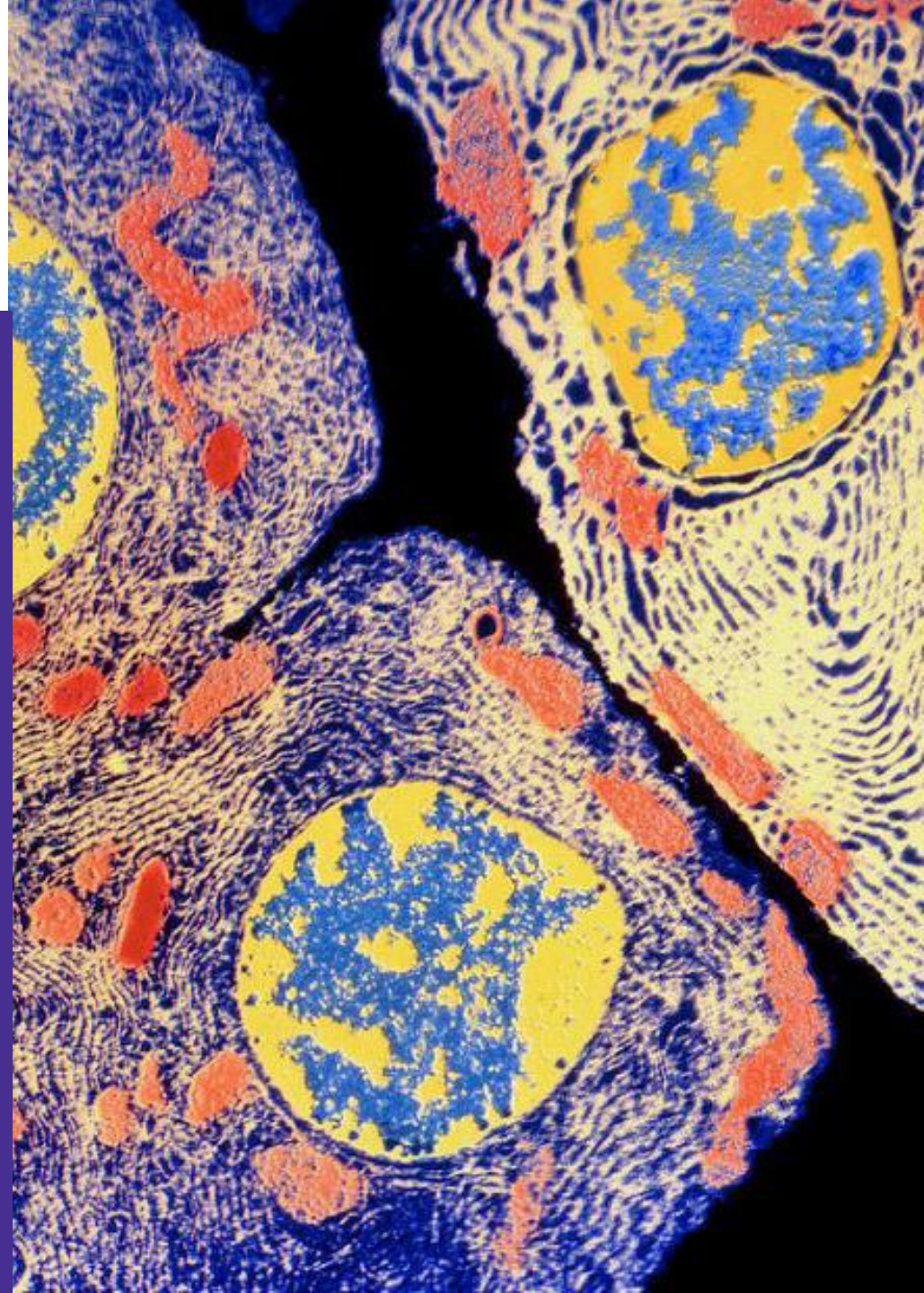
CalciMedica

Corporate Presentation

November 2026



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 Intellectual Property (IP) protections; the timing for CalciMedica's receipt and announcement of data from its clinical trials and other clinical and regulatory milestones, including expectations regarding the timing for regulatory approvals; the estimated patient populations and addressable market for CalciMedica's product candidates; and expectations regarding CalciMedica's financial position, capital requirements, and anticipated 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. These documents can be accessed on CalciMedica's web page at calcimedica.com.

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

CalciMedica: Leaders in CRAC channel inhibition

Inhibiting CRAC channels to control excessive calcium signaling and protect organ tissues

Two selective drug candidates	**Auxora (IV)** Acute hospital treatment	**CM5480 (oral)** Chronic treatment

Therapeutic Focus: Pulmonary hypertension

CRAC channel Inhibition offers a New Frontier in PH treatment:

Direct right-heart protection and improved cardiac function along with pulmonary pressure reduction

Catalysts
Mid-2027

- Auxora PH proof-of-concept Phase 1b data
- CM5480 IND submission

Cash runway
Into 2H 2027

Note: **CRAC** is Calcium Release-Activated Calcium. IND is Investigational New Drug. Enrollment in next trial in Acute Pancreatitis subject to funding

PH-focused pipeline with human proof-of-concept data expected in mid-2027

Program	Purpose	Preclinical	Phase 1	Phase 2	Phase 3	Anticipated milestones
Pulmonary hypertension						
Auxora – IV[1] PH Proof-of-concept	▪ **Immediate CRAC channel inhibition POC** ▪ **Expand into hospitalized PH patients**		→			**Ph1b data — mid-2027**
CM5480 – Oral PH patient group TBD	▪ **Oral candidate for chronic dosing**		→			**IND submission — mid-2027**
Acute critical disease						
Auxora – IV Acute pancreatitis	▪ Late-stage clinical opportunity			→		FDA-aligned —enrollment subject to funding

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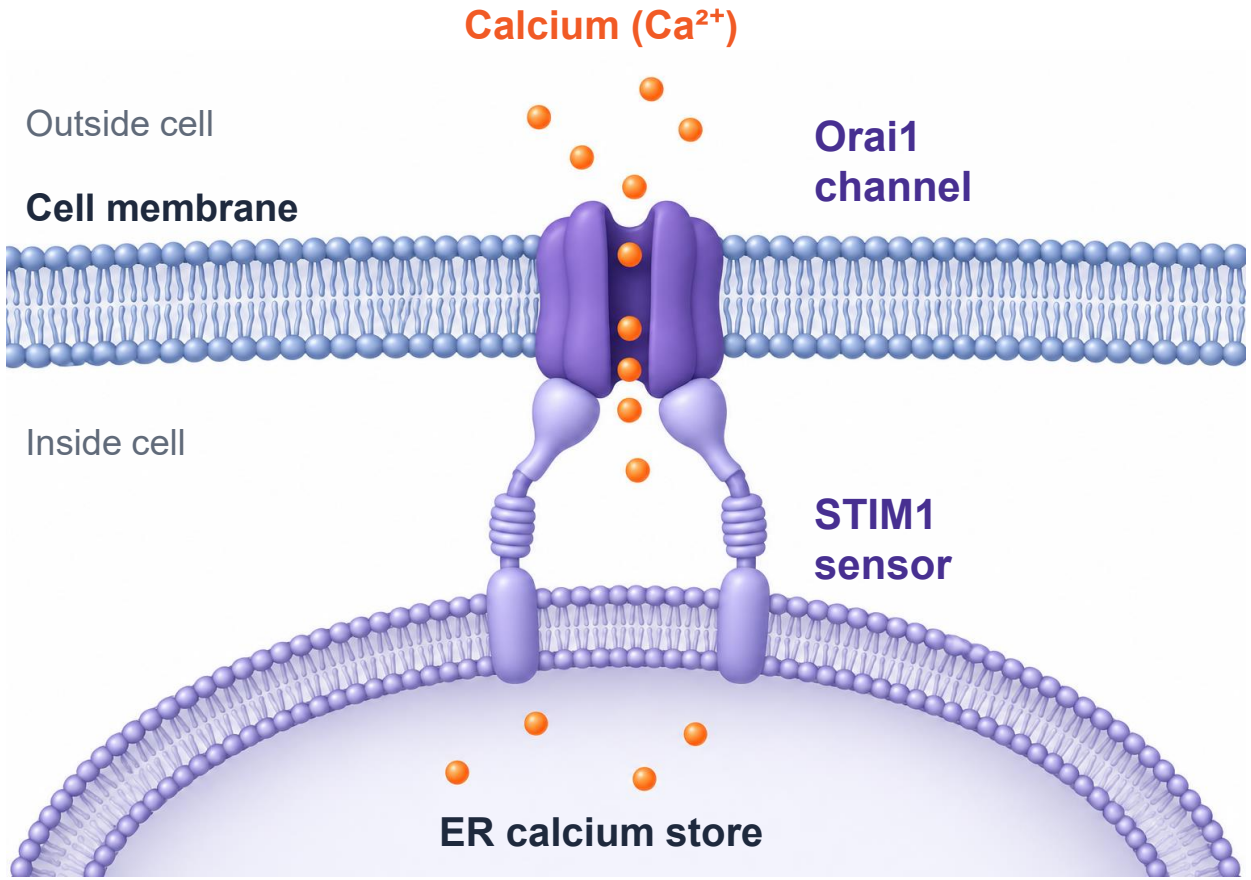
1: Auxora Ph1b trial not yet initiated; IND submission anticipated 2H 2026

CRAC channels: tightly regulated channels controlling the calcium stores in cells



IN HEALTHY TISSUES

Calcium enters when internal stores run low. Feedback signaling prevents unnecessary activation and excess calcium

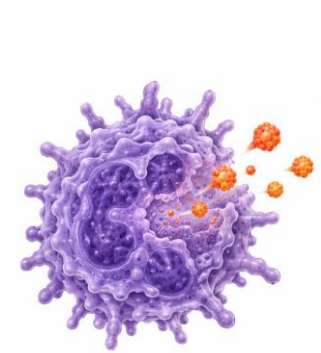
ER = endoplasmic reticulum; **STIM1** = stromal interaction molecule 1

Sources: Roos et al., J Cell Biol 2005; Prakriya et al., Nature 2006; Masson et al., Circ Res 2022; Saint-Martin Willer et al., JCI Insight 2025.

Excessive CRAC channel signaling linked to cardiopulmonary disease processes

Persistent inflammation | **Disrupted calcium homeostasis** | **Channel upregulation**

Sustained CRAC activation and Orai1-mediated calcium signaling



Persistent inflammation

+



Direct tissue injury

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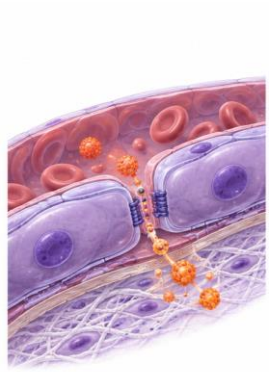

Vascular leakage and dysfunction

+



Vascular and cardiac remodeling

CRAC channel inhibition aims to limit excessive, pathological calcium signaling

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Sources: Wen L et al., Gastroenterology 2015; Mukherjee R et al., Gut 2016; Bartoli F et al., Circulation 2020; Masson B et al., Circ Res 2022; Nieto-Felipe J et al., J Biol Chem 2023; Kosuru R et al., Arterioscler Thromb Vasc Biol 2024.

Auxora has shown consistent reduction and prevention of respiratory failure, cardiac failure and mortality

	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
Years	2019	2020	2021	2024	2026 Terminated due to enrollment imbalance
# of Patients	21	30	284	216	108
Expected Mortality	<10%	15-25%	15-25%	<5%	~30-50%
Reduced Mortality		50% reduction	56% reduction (p<0.05)		Imbalance due to enrollment
Reduced Respiratory Failure	Less ventilator use	Less ventilator use	33% reduction	100% reduction (p<0.05)	Less ventilator use in survivors
Cardiac Benefit			Reduction in D-dimer and angiopoietin-2 (p<0.05)		Mortality benefit in cardiac arrest patients (n=10; nominal p<0.05)

Auxora has been well-tolerated in over 350 critically ill patients

Notes: For illustrative purposes only. Not a head-to-head comparison. Differences exist between clinical trial design and patient populations, and caution should be exercised when comparing data across trials; all data published with the exception of KOURAGE trial results

CRAC channel inhibition for pulmonary hypertension (PH)



PH is a large opportunity with unmet need across all patient groups

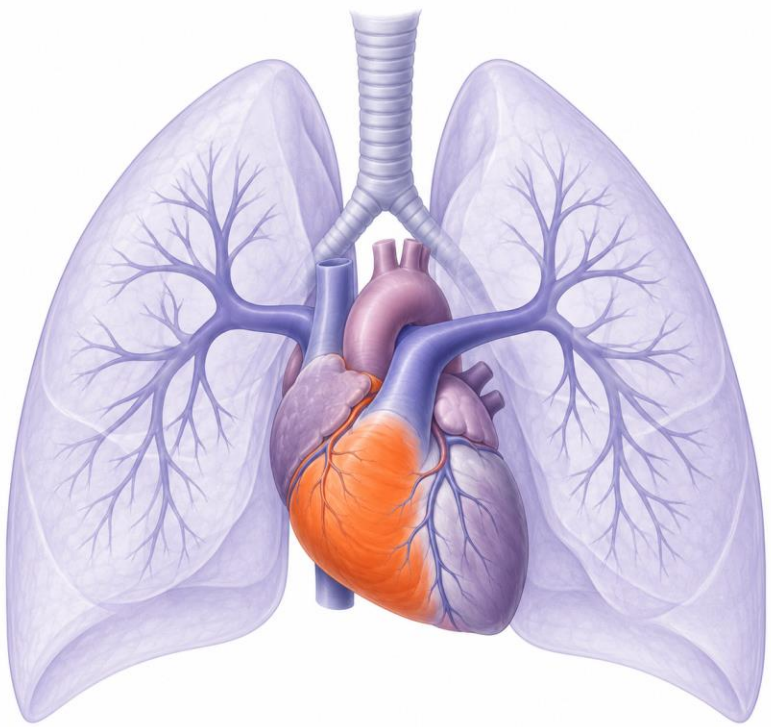
Group 1	Group 2	Group 3	Group 4	Group 5
Pulmonary Arterial Hypertension (PAH)	**Left Heart Disease**	**Lung Disease / Hypoxia**	**Chronic Thrombo-embolic PH**	**Unclear / Multifactorial Mechanisms**
~40K	**~500K**	**~80K**	**~10–17K**	
Est. US Patients $5.7B 2025 worldwide drug sales[1]	Est. U.S. patients[2] CpcPH-HFpEF	Est. U.S. patients[3] PH-ILD	Est. U.S. patients[4] CTEPH	Small numbers of patients across different diseases

CpcPH-HFpEF = combined pre- and post-capillary pulmonary hypertension associated with heart failure with preserved ejection fraction; **PH-ILD** = pulmonary hypertension associated with interstitial lung disease; **CTEPH** = chronic thromboembolic pulmonary hypertension 1. J&J and Merck, FY2025 annual reports. 2. Modeled estimate using ~3.5M U.S. HFpEF patients × 60% with PH × 25% with CpcPH. Johns Hopkins Medicine 2024; 2022 ESC/ERS PH guidelines. 3. DelveInsight, Epidemiology Forecast 2025. 4. Delcroix M et al., Eur Respir J 2021: 30–50 cases/million × 2025 U.S. Census population

PH is a large opportunity with unmet need across all patient groups

	Group 1 Pulmonary Arterial Hypertension (PAH)	Group 2 Left Heart Disease	Group 3 Lung Disease / Hypoxia	Group 4 Chronic Thrombo-embolic PH	Group 5 Unclear / Multifactorial Mechanisms
	Often genetic; narrowing of lung arteries leading to high pulmonary pressure and right ventricular (RV) failure	Often post acute event; left ventricular failure causing high pulmonary pressure and RV failure	Often idiopathic; multiple indications with lung fibrosis leading to high pulmonary pressure and RV failure	Often post traumatic or surgical event; emboli in the lung capillaries causing high pulmonary pressure and RV failure	PH patients not diagnosed with other group symptoms or etiologies
Pros	Patients remain under-treated; established clinical path	No specific approved therapy	Limited approved treatment options	Only one approved drug treatment	
Cons	Crowded market and polypharmacy	Complex patients and crowded development	Crowded development and fragmented market	Small indication with surgical treatment options	

Across *all* PH groups, elevated pulmonary pressure threatens right ventricular function



Elevated pulmonary vascular pressure → **Right ventricular (RV) failure**

Focus of existing therapies

Not directly targeted by existing therapies

Existing need: High pressure persists despite advances

Unmet need: RV failure remains the driver of poor outcomes

New Treatment Frontier: Direct RV Protection for Improved Outcomes

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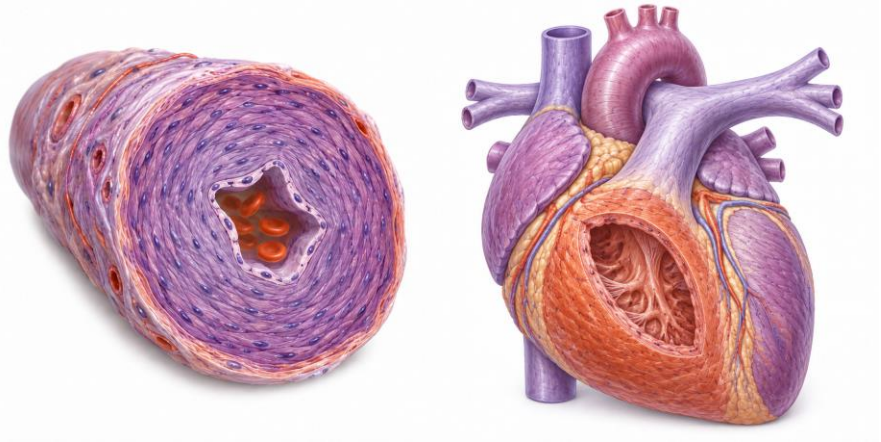
ULN = Upper limit of normal; **RV** = right ventricle; **PAP** = pulmonary arterial pressure; Note: Current therapies indirectly improve RV function through afterload reduction

1. Souza et al. Eur Respir J. 2023;62:2301107.

CRAC channel inhibition directly targets *both* elevated pulmonary pressure and reduced right ventricular function

Pulmonary vasculature

Right ventricle (RV)



Vasoconstriction and remodeling

RV dysfunction and remodeling

	Reduce pulmonary vascular pressure		Improve RV Function
Therapeutic approach	**Vasodilation**	**Vascular remodeling**	**RV protection**
Vasodilators	+++		+ Indirect
Activin pathway / TKIs (Winrevair)	++	+++	+ Indirect
CRAC channel Inhibition	++	+++	+++ **Direct**

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TKI = tyrosine kinase inhibitor (investigational in PAH). Table shows primary therapeutic axes. Vascular unloading can also improve RV function. CRAC channel inhibition findings are preclinical. No head-to-head clinical trials. 1. Saint-Martin Willer et al., JCI (Journal of Clinical Investigation) Insight 2025

CRAC channel inhibition improves lung and heart outcomes across complementary preclinical models

	Pulmonary vasculature		Heart	
Model and compound	**Pulmonary pressure ↓**	**Vascular remodeling ↓**	**Ventricular function ↑**	**Ventricular remodeling ↓**
MCT rat[1] CM5480	✓	✓	✓	✓
Sugen/hypoxia rat[2] Tool compound	✓	✓	✓	✓
Chronic hypoxia rat[2] Tool compound	✓	✓	✓*	✓
Pulmonary artery banding rat[3] CM5480	**Cardiac model** Pulmonary endpoints not assessed		✓	✓
Transverse aortic constriction mouse[4] Tool compound	**Cardiac model** Pulmonary endpoints not assessed		✓	✓

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MCT = monocrotaline

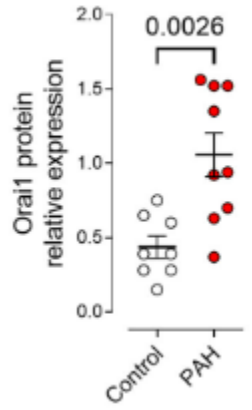
1. Saint-Martin Willer et al., JCI Insight 2025. 2. Masson et al., Circ Res 2022. 3. INSERM, shared with permission. 4. Bartoli et al., Circulation 2020.

* Chronic hypoxia did not significantly reduce cardiac output versus normoxic controls. Treatment reduced RV systolic pressure, hypertrophy, and fibrosis.

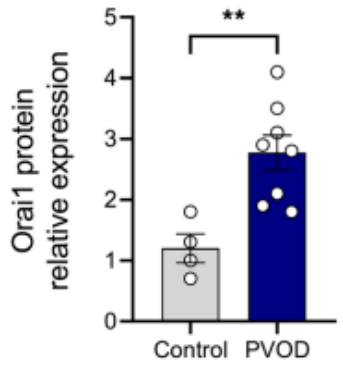
CRAC channel expression increased in patients with pulmonary vascular and cardiac disease

Pulmonary Vasculature

Pulmonary Arteries (PAH)

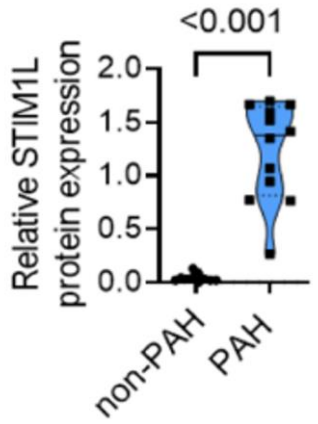


Pulmonary Veins (PVOD)

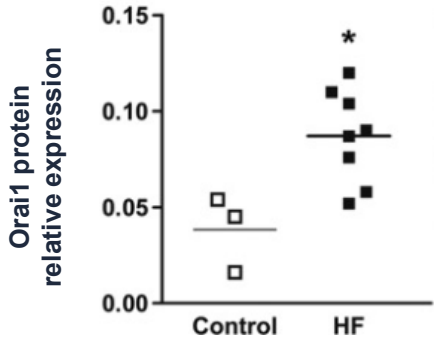


Heart

Right Ventricle (PAH)



Left Ventricle (Heart Failure)



CRAC channel overactivation linked to lung and heart remodeling and hypertrophy

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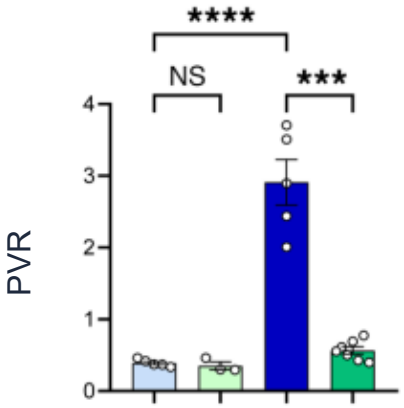
PAH: pulmonary arterial hypertension**; PVOD**: pulmonary veno-occlusive disease**; HF**: heart failure; **STIM1L** = long isoform of stromal interaction molecule 1

Sources: Masson B et al., Circ Res 2022; Saint-Martin Willer A et al., JCI Insight 2025; Antigny F et al., Circ Heart Fail 2025; Ross GR et al., Biol Open 2017.

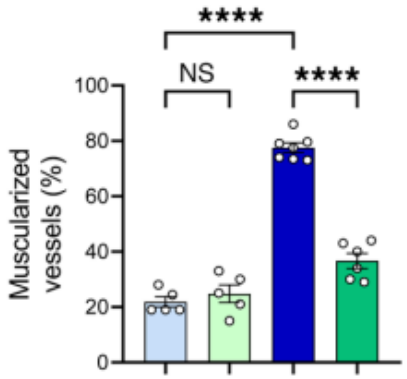
CM5480 improved function and reduced remodeling in the lungs and heart in the MCT rat PAH model

Pulmonary Vasculature

Reduced PVR[1]

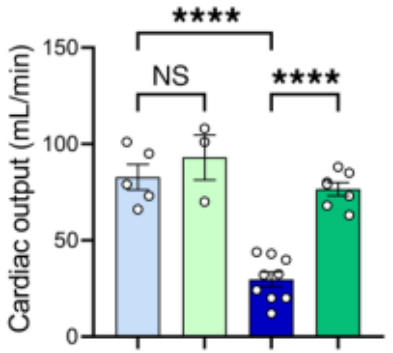


Reduced Pulmonary Vascular Remodeling

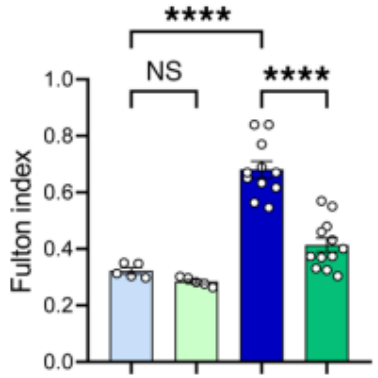


Heart

Improved Cardiac Output



Reduced Right Ventricular (RV) Remodeling[2]



Control + vehicle Control + CM5480 MCT + vehicle MCT + CM5480

CM5480 also showed additive benefit in combination with vasodilators (sildenafil or ambrisentan)

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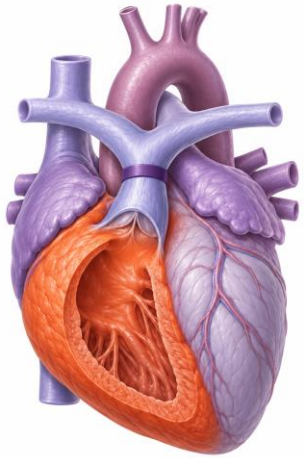
MCT = monocrotaline; **RVSP** = right ventricular systolic pressure; **CO** = cardiac output; **LV** = left ventricle; **NS** = not statistically significant

1. PVR (Pulmonary Vascular Resistance) = RVSP / CO, a surrogate of true PVR 2. Fulton index and RV/tibia length measure RV hypertrophy; Fulton index = weight ratio of RV to the sum of the LV + septum. Publication: Saint-Martin Willer et al., JCI Insight 2025

Direct right ventricle (RV) protection differentiates CM5480 from other therapies (unpublished data)

Pulmonary artery banding model (rat)



Isolates direct cardiac effects from indirect pulmonary effects

Metric	PAB untreated	CM5480[1]	Sotatercept[2]	Imatinib[3]	Tadalafil[4] (vasodilator)
RV systolic function	↓	↑	↔ / ↓	↓	↔
RV diastolic function	↓	↑	↔	↓	↔
RV hypertrophy	↑	↓	↓	↑	↔
RV fibrosis	↑	↓	↓	↑	↔

Data support direct RV-protective activity of CM5480 but not other drugs or drug candidates

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PAB = pulmonary artery banding; **RV** = right ventricle

1. CM5480 data from INSERM (Antigny & Sabourin), shared with permission 2. Lemay SE, "Sotatercept impairs right ventricular function: insights from multi-center preclinical studies," PVRI 2026 Congress, Jan 2026 3. Zeng, Br J Pharmacol 2025;182:2560–2581 4. Balsa, Int J Mol Sci 2023;24:15539

Note: Untreated PAB vs sham; treatments vs PAB vehicle. Results from separate studies

TAC model of left heart stress supports CRAC channel inhibition for Group 2 (heart failure) PH

Transverse Aortic Constriction Model (TAC) Results[1]

Mice: 5 weeks of left ventricle (LV) pressure overload, then 3 weeks of a tool Orai1 inhibitor or vehicle

EJECTION FRACTION

56.9% → 71.2%

+14.3 points

p = 0.001

END-SYSTOLIC VOLUME

0.089 mL → 0.044 mL

−51%

p = 0.003

LV–ARTERIAL COUPLING

1.36 → 2.86

2.1× higher

SV / ESV

FIBROTIC GENE EXPRESSION

Col1a1 · Col3a1

Prevented

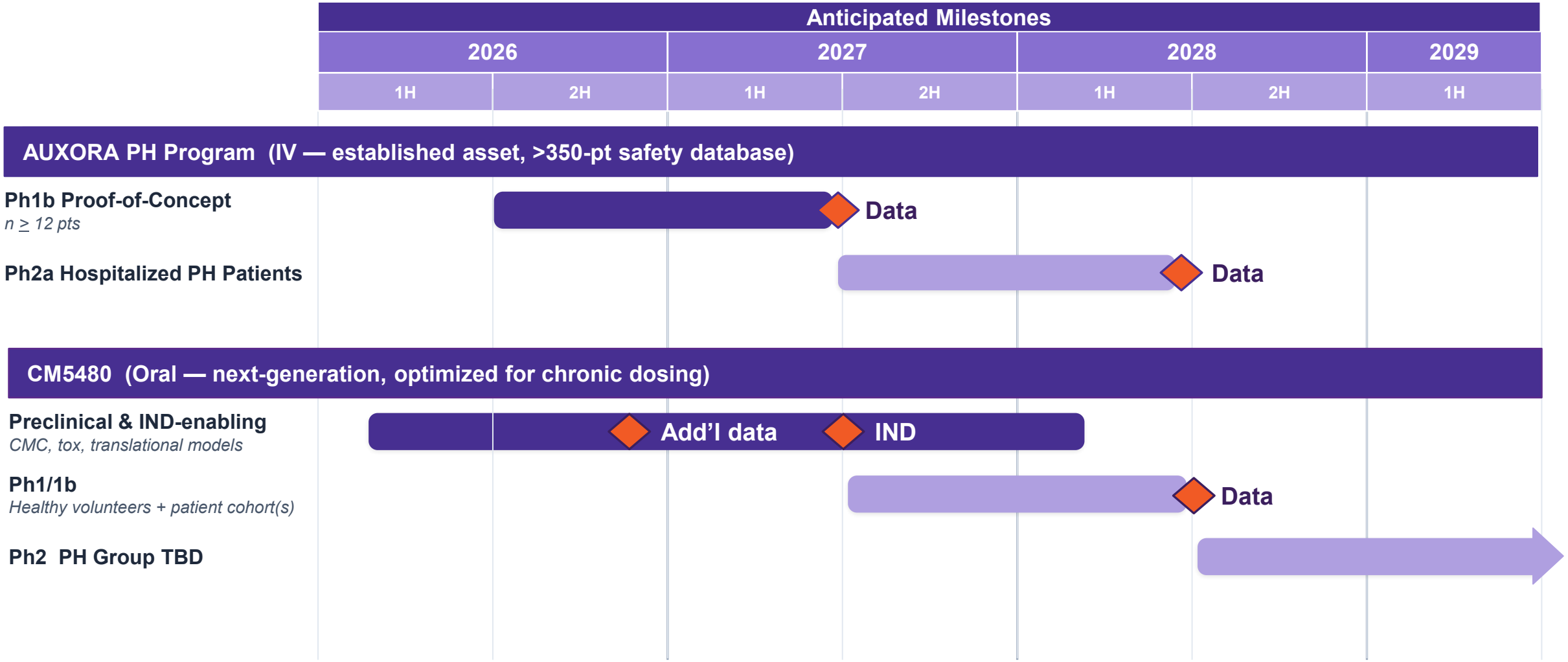
p < 0.05 vs. vehicle

LV = left ventricle; **SV / ESV** = stroke volume / end-systolic volume

Note: Study used JPIII, a small-molecule Orai1 inhibitor used as tool compound for target validation; LV–arterial coupling shown here is calculated as SV/ESV; the authors do not report a coupling ratio.

Sources: 1. Bartoli F et al., Circulation 2020. 2. Saint-Martin Willer et al., JCI Insight 2025. 3. Fayyaz AU et al., Circulation 2018. 4. Ross GR et al., Biol Open 2017.

PH Development Plan: Auxora PH data and CM5480 IND submission are mid-2027 milestones



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Note: Lighter shading indicates activities not reflected in the current cash runway.

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Auxora for acute pancreatitis



Acute pancreatitis: substantial unmet need and a potential $2 billion U.S. market

High unmet need

~255K U.S. AP admissions annually[1]

0 approved therapies in U.S. — care is supportive only

~$3.0B annual U.S. hospital costs[1]
>1.1M hospital days

Potential market opportunity

~$1.6–2.0B

Potential annual U.S. market

~79,000 episodes × $20,000–25,000/course

255K admissions × 62% with SIRS
× 50% with LDH >240 U/L (enrichment approach)

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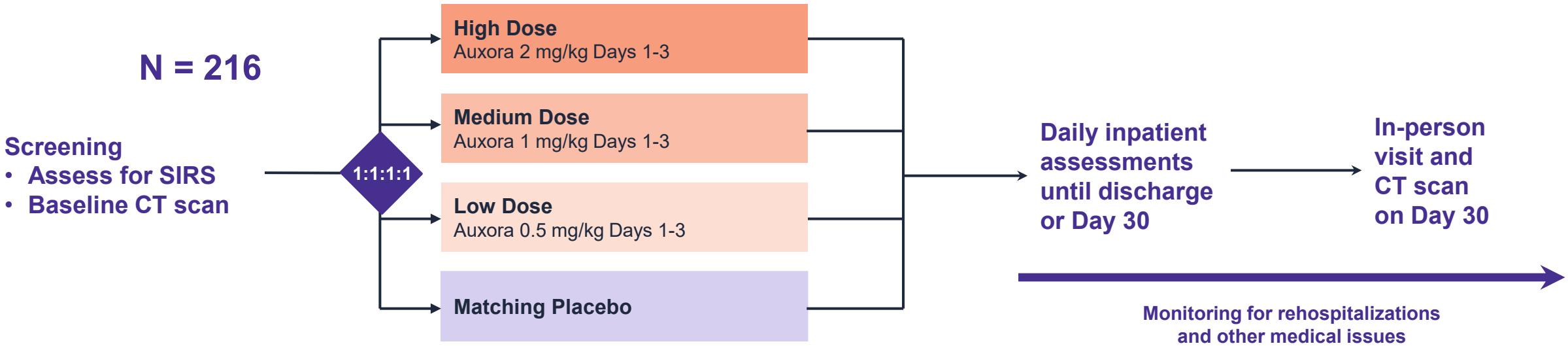
AP = acute pancreatitis; **SIRS** = systemic inflammatory response syndrome
Illustrative market size assumes one course per modeled episode at full penetration. Pricing and eligibility are assumptions.
1. Peery AF et al., Gastroenterology 2025; 2021 National Inpatient Sample; CARPO: clinical results in following slides.

CARPO: completed Phase 2b trial in AP with SIRS

Dose-ranging study to establish efficacious dose, safety, target patient population and regulatory endpoints



Endpoints

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

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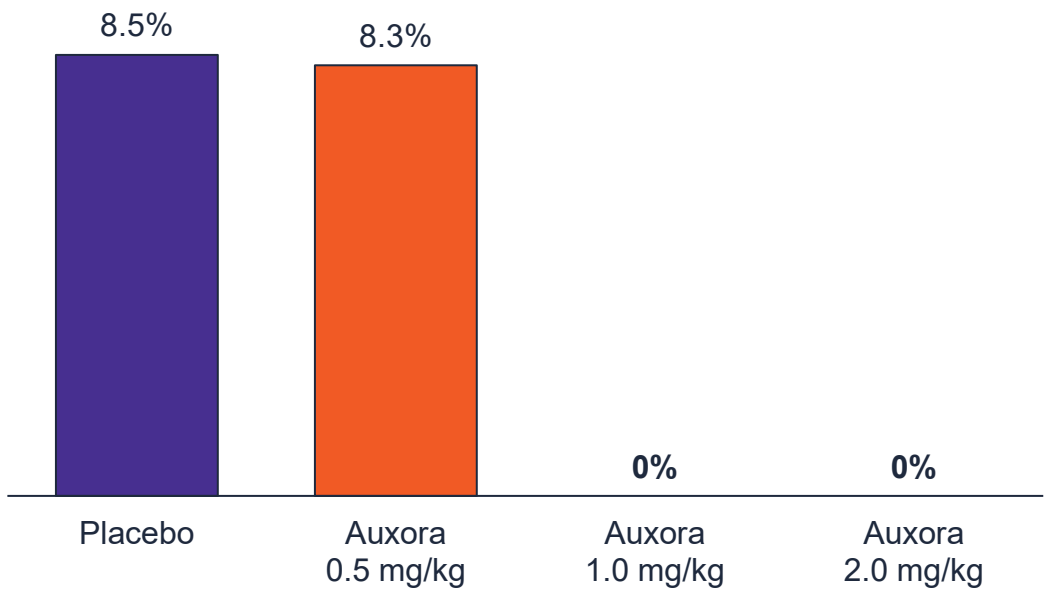
AP = acute pancreatitis; **CT** = computed tomography; **SIRS:** Systemic Inflammatory Response Syndrome

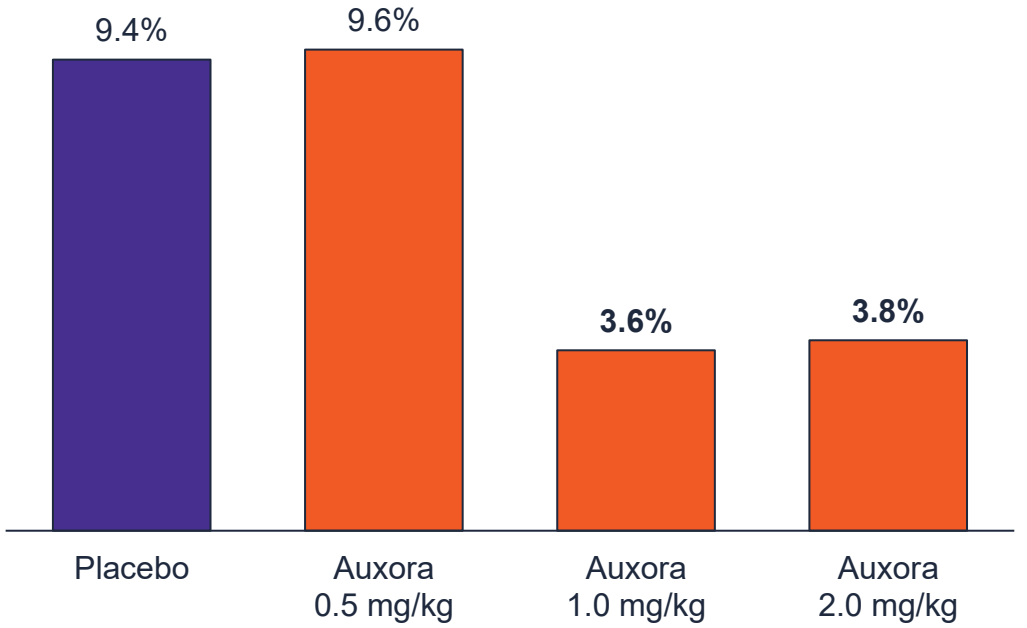
Auxora prevented new severe respiratory failure

100% reduction in new severe respiratory failure[1]



Each p<0.05 vs. placebo

60% reduction in severe organ failure[2]



Stratified Win Ratio Composite including mortality, respiratory failure, pancreatic necrosis and recovery:

1.64 (95% CI 1.03-2.61, p=0.037)[3]

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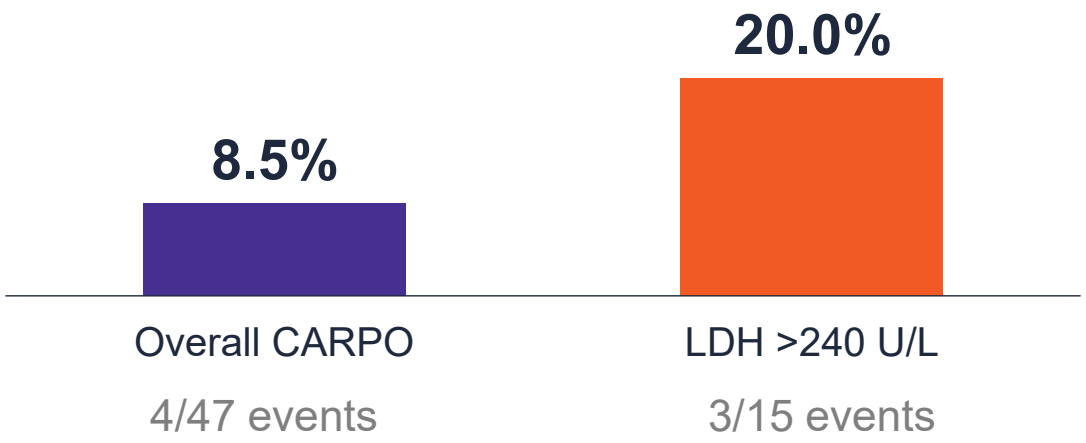
1. mITT (modified intention-to-treat) excluding baseline respiratory failure (n=197) 2. mITT (N=214); severe organ failure includes severe respiratory failure, severe renal failure, and severe cardiovascular failure 3. Exploratory stratified win ratio: Auxora 2.0 mg/kg vs placebo

CARPO suggests a ~20% placebo event rate with LDH enrichment

CARPO analysis

New-onset severe respiratory failure on placebo



6 of 8 **new severe respiratory-failure cases across all arms had LDH >240 U/L[1]**

Independent publication

LDH (lactate dehydrogenase) was the study's strongest individual predictor of ARDS[2]

111 ICU patients with hypertriglyceridemic acute pancreatitis

Closely aligned LDH cutoffs

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>240 U/L	**249.5 U/L**

Published after CalciMedica selected its cutoff

A routine marker to enrich for patients at greater risk of severe outcomes

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CARPO: retrospective analysis excluding baseline respiratory failure.
1. Remaining cases: one had LDH 238 U/L; one had no LDH result. **LDH** = lactate dehydrogenase; **ARDS** = acute respiratory distress syndrome
2. Zhu K et al., Emerg Med Int. 2026;2026:8368299, Tables 4–5

FDA-aligned on the planned Phase 2b design expected to inform a potential future registrational study in AP

FDA-aligned design

Following a Type C Meeting

First potential registrational endpoints in AP

Establishes the first clinical-trial endpoint framework in AP

Primary Endpoint:
New-onset Severe Respiratory Failure

Key Secondary Endpoints:
Multi-organ Failure
Time to Medically Indicated Discharge

LDH enrichment marker

Evaluating elevated LDH to identify patients at higher risk of severe respiratory failure

CARPO analysis suggests

~20% New-onset severe respiratory failure in placebo patients with elevated LDH

Preparations for the trial are underway; initiation is subject to additional funding

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LDH = lactate dehydrogenase; **AP** = acute pancreatitis

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Catalysts



Investment highlights and milestones

CRAC channel inhibition: new frontier in pulmonary hypertension

Advancing two drug candidates, Auxora and CM5480, with recent financing

- Pulmonary vascular and direct cardiac protection observed in robust preclinical package
- Pulmonary and lung benefits observed in clinical trials with Auxora

Auxora PH data	CM5480 IND Submission	Cash runway
Mid-2027	Mid-2027	Into 2H 2027

PH = pulmonary hypertension; **PAH** = pulmonary arterial hypertension