



PROTECTING THE HEART

MRS2339 AS A FIRST-IN-CLASS NOVEL PROTECTIVE DRUG

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MRS2339 is a first-in-class drug to treat patients with systolic heart failure without causing any drop in blood pressure or change in heart rate.



- The rationale: The heart's pumping ability is severely reduced, associated with low blood pressure, particularly in those with Class IIIb and Class IV heart failure.
- The problem: All current drugs lower blood pressure, causing concern by providers and lack of compliance from patients.
- The solution: MRS2339 can benefit these patients and address an unmet medical need with oral, SQ & IV formulations to treat the full spectrum of heart failure;
- Very high disease burden: 3-month readmission rate is up to 40% and 4-year mortality rate after advanced heart failure diagnosis is nearly 80%;
- Very high economic burden: cost projected to reach \$70B by 2030 in the U.S. alone;
- We aim to raise \$32m: Phase 1b (\$7m) with dose escalation on Class IIIb/Class IV patients and Phase 2 trial (\$25m) for POC as an acute therapy for hospitalized patients with acute decompensated heart failure and as a SQ therapy for bridging to outpatient setting.

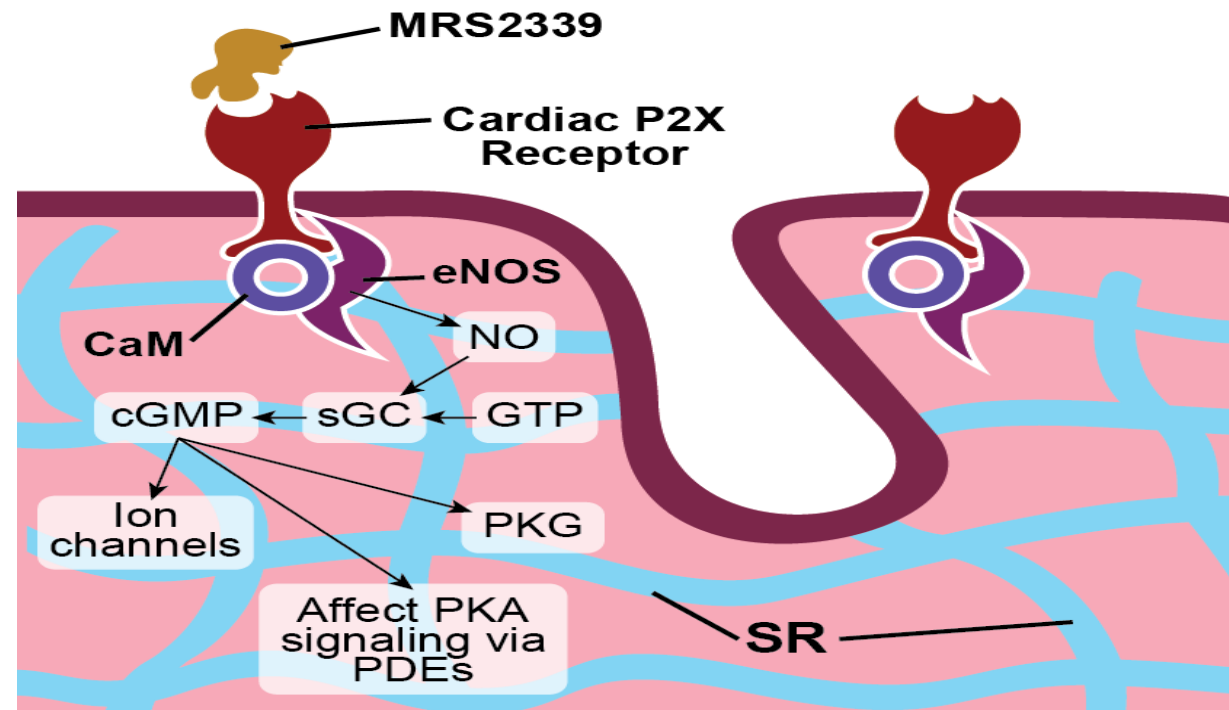


MRS2339 has a unique mechanism of action with cardiac-specific increase in cyclic GMP which is an established cardioprotective molecule

- MRS2339 is a cardiac P2X receptor agonist that is a hydrolysis-resistant adenosine monophosphate derivative;
- Physical association of P2X receptors with endothelial Nitric Oxide Synthase (eNOS) in the heart;
- MRS2339 is without vasodilator effect or effect on immune cells;
- Increase stroke volume and cardiac output & reverse the maladaptive remodeling;
- Cardioprotective with benefits lasting for at least one month post-dose;
- Efficacious in multiple animal models of heart failure;
- Can be additive to other heart failure drugs and not replacing them.

MRS2339 differs from nonselective cyclic GMP stimulating drug which tends to cause hypotension in sick patients

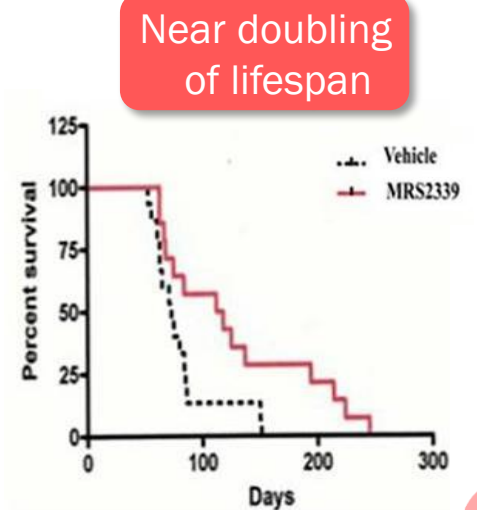
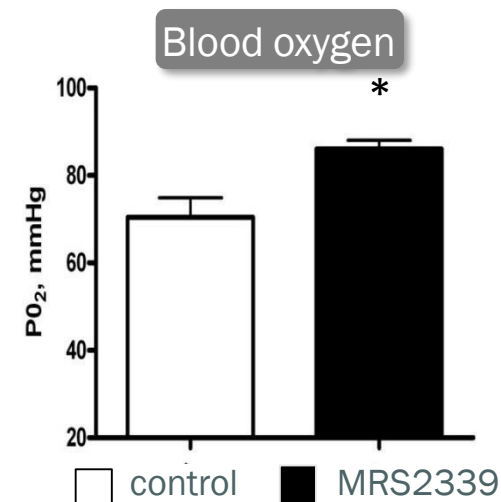
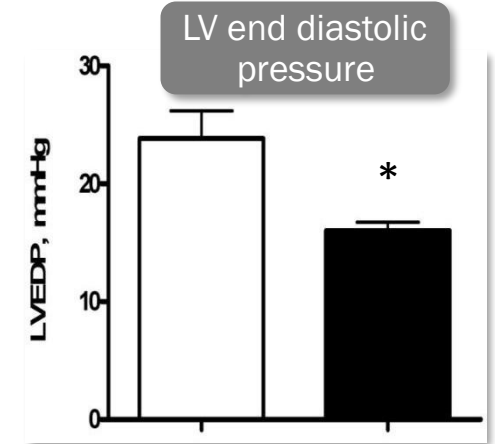
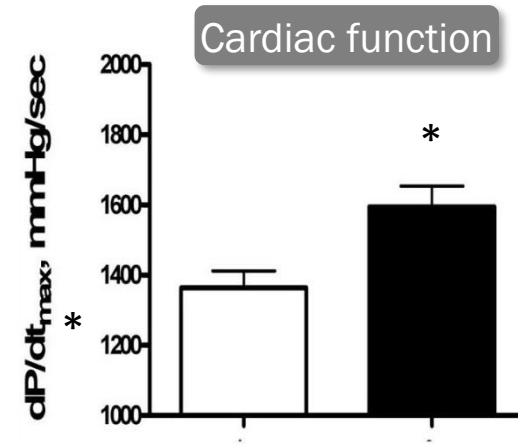
Proposed Mechanism of Action



MRS2339 increases nitric oxide and subsequent increase in cyclic GMP with both being localized to heart

MRS2339 improves heart function and prolongs lifespan in animal models

- MRS2339 improved contractile function, oxygenation and reduced lung congestion due to decreased left ventricular end diastolic pressure (LVEDP) which is equal to the pressure in the lungs (higher pressure impairs oxygenation)-saw improvement in just 4-5 dogs.
- MRS2339 preserved LV wall thickness, increased stroke volume and decreased LV remodeling
- Extended survival in a mouse model of severe dilated cardiomyopathy
- Large therapeutic index (ratio of dosage causing adverse effects to that leading to efficacy): 100-fold



* P<0.05 vs control dogs

Mouse



No Competition in Class IIIb and Class IV Heart Failure Patients

Company	Product	Likely Effect on BP in Class III & IV	% Class IV in Phase 3 Trial	Clinical Benefit in Class IV Patients
AstraZeneca	farxiga® (dapagliflozin) 5mg & 10mg tablets	↓	< 1% in DAPA-HF	No
Boehringer Ingelheim	Jardiance® (empagliflozin) tablets 10 mg/25 mg	↓	0.5% in EMPEROR-REDUCED	No
MERCK	Verquvo® (vericiguat) tablets 2.5 mg, 5 mg, 10 mg	↓	1.4% in VICTORIA	Not Shown for Class IV
novo nordisk	Victoza® liraglutide injection 1.2 mg 1.8 mg		FIGHT	Worse
NOVARTIS	Entresto® Sacubitrilo-Valsartan	↓	100% in LIFE	No

MRS2339 does not cause hypotension while producing benefits in many animal models of systolic HF. MRS2339 is different from Verquvo which non-selectively increases cyclic GMP throughout and risks causing decreased blood pressure. We expect that MRS2339 will have little competition in late/end stage HF. FDA rejected approval of Cytokinetic’s Omecamtiv Mecarbil in March 2023.



Provascor Leadership and Operation



Bruce Liang, MD
Cardiologist/ Scientist,
Dean of UConn School of
Medicine,
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Mark Van Allen
Chief Operating
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Martin Bexon, MD,
Bexon Clinical, Inc.
Medical Monitor,
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Behring and Roche



William White, MD
Clinical
Pharmacologist,
Point on Clinical and
Cardiovascular
Safety Endpoint



Mary E ("Beth")
P Goad, DVM,
PhD, Board-
Certified
Veterinary
Pathologist and
Toxicologist
With >30 Years
of Experience.



Donna Mancini,
MD, Clinical
Development
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Advisor on
Heart Failure,
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Advanced Heart
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Cardiac
Transplant
Programs at
Columbia and
Mount Sinai

James
Heym, PhD

Science Advisor,
Led Drug
Discovery and
Development As
Vice President
at Pfizer



MRS2339 testing is completed in Phase 1a study on healthy human volunteers without safety concerns or serious adverse effect

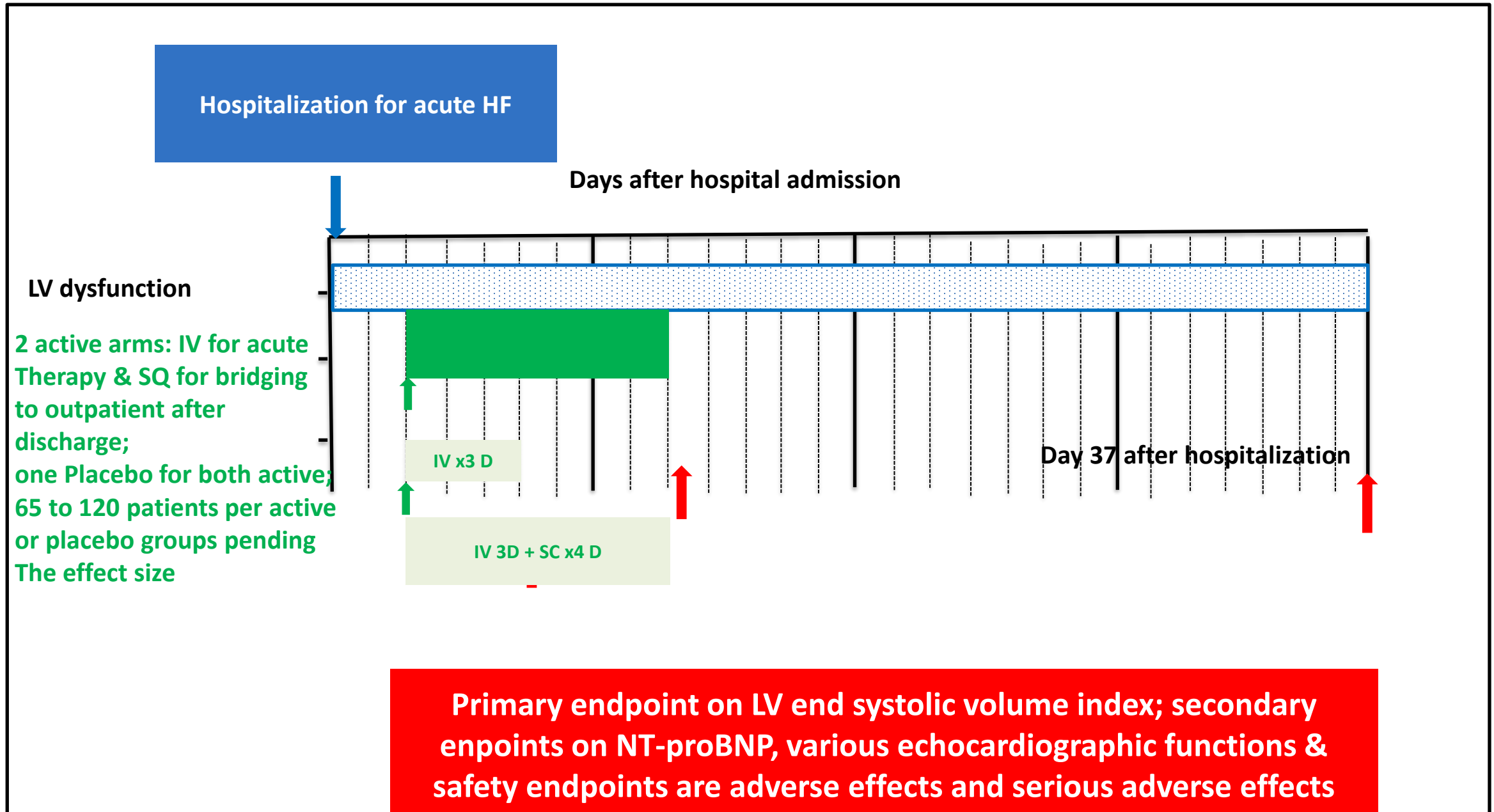
Phase 1a – First-in-Human Study

- Randomized, double blind, single ascending dose (SAD) in healthy volunteers (HV)
- Assess the safety, tolerability, and pharmacokinetics (PK)
- 24hr IV infusion and 24hr monitoring (in-house) for 3 days: day-1, Day 1, Day 2
- 3 cohorts with 8 healthy subjects (4 males and 4 females) per cohort and total of 5 dosings.

The highest of the 5 dosing levels is without any safety concerns or change in blood pressure or heart rate.

*This highest dosing level is 16 -fold the anticipated efficacious dosage in humans. We expect a wide therapeutic range in patients. The lack of blood pressure or heart rate changes is a unique property, making the drug candidate suitable for all patients including severe heart failure. FDA agrees with the results of the 1a study and deems the drug safe in HV. **PD effect with target engagement is already evident.***

Phase 2 POC for those with Class IIb & IV heart failure using the \$25m



Timeline on the Phase 2 trial for the two indications-IV and SC using the \$25m

Mid 2024 – Mid/Late 2025-completed

Milestone 4

Phase 1a Clinical trial in
Healthy Subjects IV infusion

Early 2026 – Mid/Late 2027

Milestone 5

Phase 1b Clinical Trial in
Class III, IV with IV infusion

2027 – 2029

Milestone 6

Phase 2 POC using IV &
SC formulations

2029-2030 – exit options

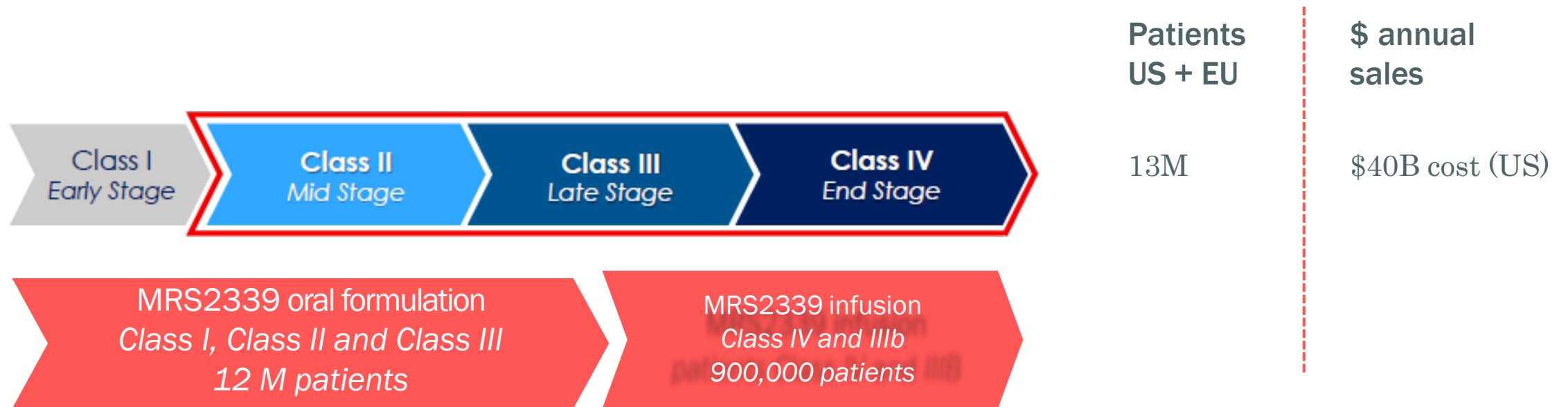
Milestone 7

Partnership or acquisition by pharma, IPO

IV or SQ infusion is for Class IIIb & Class IV patients;
Oral ingestion is for chronic use in milder cases

The annual gross revenue is based on \$5,000-\$7,000 for one infusion cycle of and 20% market penetration for \$0.9B-\$1.26B. Repeat cycle can be considered for each episode of acute heart failure with doubling or tripling of gross sale.

Oral therapy anticipates \$16.8B of annual gross sale.



Preclinical and clinical plans on the oral formulation-need \$3m for Phase 1 & \$25m-\$27m for Phase 2 POC in Class II and Class III heart failure

Late 2025-Mid 2026

Milestone 1

Successful development and testing in preclinical animal model

Mid 2026 – Late 2026

Milestone 2

IND submission for an open IND in Phase 1 Clinical Trial on Class I, II or III heart failure patients

Late 2026 – Mid 2027

Milestone 3

Analyze data on clinical POC from Phase 2 IV&SC trial & Ready for Phase 1 trial using oral drug

Mid 2027 – Mid 2028

Milestone 4

Fund raising and conducting Phase 1 trial on oral drug in patients with mild HF

Lead and co-lead oral formulations as stable emulsions have been developed and are feasible to manufacture.

Cost Reductions & Revenue Reimbursements

- Hospitals will likely be users.
- Insurers will likely be buyers due to
 1. savings from reduced hospitalization and reduced cost per episode of care;
 2. patients wanting to take the drug for improved quality of life, reduced morbidities or even mortality.
- Patients may pay cash if the drug prolongs life.
- Compassionate use.
- Purchase by integrated delivery systems such as VA, Kaiser Permanente, etc

