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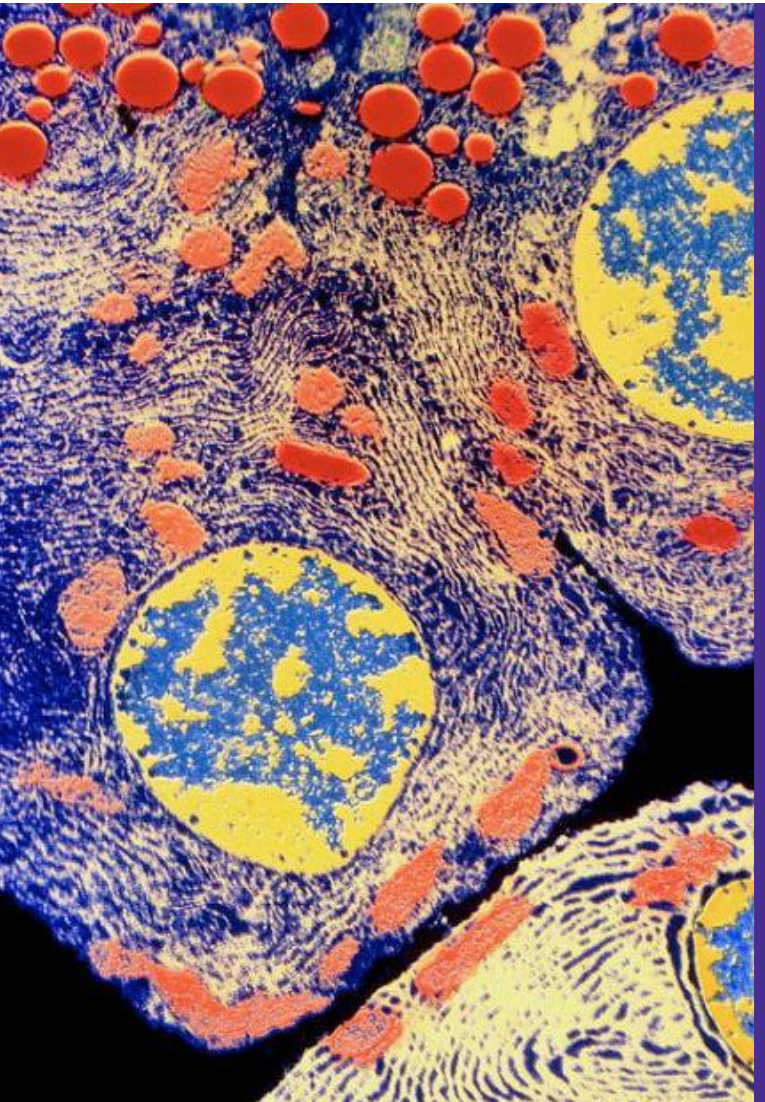

Investor Update

June 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 of the date of this presentation. CalciMedica disclaims any obligation to update these forward-looking statements, except as may be required by law.

Pioneering CRAC channel inhibition in Pulmonary Hypertension

PLATFORM

Leader in CRAC channel inhibition

- Proven Orai1 / CRAC inhibitor clinical experience
- Proprietary chemistry and internal pipeline
- Two current drug candidates: CM5480 (oral) and Auxora (IV)
- IP out to 2041+ (Auxora) and 2046+ (CM5480)

DISEASE BIOLOGY

Central to PH pathology

- Orai1 upregulated in diseased pulmonary vasculature, RV, and LV[1]
- Linked to proliferation, inflammation, vasoconstriction and hypertrophy
- Relevant to RV failure—key outcomes driver[2]

DIFFERENTIATION

Anti-remodeling in both lung & heart

- CRAC inhibition activity in both lung and heart tissue
- Potential direct RV support and anti-remodeling
- Broad PH potential across disease groups

DEVELOPMENT STRATEGY

Fast human POC data, followed by optimized oral development

- Auxora IV Ph1b POC in PAH expected mid-2027
- CM5480 oral IND targeted mid-2027; data expected mid-2028
- Auxora POC trial designed to de-risk CM5480 in PH and potentially advance Auxora for hospitalized PH

Key Anticipated Catalysts: Auxora Ph1b data in PAH (mid-2027) | CM5480 IND clearance (mid-2027)

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1. Saint-Martin Willer et al., JCI Insight 2025; Masson et al., Circ Res 2022; Bartoli et al., Circulation 2020; Antigny et al., Circulation HF 2025
2. Vonk Noordegraaf A, et al. Cardiovascular Research 2015

RV = Right Ventricle; **LV** = Left Ventricle; **PH** = Pulmonary Hypertension; **POC** = Proof of Concept

Two well-characterized drug candidates, built on deep CRAC channel expertise

Auxora

CLINICAL · IV

Zegocractin · 4-hour infusion, 3–5 days

CLINICAL EVIDENCE

- Multiple Phase 2 trials: acute pancreatitis, COVID-19 pneumonia, and acute kidney injury
- Statistically significant reduction in severe respiratory failure observed across studies

BIOMARKER VALIDATION

- Normalized inflammatory cytokines (IL-6, TNF-α, IL-17)
- Improved markers of endothelial damage and microcoagulation (D-dimers, Ang-1, Ang-2)

CM5480

PRECLINICAL · ORAL

Selective, potent oral CRAC inhibitor

PRECLINICAL EVIDENCE

- Active across PAH, rheumatoid arthritis, ulcerative colitis, asthma, and chronic pancreatitis

PHARMACOLOGY

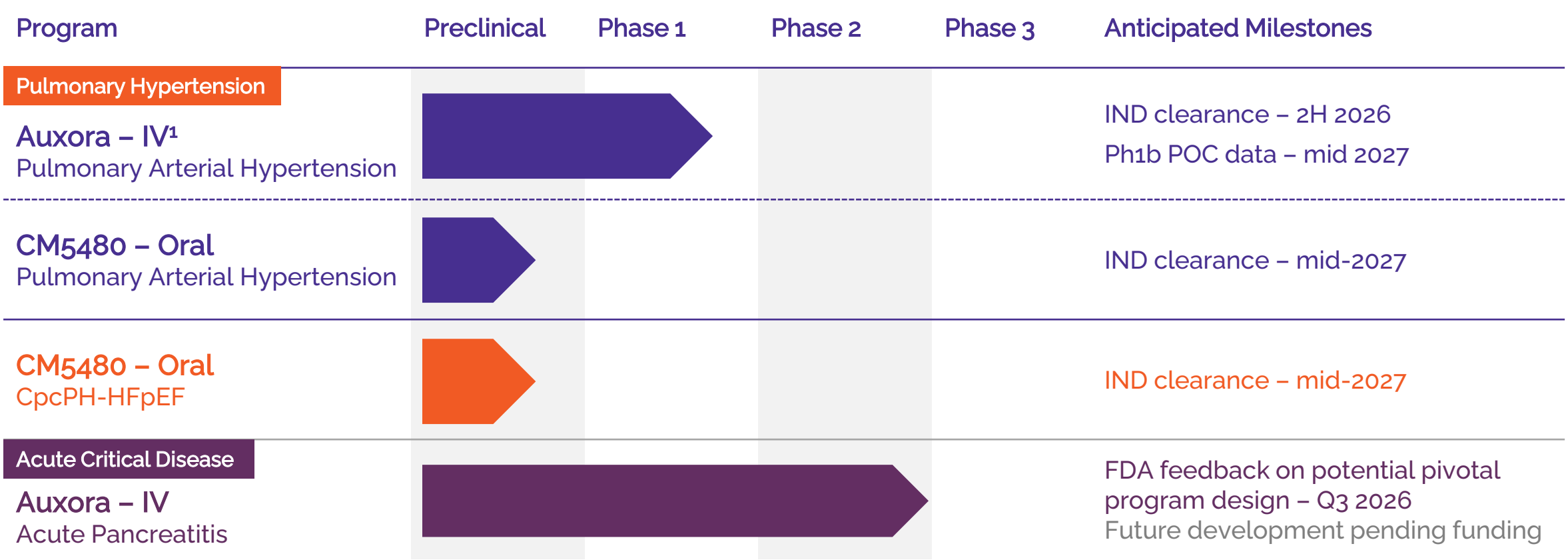
- Anti-inflammatory, tissue-protective, and anti-proliferative activity
- PK, dosing, and toxicology conducted in three species (unpublished)

DEVELOPMENT STATUS

- IND-enabling and formulation studies ongoing

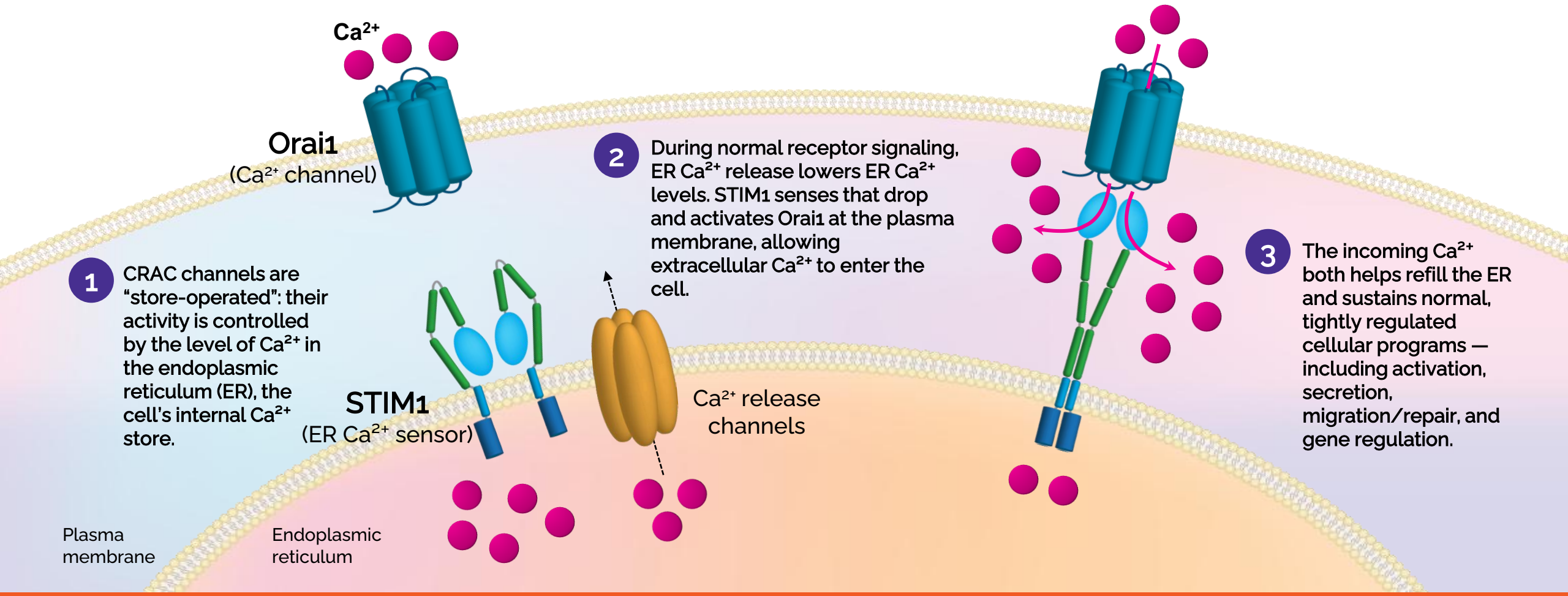
Link between the two assets: Potential for Auxora to de-risk CM5480 in Pulmonary Hypertension

PH-focused pipeline designed to generate human POC data by mid-2027 with next-gen compound to follow



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

CRAC channels: A store-operated calcium signaling system



In healthy cells, CRAC signaling is tightly regulated, localized, and self-limited

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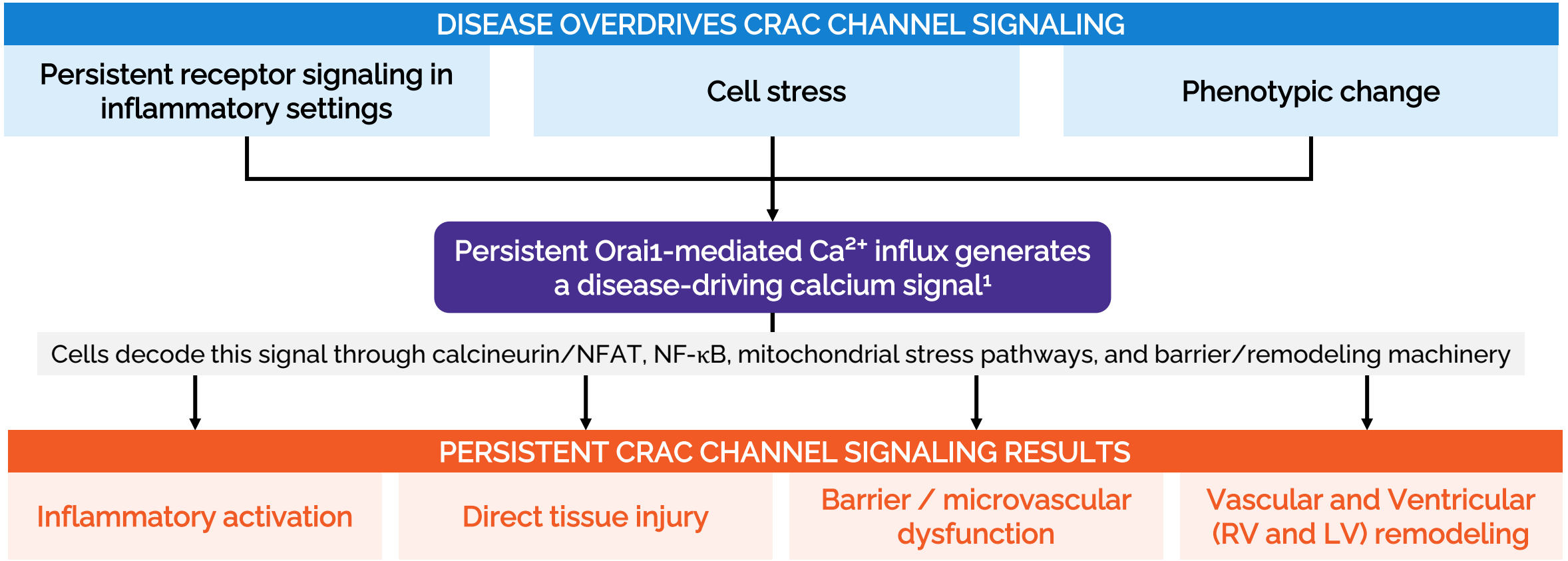
Adapted from Roos,…Stauderman, J. Cell Bio. 2005; Zhang…Stauderman, Cahalan, Nature, 2005; Zhang…Stauderman, Cahalan, PNAS, 2006.

Disease can overdrive CRAC channel signaling, creating a persistent, pathologic calcium signal



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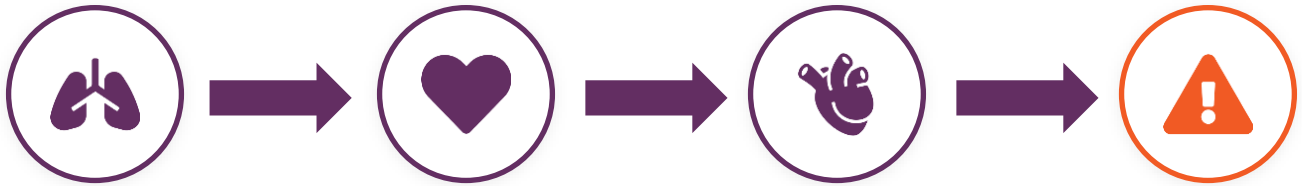
1. Masson et al., Circulation Research 2022 (among others)
RV = Right Ventricle; **LV** = Left Ventricle

Pulmonary Hypertension spans diverse etiologies, but RV failure drives prognosis across groups

Initial Development Pathways

Group 1	Group 2	Group 3	Group 4	Group 5
Pulmonary Arterial Hypertension (PAH)	**PH due to Left Heart Disease**	**PH due to Lung Disease / Hypoxia**	**PH due to Pulmonary Artery Obstruction**	**PH with Unclear / Multifactorial Mechanisms**
Idiopathic • Heritable • CTD-associated • Drug-induced	HFpEF, including CpcPH-HFpEF • HFrEF • Valvular disease	COPD • ILD • Sleep-disordered breathing	CTEPH • Chronic thromboembolic disease	Sarcoidosis • Hematologic / metabolic disorders

Shared consequence across PH pathologies: progressive right ventricular failure



Why it matters: RV function is a major determinant of symptoms, functional decline & survival across PH groups

Therapeutic gap: Current therapies primarily target the pulmonary circulation — not the failing RV directly

CalciMedica opportunity: CRAC channel inhibition is active in both pulmonary vascular and RV tissue, creating the potential for a differentiated lung–heart profile

CRAC channel inhibition as a potential therapy for PAH


JCI insight

RESEARCH ARTICLE

Combination of Orai1 inhibitor CM5480 with specific therapy mitigates pulmonary hypertension and its cardiac dysfunction

Anaïs Saint-Martin Willer,[1] Grégoire Ruffenach,[1] Bastien Masson,[1] Kristelle El Jekmek,[1] Angèle Boët,[1] Rui Adão,[2,3,4,5] Mathieu Gourmelon,[1] Antoine Beauvais,[1] Jessica Sabourin,[6] Mary Dutheil,[1] Maria-Rosa Ghigna,[1] Laurent Tesson,[7] Séverine Ménoret,[7,8] Ignacio Anegon,[7] Fabrice Bauer,[1,9] Vincent de Montpréville,[10] Sudarshan Hebbar,[11] Carmen Brás-Silva,[2] Kenneth Stauderman,[11] Marc Humbert,[1] Olaf Mercier,[1] David Montani,[1] Véronique Capuano,[1] and Fabrice Antigny[1]

"Despite recent improvements in the treatment of PAH, it remains a severe disease for which there is no cure, and patients often progress to RVF. We continue to search for new potential drugs with novel mechanisms that can enhance current treatment strategies. Our translational work has suggested that CRAC channel inhibition could offer such a mechanism"

Dr. Marc Humbert, Université Paris-Saclay, INSERM

"These preclinical results show that targeting Orai1 delivered several key benefits: it improved pulmonary vascular remodeling by reducing pulmonary arterial smooth muscle cell and pulmonary endothelial cell dysfunctions; it improved RVD; and combination therapy with CM5480 provided significantly greater benefits…compared to monotherapies."

Dr. Fabrice Antigny, Université Paris-Saclay, INSERM

Over a decade of research by a world-class team at INSERM supports CRAC channel inhibition in pulmonary hypertension (select publications highlighted in next slide)

CRAC channel inhibition shows activity across pulmonary vasculature, RV, and LV in preclinical PH models

Model	Observations		Why it matters
MCT rat (CM5480)[1]	• PVR ↓ • Cardiac output restored • RV hypertrophy ↓	• RV fibrosis ↓ • RNA-seq: broad reversal of disease-associated genes in lung and RV	• Widely used and standard PAH model • **CM 5480 observed to improve lung and cardiac function and showed anti-remodeling activity in both lung and RV** • Additive benefit when combined with sildenafil or ambrisentan
Sugen/Hypoxia rat (tool compounds)[2]	• PVR ↓ • Cardiac output restored • RVSP ↓	• Pulmonary vascular remodeling ↓ • RV hypertrophy ↓ • RV fibrosis ↓	• Su/Hx is considered the most clinically translatable PAH model • **Reproducibility across a second preclinical PAH model supports the robustness of the observed effect** • In prior preclinical studies, CM5480 demonstrated activity consistent with the tool compounds evaluated in these models
Pulmonary artery banding rat (CM5480)[3]	• RV systolic function ↑ (TAPSE, FAC) • RV diastolic function ↑	• RV hypertrophy ↓ • RV fibrosis ↓	• PAB isolated the RV effect from any pulmonary vascular effect • **Evidence of direct RV benefit extends the potential opportunity from Group 1 to any PH-driven RV failure** • Potential differentiation vs. TGF-β/activin MOA
Transverse aortic constriction mouse (tool compound)[4]	• LV systolic function preserved (EF, FS) • End-systolic volume ↓	• Fibrosis ↓ • Improved LV-arterial coupling • Normalized Ca^{2+} handling	• Established that the cardiac protective effect generalizes from RV to LV under pressure overload • **Provided mechanistic rationale for Group 2 PH (PH-LHD)**

In addition, gene expression data from patient tissues, model animal tissues, and knock-out models offer further evidence of CRAC channel involvement in PH disease processes

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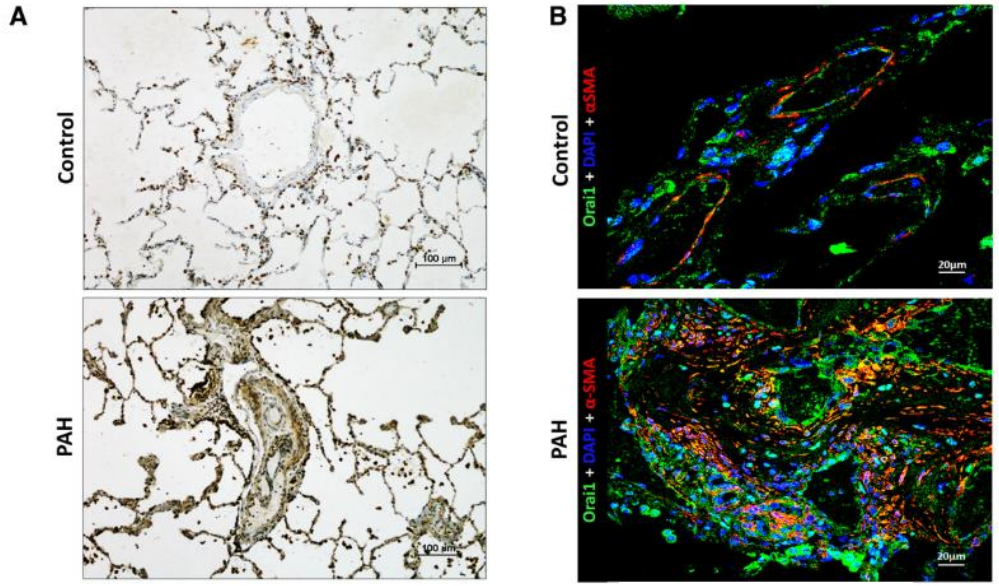
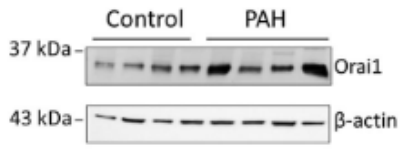
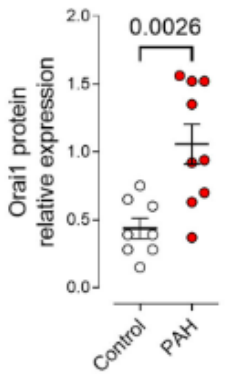
1. Saint-Martin Willer et al., JCI Insight 2025 2. Masson et al., Circ Res 2022 3. Research results from INSERM lab conducted by Antigny and Sabourin; shared with permission. Unpublished data 4. Bartoli et al., Circulation 2020;
PVR = Pulmonary Vascular Resistance; **RVSP** = RV Systolic Pressure; **TAPSE** = Tricuspid Annular Plane Systolic Excursion; **FAC** = Fractional Area Change; **EF** = Ejection Fraction; **FS** = Fractional Shortening; **MOA** = Mechanism of Action; **RVF** = Right Ventricular Failure

CRAC channels (Orai1/STIM1) are upregulated in lung vasculature in patients with PAH & PVOD

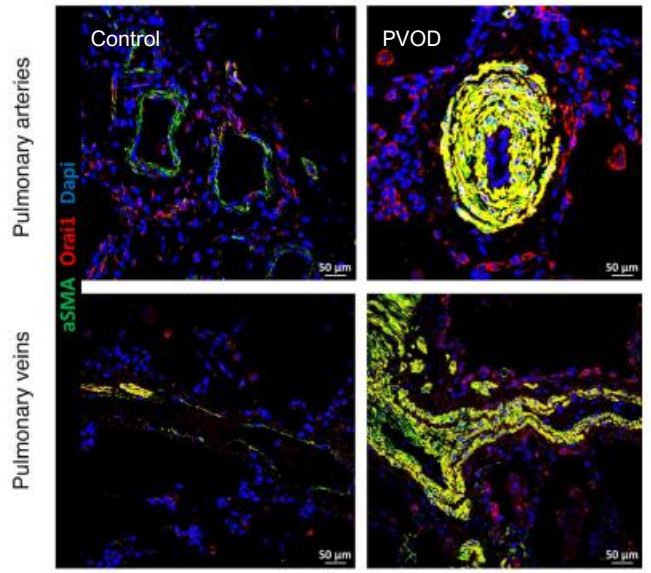
Lung Tissues from PAH Patients

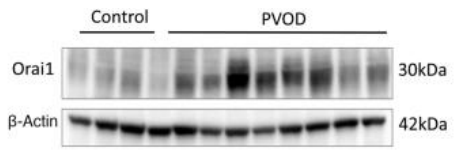


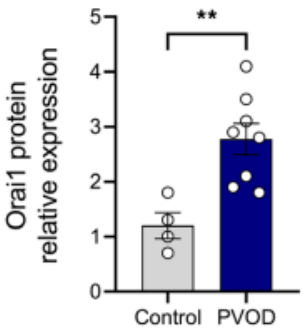




Lung Tissues from PVOD Patients







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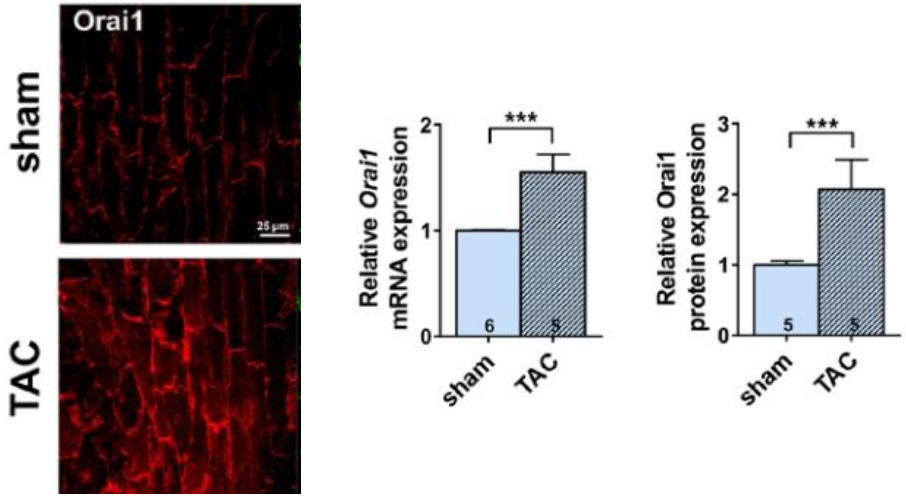
PVOD = Pulmonary Veno-Occlusive Disease; Masson et al., *Circulation Research* 2022 and Saint-Martin Willer et al., *JCI Insight* 2025

Additionally, CRAC channels (Orai1/STIM1) are upregulated in both sides of the heart when under pressure overload

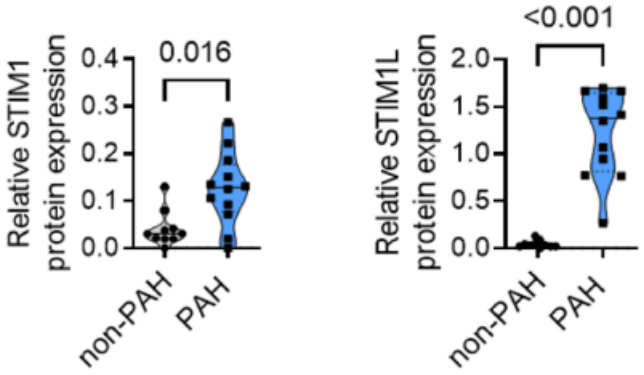
Left-Ventricle

Transverse aortic constriction (TAC) mouse model forces the LV to pump against high pressure

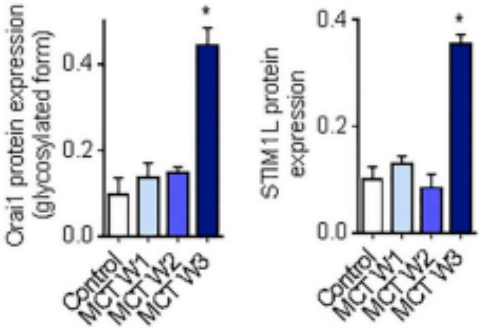


Right-Ventricle

Human RV tissue from PAH patients obtained at heart-lung transplant, representing end-stage RV pressure overload in the clinical disease



Monocrotaline (MCT) rat model causes pulmonary vascular disease, forcing RV to pump against high pressure (PAH model)



Note: Glycosylated form of Orai1 refers to functional (membrane-localized) Orai1;
STIM1L is a long splice isoform of STIM1 that enables faster, repetitive SOCE activation.
Sources: Bartoli et al, Circulation 2020 (TAC mouse, Fig 1B–C) · Antigny et al, Circ Heart Fail 2025 (human PAH RV, Fig 8C) · Sabourin et al, J Mol Cell Cardiol 2018 (monocrotaline rat, Fig 7A)

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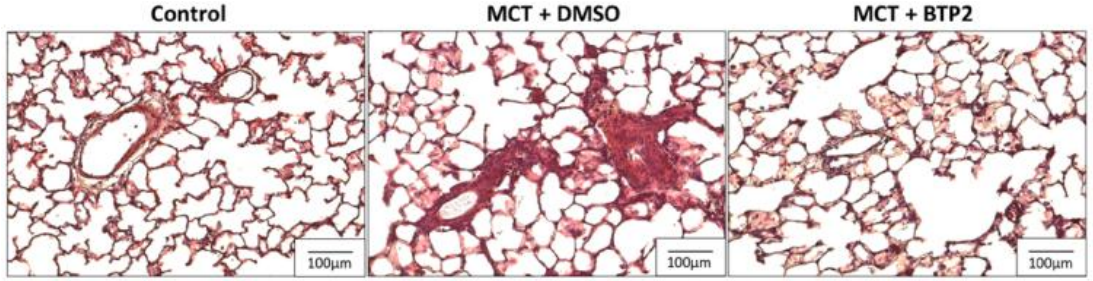
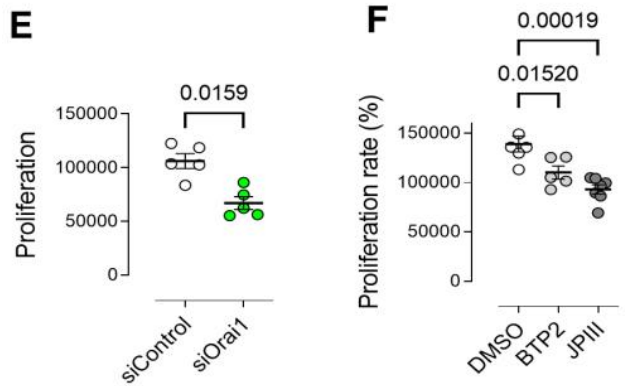
Prior studies linked Orai1 to remodeling/hypertrophy in both the pulmonary arteries and the heart

PASMCs: Orai1 inhibition reverses proliferative, migratory, apoptosis-resistant phenotype

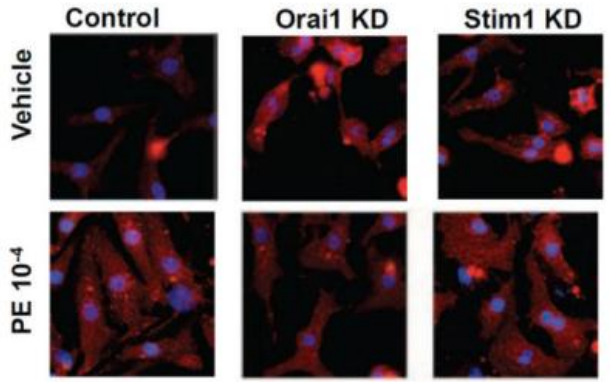
In vivo MCT rats (top); human PAH-PASMCs (bottom)

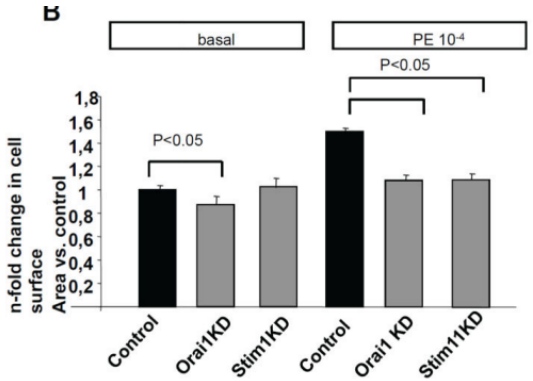




Cardiomyocytes: Orai1 silencing blocks hypertrophic growth

Neonatal rat cardiomyocytes, PE-induced hypertrophy





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Masson et al., Circ Res 2022;131:e102–e119; Voelkers et al., J Mol Cell Cardiol 2010;48:1329–1334

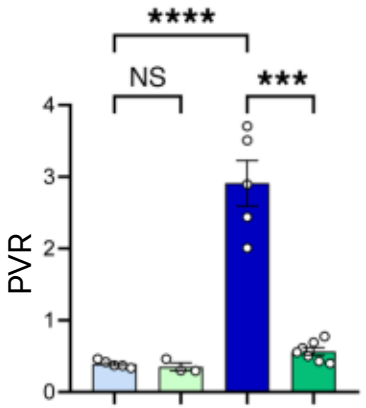
PASMC = Pulmonary Artery Smooth Muscle Cell

CM5480 demonstrated anti-remodeling activity in the lung and showed reduction in pulmonary vascular resistance (PVR) in MCT PAH model

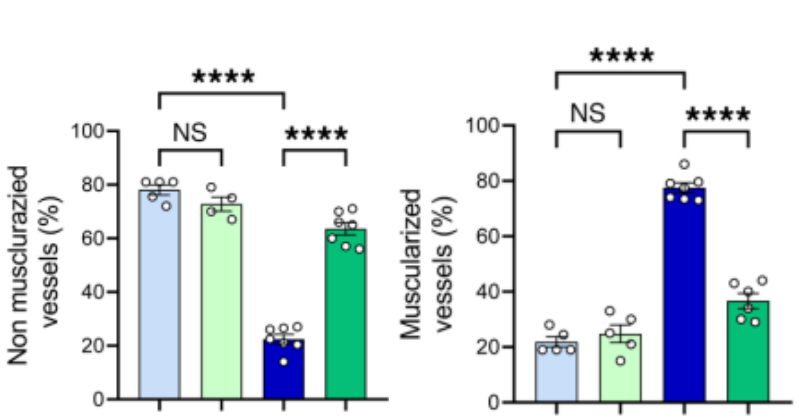
- CM5480 Monotherapy observed to reduce PVR and pulmonary vascular remodeling
- Combination with two SOC drugs showed additive benefit

CM5480 as Monotherapy

Reduced PVR

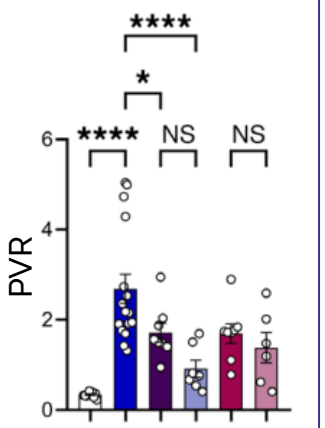


Reduced Pulmonary Vascular Remodeling

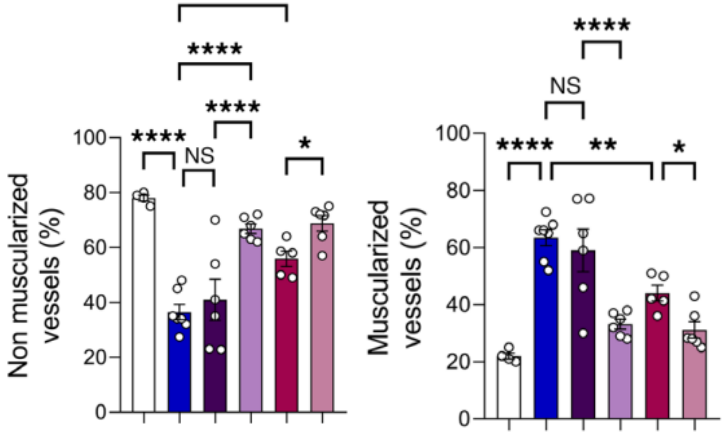


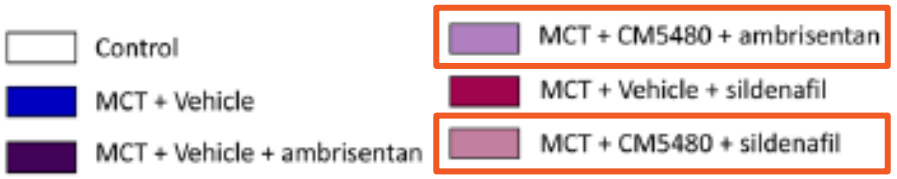
CM5480 in Combination with SOC

Reduced PVR



Reduced Pulmonary Vascular Remodeling





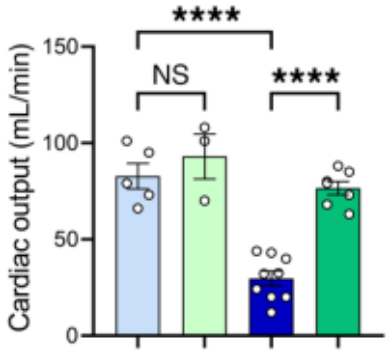
Note: PVR (Pulmonary Vascular Resistance) = RVSP / CO

CM5480 has been shown to improve cardiac output and RV remodeling in MCT PAH model

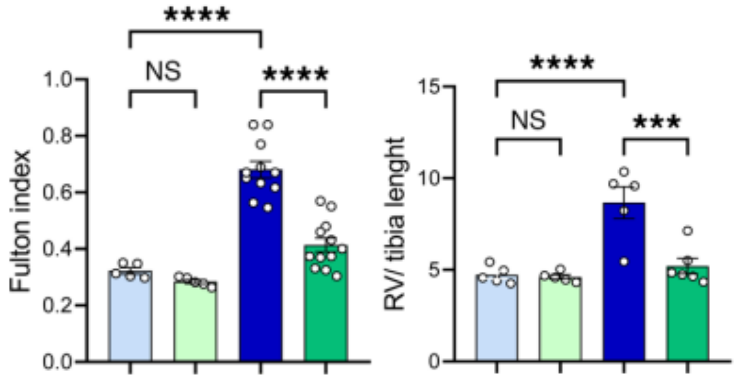
- CM5480 Monotherapy observed to improve cardiac output and reduce right ventricular remodeling
- Combination with two SOC drugs showed additive benefit

CM5480 as Monotherapy

Improved Cardiac Output

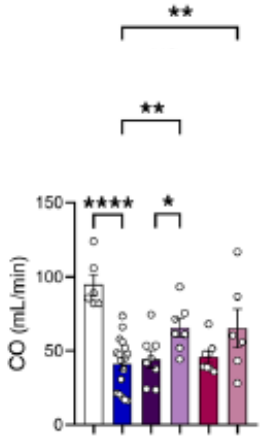


Reduced Right Ventricular (RV) Remodeling

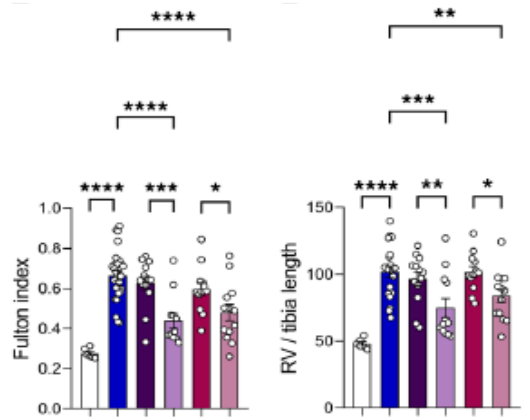


CM5480 in Combination with SOC

Improved Cardiac Output



Reduced Right Ventricular (RV) Remodeling[1]



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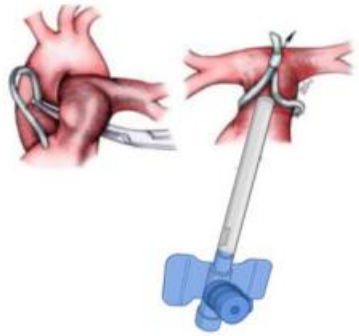
1. Fulton index and RV/tibia length measure RV hypertrophy; Fulton index = weight ratio of RV to the sum of the LV + septum
Publication: Saint-Martin Willer et al., *JCI (Journal of Clinical Investigation) Insight* 2025

CM5480 demonstrated direct RV-protective activity in the PAB model

The pulmonary artery banding (PAB) rat model created fixed RV pressure overload without primary pulmonary vascular remodeling, enabling assessment of direct RV effects independent of the pulmonary vasculature

Purpose of Model



- Enables assessment of RV activity independent of pulmonary vascular effects

Endpoints Assessed

- RV systolic and diastolic function
- RV hypertrophy and remodeling
- RV fibrosis
- Hemodynamic parameters

CM5480 Demonstrated Effect

- Improved RV function
- Reduced RV hypertrophy
- Reduced RV fibrosis
- Consistent with direct RV-protective activity

CM5480 showed direct RV benefit in a model isolating RV protection; inhibitor of TGF-β/activin receptor kinases (sotatercept related-MOA) did not show comparable effects in the same model at the same institution[1]

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1. From CalciMedica discussions with INSERM team; **MOA** = Mechanism of Action
Source: F. Antigny and J. Sabourin (INSERM), personal communication; shared with permission. Unpublished data.

Left ventricular function rescue under pressure overload: Rationale for CRAC channel inhibition in Group II PH

- TAC mouse model surgically induced LV pressure overload and systolic dysfunction mimicking LV pathology in Group II PH
- Orai1 inhibition preserved LV systolic function and improved left ventricular efficiency

EJECTION FRACTION

56.9% → **71.2%**

+14.3 pts

p = 0.001

Systolic pump function restored toward sham

END-SYSTOLIC VOLUME

0.089 mL → **0.044 mL**

−51%

p = 0.003

Less residual blood after each contraction

LV–ARTERIAL COUPLING

1.36 → **2.86**

2.1× efficiency

SV / ESV

Greater stroke output per unit of end-systolic volume

TAC MOUSE MODEL | 3-WEEK JPIII INFUSION | N = 5/ARM

Parameter (TAC)	Vehicle	JPIII	P-value
Heart rate (bpm)	534 ± 16	543 ± 15	0.68
Ejection fraction (%)	56.9 ± 1.3	**71.2 ± 3.8**	**0.001**
LV internal diameter, end-systole (mm)	3.27 ± 0.12	**2.82 ± 0.17**	**0.036**
End-systolic volume (mL)	0.089 ± 0.008	**0.044 ± 0.011**	**0.003**
End-diastolic volume (mL)	0.21 ± 0.022	0.17 ± 0.02	0.12
Stroke volume (mL)	0.121 ± 0.013	0.126 ± 0.005	0.76

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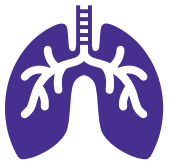
Note: JPIII: small-molecule Orai1 inhibitor used as tool compound for target validation
Bartoli F et al, 2020 Circulation

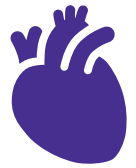
CM5480 reversed PAH-mediated genetic changes in both the lung and right ventricle of the heart

Transcriptomic profiling of CM5480 Treatment in the MCT Rat Model of PAH



305 dysregulated genes in the lung were restored by CM5480 in MCT-treated rats
(vs. 100 with amplified dysregulation)

- Pathways restored include metabolism and inflammation/immune response



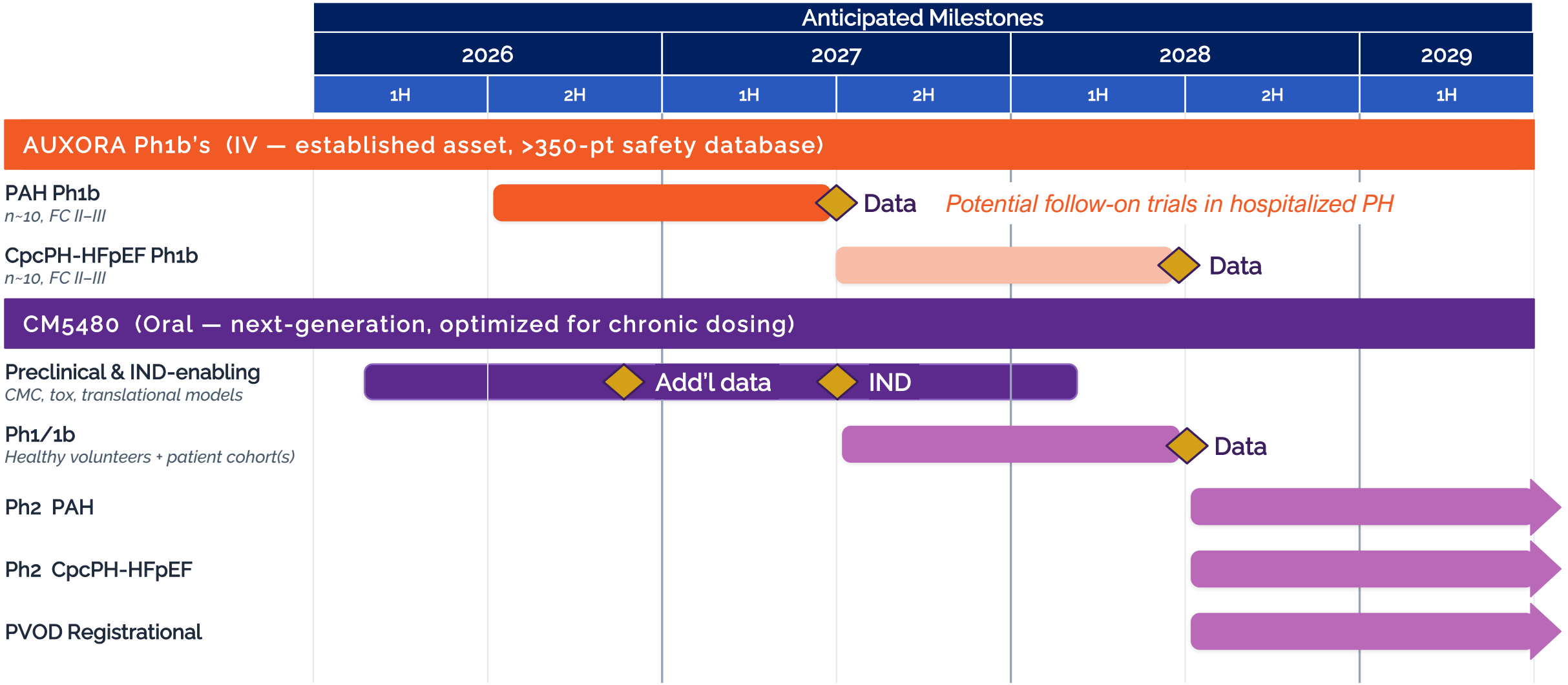
2,358 dysregulated genes in the RV were restored by CM5480 in MCT-treated rats
(vs. only 9 with amplified dysregulation)

- Restoration of gene expression was most striking in the RV
- Pathways restored include inflammation and heart contraction

CM5480 is potentially disease-modifying and potentially restores RV function in PAH

Publication: Saint-Martin Willer et al., *JCI (Journal of Clinical Investigation) Insight* 2025

Efficient path to potentially validate CRAC channel inhibition in PH and expand across multiple indications



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

Auxora Ph1b: PAH data with CRAC channel inhibitor anticipated by mid-2027

Capital-efficient Ph1b study using an established IV asset with a **>350-patient safety database** — delivering potential first-in-human CRAC channel inhibitor signals in pulmonary arterial hypertension expected in mid-2027

POPULATION

PAH

Functional class II and III

- **~10 patients**
- Baseline PVR ≥5 Wood units
- Stable on SOC incl. sotatercept

TREATMENT

5-day IV course

Single treatment course

- IV infusion daily for 5 consecutive days
- Administered in Phase 1 unit

ENDPOINTS

RV and LV hemodynamics

RHC / ECHO / CMR + biomarkers

- LV & RV function: contractility, strain, TAPSE, RA size
- Hemodynamics: PVR, mPAP, PCWP, CI
- EmPHasis-10 questionnaire
- NT-proBNP, Cystatin-C
- Assessed at Day 5, weekly, and Day 35[1]

ANTICIPATED TIMELINE

Data mid-2027

Advancing to IND submission

- YE 2026: Trial enrolling
- Mid-2027: Data

STRATEGIC OBJECTIVES

De-risk CM5480 in PAH

First potential human signal for CRAC channel inhibition in PAH — expected to inform and de-risk our oral chronic-dosing program (IND clearance anticipated mid-2027).

Establish Auxora as a potential IV therapy in hospitalized PH

Potential acute / decompensating indications; high unmet need; registration studies could begin in 2027.

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1. Measurement frequency dependent on endpoint

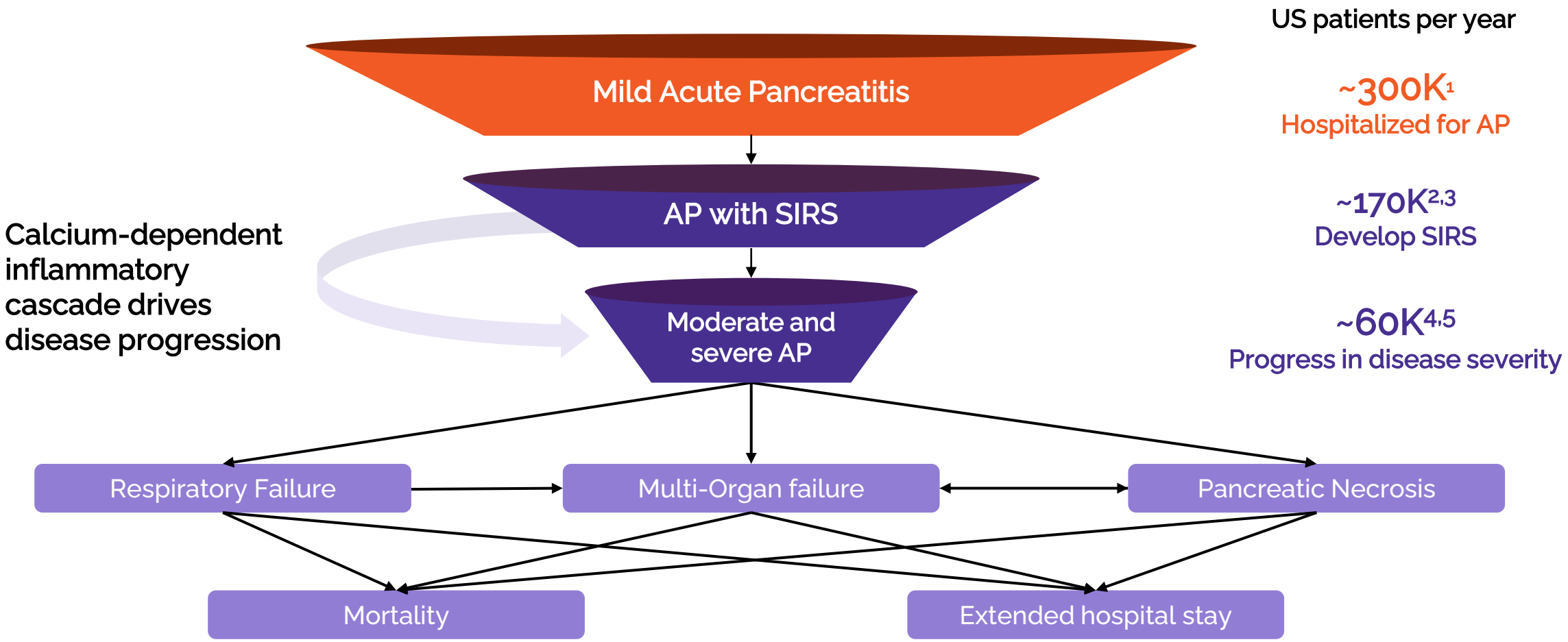
RHC = Right Heart Catheterization; **CMR** = Cardiac Magnetic Resonance; **TAPSE** = Tricuspid Annular Plane Systolic Excursion; **mPAP** = mean Pulmonary Artery Pressure; **PCWP** = Pulmonary Capillary Wedge Pressure; **CI** = Cardiac Index

Anticipated milestones

Auxora in PAH	• Ph1b proof-of-concept data extpected mid-2027
CM5480 in PH	• Additional preclinical data in PH models expected 2H 2026 • IND submission expected mid-2027
Auxora in AP	• FDA feedback on pivotal program design expected in 3Q 2026
Cash Runway	• Cash expected to fund current operations into 2H 2027

Appendix: Auxora for Acute Pancreatitis (AP)

AP: common, costly, and without approved treatments



US patients per year

~300K[1]
Hospitalized for AP

~170K[2,3]
Develop SIRS

~60K[4,5]
Progress in disease severity

Economic burden: >1M hospital days and ~$2.5B in U.S. costs annually

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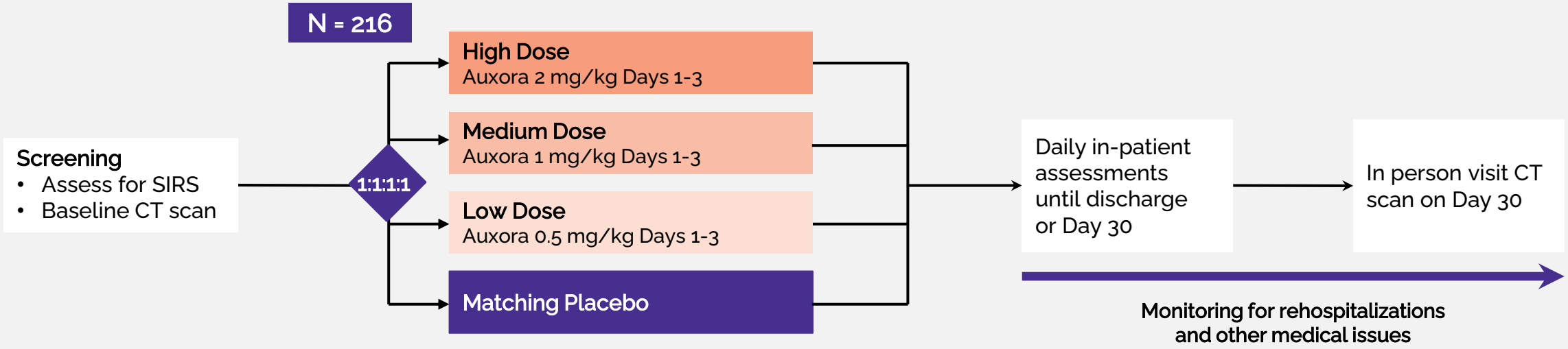
1, Peery AF et al. Gastroenterology. 2022;162(2):621–44; 2. Machicado JD et al. United European Gastroenterol J. 2021;9(2):139–49.; 3. Singh VK et al. Clin Gastroenterol Hepatol. 2009;7(11):1247–51.; 4. Boxhoorn L et al. Lancet. 2020;396(10252):726–34; 5. Metri A et al. Surg Open Sci. 2024;19:109–17.; SIRS = Systemic Inflammatory Response Syndrome

CARPO Phase 2b clinical trial in AP with SIRS

Endpoints

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



Primary Objective: Dose Response on Primary and Secondary Endpoints

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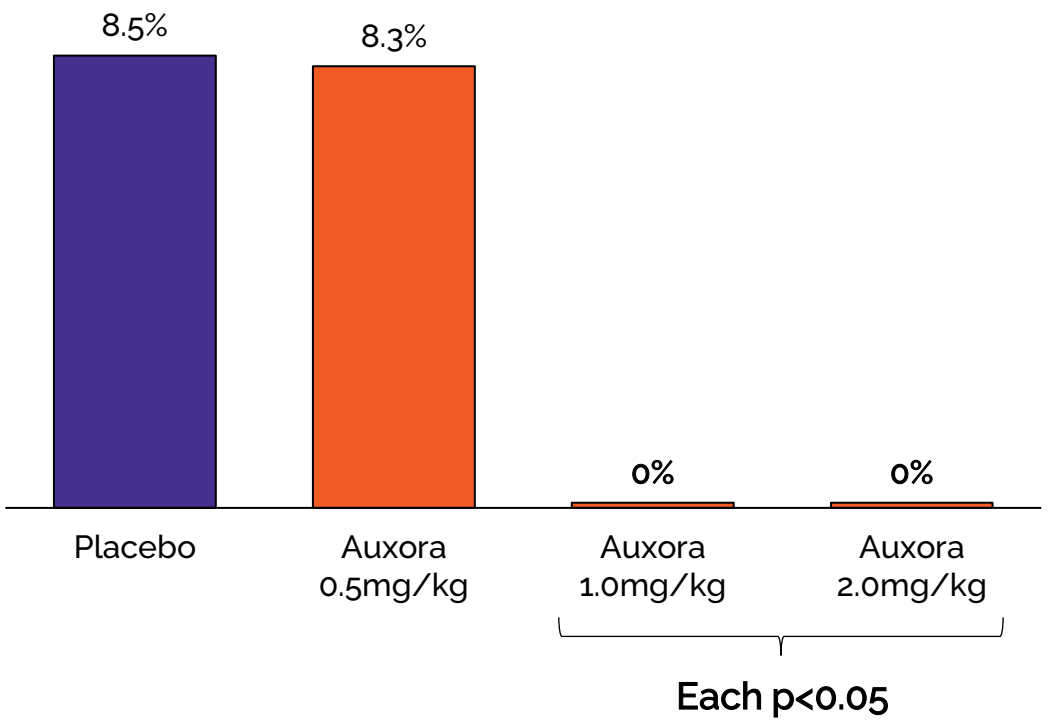
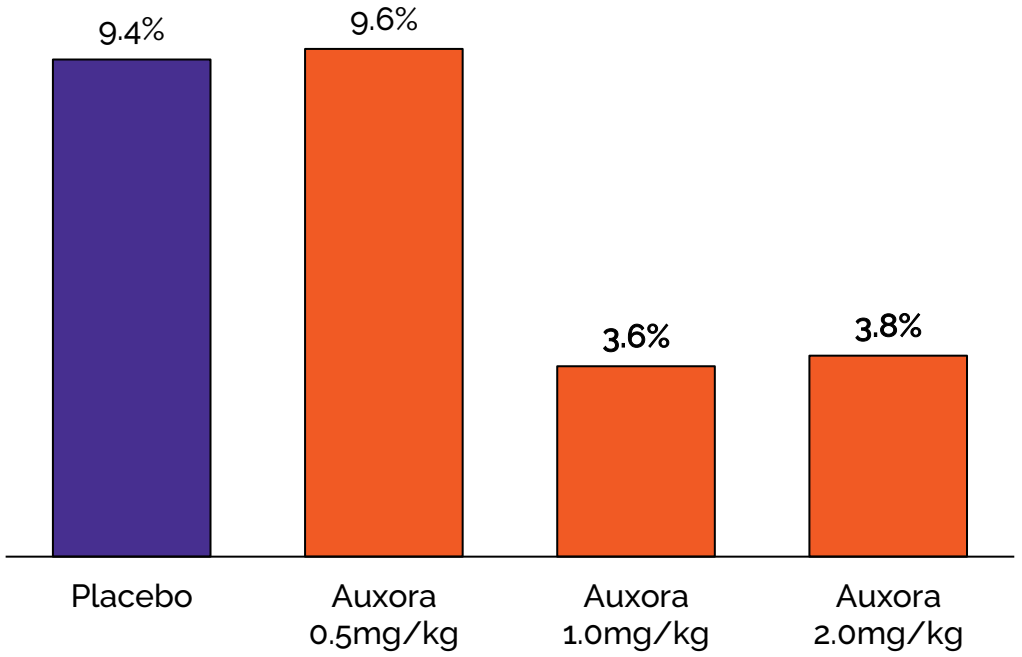
SIRS: Systemic Inflammatory Response Syndrome

Auxora prevented new severe respiratory failure

Observed 100% reduction in new severe respiratory failure[1]



Observed 60% reduction in severe organ failure[2]



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1. mITT excluding baseline respiratory failure (n=197)
2. mITT (N=214); severe organ failure includes severe respiratory failure, severe renal failure, and severe cardiovascular failure

Win-ratio analysis favors Auxora across key clinical outcomes

	% of patient-pair comparisons won		
Endpoint	Placebo (n = 53)	Auxora 2.0 mg/kg (n = 52)	Favored arm
All-cause mortality	-	-	(no events)
New onset severe respiratory failure	0.0%	7.5%	✓ Auxora
New onset necrotizing pancreatitis	13.6%	22.3%	✓ Auxora
Time to medically indicated discharge	19.8%	26.5%	✓ Auxora
Across all hierarchical comparisons	33.4%	56.3%	✓ Auxora

Win-Ratio = 1.64 (95% CI: 1.03–2.61, p = 0.037)

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Win-ratio (Finkelstein-Schoenfeld): Patient pairs compared hierarchically across endpoints. Percentages represent proportion of comparisons won. Totals <100% because 10.3% of comparisons were ties. CI = confidence interval

Advancing towards a potential pivotal program in AP

- Ongoing constructive discussions with the FDA regarding the design of a pivotal program in AP
- Leveraging AI-enabled analyses with Telperian to refine patient selection and endpoint strategy, with the goal of an enriched, efficient study design
- FDA feedback on pivotal program design expected in 3Q 2026

Appendix: Additional Slides

To-date, CRAC channel pathway demonstrated that it does not interfere with and is not modulated by pathways targeted by existing PAH therapies

Effect of Orai1 Knockdown on mRNA Expression of Targeted Pathways in Human PAH-PASMCs

mRNA	Effect of Orai1 Knockdown
Endothelin Receptor Type A	**No change**
Endothelin Receptor Type B	**No change**
Phosphodiesterase 5 (PDE5)	**No change**
BMPR2	**No change**
BMPR1A	**No change**
TGFBR2	**No change**
TGBR3	**No change**
TGFBR1	**Decreased**

Effect of PAH Drugs on Orai1 Protein Expression in Human PAH-PASMCs

Drug Class	Drug	Orai1 Protein Expression
PDE5 inhibitor	Sildenafil	**Increased**
Endothelin inhibitor	Ambrisentan	**No effect**
Monoclonal antibody inhibitor of activin type II receptors	Bimagrumab	**No effect**
Tyrosine kinase inhibitor	Imatinib	**No effect**

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PASMC = pulmonary artery smooth muscle cell
Publication: Saint-Martin Willer et al., *JCI (Journal of Clinical Investigation) Insight* 2025