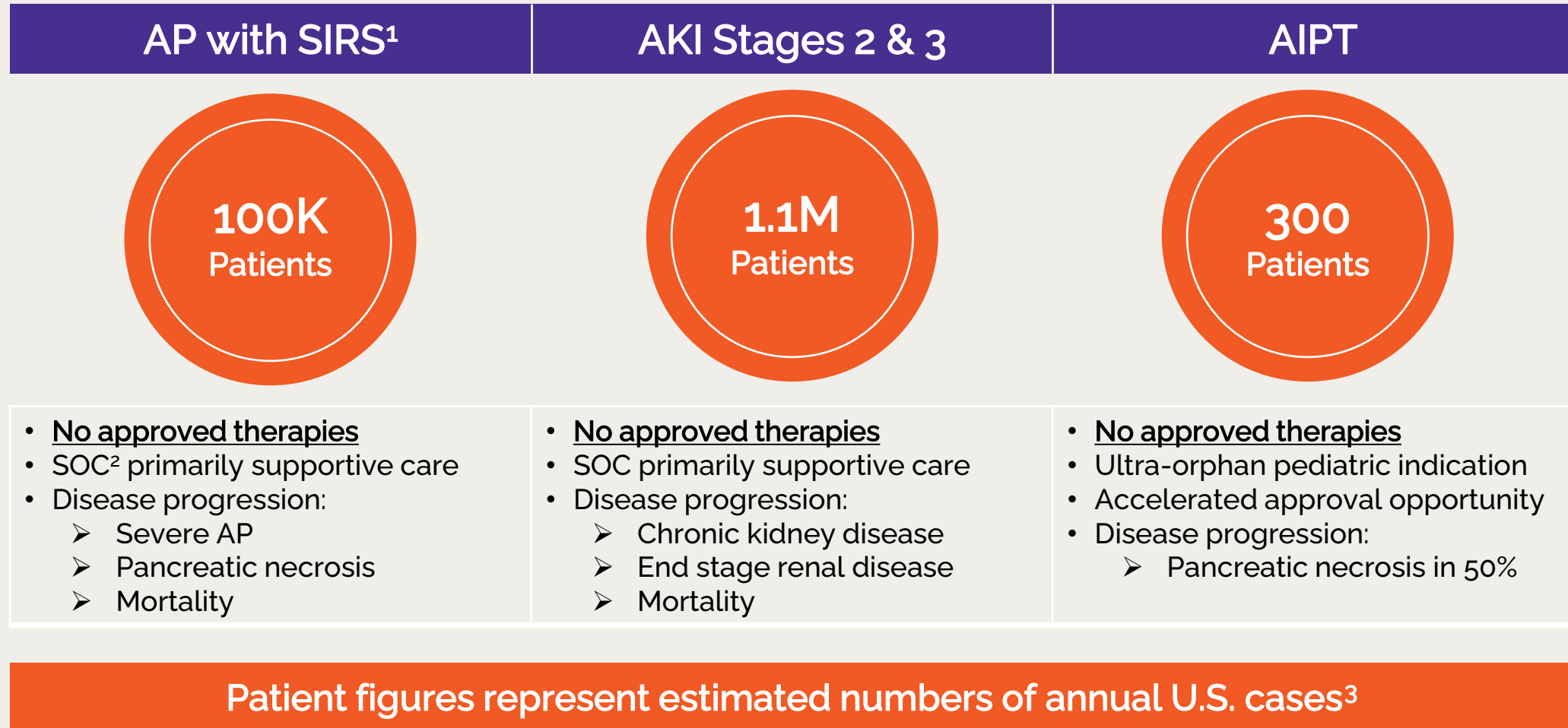
Rapid onset of immunomodulatory action reaches peak by the end of 4-hour infusion



Recovery within 24-48 hours of dosing limits the potential for long-term immunosuppression

¹) Zegocractin is the active pharmaceutical ingredient in Auxora

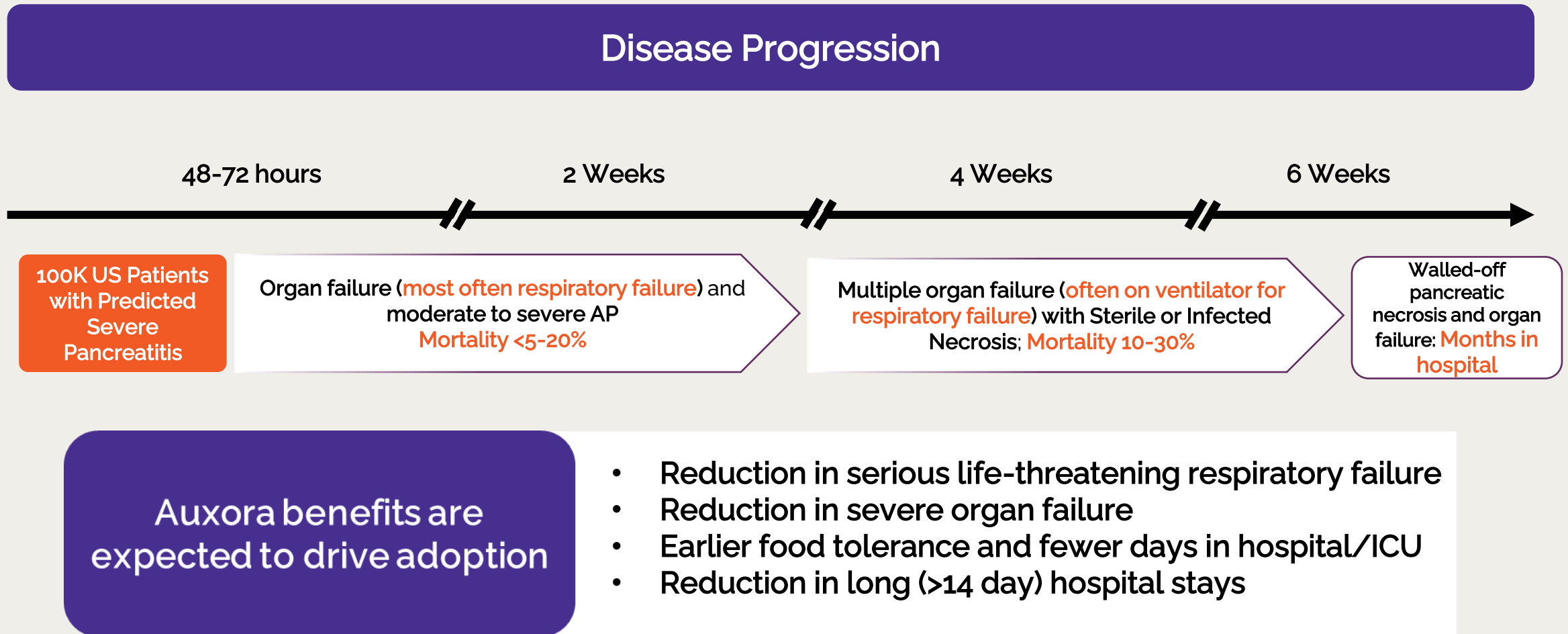
Large U.S. Market Opportunity in Acute Inflammatory Diseases



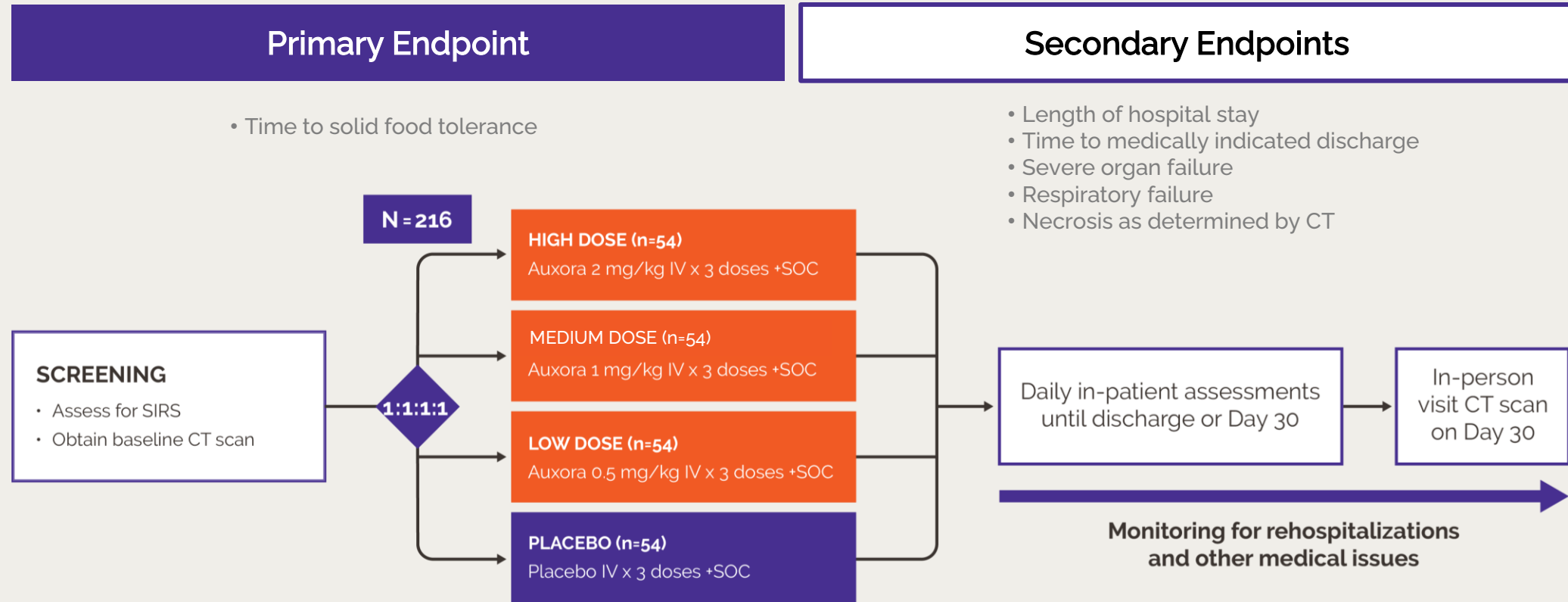
1) **SIRS**: Systemic Inflammatory Response Syndrome; 2) **SOC**: Standard of Care; 3) Sources: Primary Market Research, KOLs, Healthcare Cost and Utilization Project, Pancreatitis Foundation, and <https://www.hcup-us.ahrq.gov/reports/statbriefs/sb231-Acute-Renal-Failure-Hospitalizations.pdf>
Criteria: Based on RIFLE staging criteria for AKI classification; Serum creatinine increase over baseline

Auxora for Acute Pancreatitis (AP)

Patient Journey and Auxora Treatment in Severe AP



CARPO Phase 2b Clinical Trial in AP



Primary Objective: Dose Response on Primary and Secondary Endpoints

CARPO Topline Takeaways

- Primary objective was met with a dose response for multiple endpoints
 - Statistically significant for time to solid food tolerance in high hematocrit patients
 - Statistically significant for severe organ failure in the entire population
 - >60% reduction in organ failure for high+medium dose vs placebo+low dose cohorts
 - Most notable reduction in respiratory failure
- Reduction in severe organ failure increases confidence in our KOURAGE AKI trial
 - KOURAGE patients have respiratory failure
- High and medium CARPO doses (2.0 mg/kg and 1.0 mg/kg doses) representative of KOURAGE dosing (single 2.0 mg/kg dose followed by four 1.6 mg/kg doses)
- Auxora was well-tolerated
- Next step: End-of-Phase 2 meeting with FDA

Time to Solid Food Tolerance

Statistical significance achieved on dose response in patients with hyperinflammatory AP

		Placebo	2.0 mg/kg	1.0 mg/kg	0.5 mg/kg
n= 122		n= 33	n= 29*	n= 31	n= 28
Low Hematocrit	25 th %	36.0	25.0	28.0	19.0
	Median hours	62.0	65.0	68.0	67.0
	75%	137.0	100.0	353.0	184.0
n= 92		n= 20	n= 23*	n= 25	n= 24
High Hematocrit	25 th %	41.5	13.0	20.0	37.0
	Median hours	113.5	67.0	64.0	78.0
	75%	187.0	117.0	113.0	187.5

*One hematocrit missing at baseline

Determination of solid food tolerance

- Patient offered a low fat, ≥500-calorie solid meal
- Patient consumes ≥50% of the meal without vomiting or an increase in abdominal pain in the two hours after the meal (as confirmed by clinical trial nurse)

CARPO: Severe Organ Failure

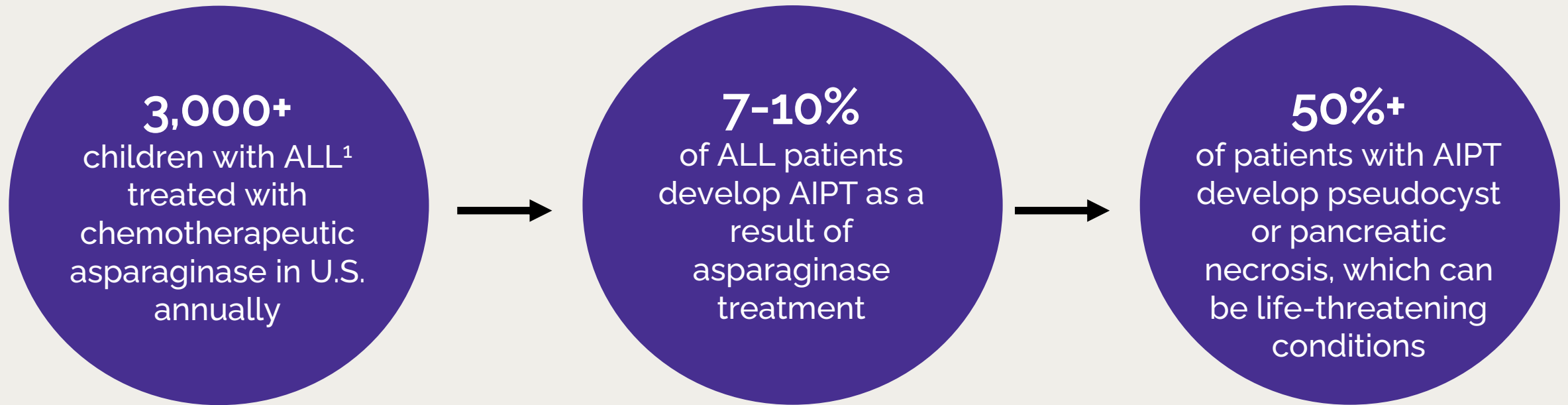
Statistical significance achieved on dose response

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

Definition of severe organ failure

- Severe respiratory failure defined as those patients receiving invasive mechanical ventilation (IMV) or those receiving for ≥ 48 hours use of either high flow nasal cannula (HFNC) or non-invasive mechanical ventilation (NIMV) (Use of NIMV for the treatment of obstructive sleep apnea not considered as meeting the definition of severe respiratory failure)
- Severe renal failure defined as the initiation of renal replacement therapy
- Severe cardiovascular failure defined as the use of vasopressor or inotropic support for ≥ 48 hours

Potential Clinical Benefits to Children with AIPT



Auxora has potential to rapidly resolve AIPT with improvement in food tolerance and pain while preventing development of further complications such as pancreatic necrosis

1) **ALL:** Acute Lymphoblastic Leukemia

2) Sources: Liu C, Yang W, Devidas M, et al. Clinical and Genetic Risk Factors for Acute Pancreatitis in Patients With Acute Lymphoblastic Leukemia. J Clin Oncol. 2016. Abaji R, Gagne V, Xu CJ, et al. Whole-exome sequencing identified genetic risk factors for asparaginase-related complications in childhood ALL patients. Oncotarget. 2017;8: 43752-43767. Rank C, Wolthers B, Grell K, et al. Asparaginase-associated pancreatitis in acute lymphoblastic leukemia: results from the NOPHO ALL 2008 treatment of patients 1-45 years of age. J Clin Oncol. 2019 38:145-154.

Proof-of-Concept Ongoing in AIPT

Pediatric Patients Had Rapid Resolution of Pain and Food Intolerance

CRSPA Phase 1/2 Trial in Pediatric AIPT

- Investigator-initiated open-label trial being conducted at St. Jude Children's Research Hospital
- Assess the safety in pediatric patients with ALL who have developed AIPT
- Estimate the efficacy of Auxora to prevent pseudocyst or necrotizing pancreatitis in pediatric patients with AIPT

Trial Status

- Cohort 1 complete (9 patients)
 - 8 patients received four daily infusions of Auxora and had rapid resolution of pain and food intolerance
 - 1 patient received less than a single infusion of Auxora and developed pancreatic necrosis
 - Blinded matched, historical control comparison for Cohort 1 completed
- Cohort 1 dosing selected as recommended dose for patients
- Expanding to additional sites to complete trial (24 patients) with data expected in 2025

Results for First Cohort Compared to Blinded, Matched Historical Controls Presented at ASH 2023

CRSPA First Cohort Data: Presented at ASH 2023

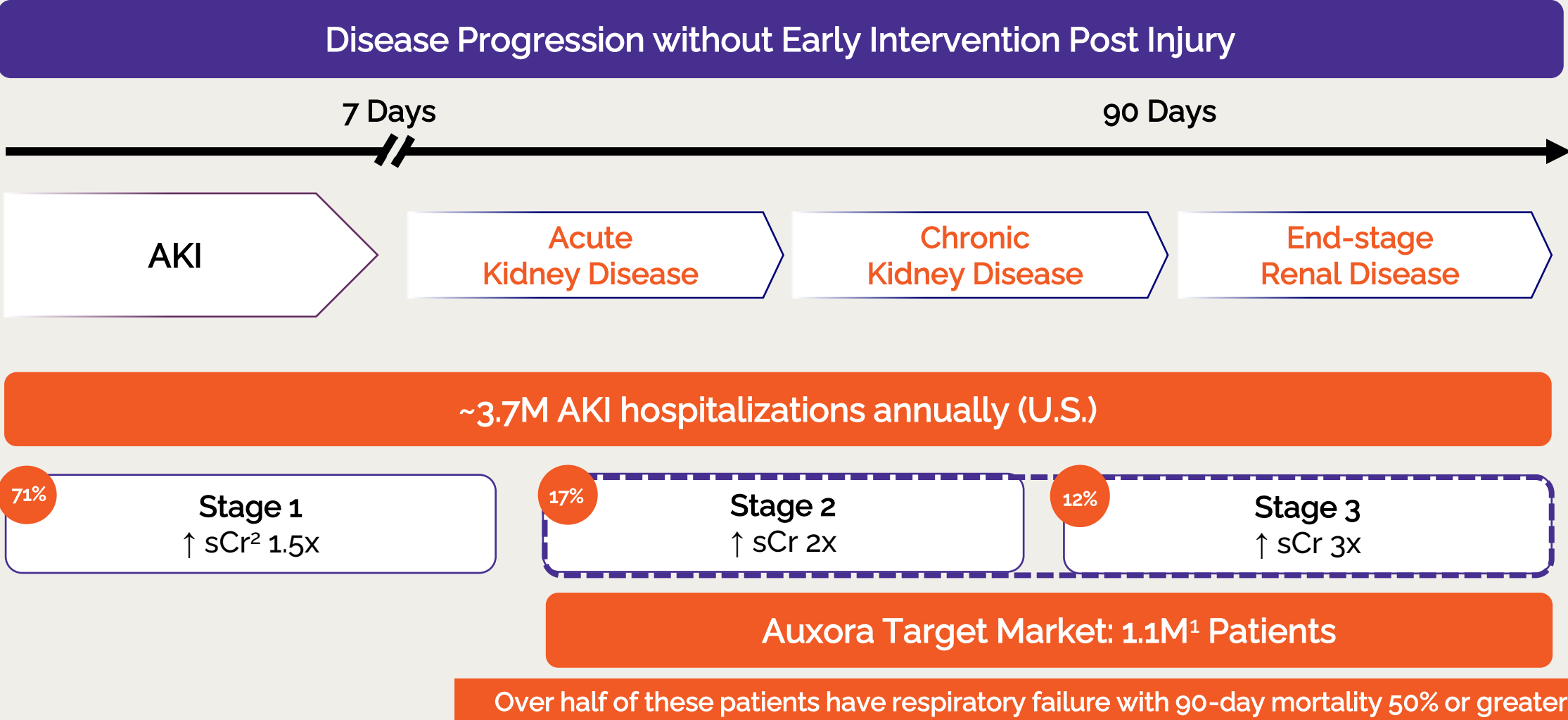
	Total 16 (T16): All AIPT	Matched T16 AIPT cohort	CRSPA evaluable for efficacy
Patients with AIPT	51	16	8
Age: mean (range)	10.3 (2.2-19.4)	9 (2.2-18.4)	8.2 (3.1-17.6)
Female (%)	17 (33.3%)	5 (31.3%)	3 (37.5%)
Low-risk therapy (%)	9 (17.6%)	1 (6.3%)	2 (25%)
Hospital days (range)	12.1 (2-70)	13.4 (2-27)	6.3 (5-8)
ICU needed (%)	11 (21.6%)	3 (18.8%)	1 (12.5%)
ICU days mean (range)	5.1 (1-9)	5 (3-7)	3
TPN needed (%)	27 (52.9%)	11 (68.8%)	0
TPN days mean (range)	37.7 (3-153)	27.2 (4-63)	NA
≥30% pancreatic necrosis (%)	NA	4 (26.7%) *	0
CTSI mean (range)	NA	5.4 (0-10) *	2.4 (0-4)
CTSI ≥ 7 (%)	NA	4 (26.7%) *	0

*One patient in matched T16 cohort was unable to be evaluated for pancreatic necrosis or a CTSI score

CTSI score definitions: 0-3 mild acute pancreatitis, 4-6 moderately severe acute pancreatitis, ≥7 severe acute pancreatitis

Auxora for Acute Kidney Injury (AKI)

Patient Journey in AKI



1) Source: <https://www.hcup-us.ahrq.gov/reports/statbriefs/sb231-Acute-Renal-Failure-Hospitalizations.pdf>
Criteria: Based on RIFLE staging criteria for AKI classification; Serum creatinine increase over baseline
2) sCr: Serum Creatinine

Potential Clinical Benefits to Patients with AKI

Current standard of care is limited to supportive therapy

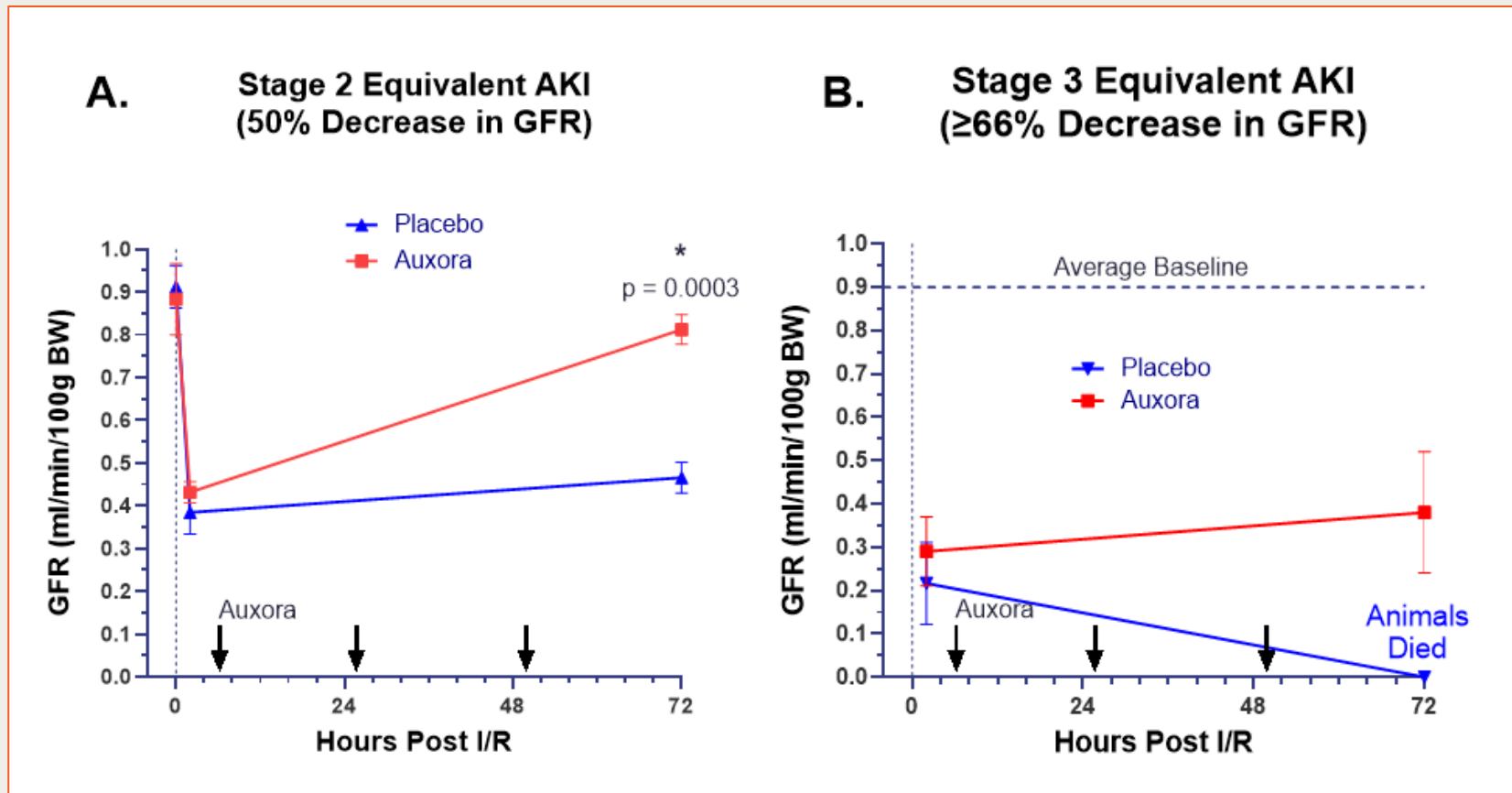
- Fluid resuscitation / Diuretics
- Nutrition
- Correction of underlying cause

Auxora benefits are expected to drive adoption

- Reduced need for dialysis
- Reduced risk of mortality
- Greater recovery of renal function

Auxora Improved Kidney Recovery and Survival in Severe AKI models

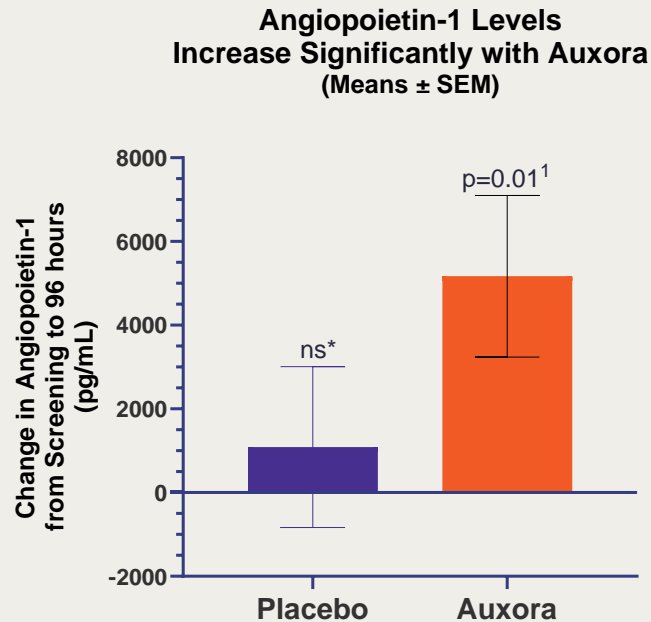
Three doses of Auxora or placebo were administered daily starting 6 hours after ischemia/reperfusion injury



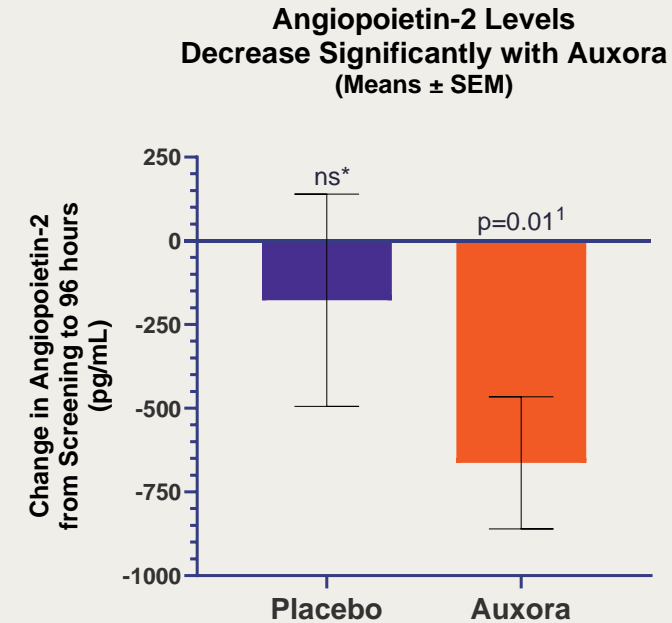
Note: GFR is Glomerular filtration rate and data is courtesy of David Basile, PhD, Indiana University

Phase 2 CARDEA Trial: Evidence of Renal Protection

Ang-1/Tie2 signaling maintains vascular integrity



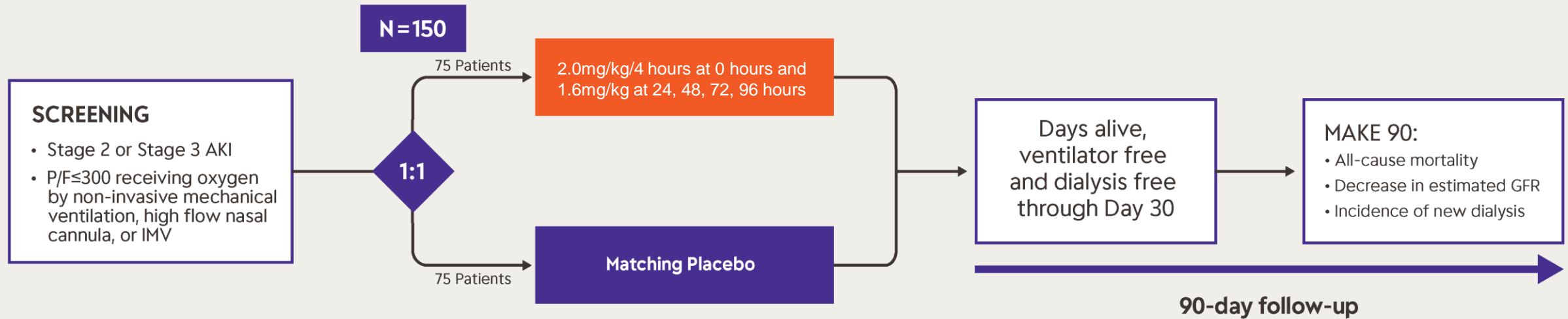
Ang-2/Tie2 results in endothelial inflammation with increased endothelial permeability



Clinical Observations

- Mortality benefit with Auxora vs Placebo observed in patients with compromised kidney function (low GFR) at time of enrollment
- ~40% reduction in reported AKI with Auxora vs Placebo

KOURAGE: Acute Kidney Injury with associated AHRF Phase 2 Trial Design



Auxora for Acute Respiratory Distress Syndrome (ARDS)

Promising Phase 2 Data from Trials in COVID-19 Pneumonia and in Ventilated Patients with Respiratory Failure

CARDEA Phase 2
Severe and Critical COVID-19
Pneumonia Patients
N=284

Trial Complete

- 56% reduction in mortality at Day 30 ($p=0.0165$)
- 33% reduction ventilation ($p=0.18$)
- Three-day shorter hospital stay ($p=0.09$)

Phase 2
COVID-19 Ventilated
Patients **N=9**

Trial Ongoing; Data Analysis Underway

- Reduction in inflammatory cell-type gene expression by macrophages in lungs
- No reduction in mitochondrial and ribosomal gene expression

Platform Application for CRAC Channel Inhibition

Preclinical Results Supporting Other I&I Indications

Indication	Intended Formulation	Preclinical Observations	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

Platform Application for CRAC Channel Inhibition

Anticipated Milestones

AP	CARPO Phase 2b Completed and Topline Data Announced Full Data Expected 2H2024; Phase 3 Initiation Expected in 2025
AKI	KOURAGE Trial Underway 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 2H25