Provascor

PROTECTING THE HEART

MRS2339 AS A FIRST-IN-CLASS NOVEL PROTECTIVE DRUG

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A new heart failure drug without hemodynamic depression is needed: Provascor has developed MRS2339 as a new heart-specific protective drug without vasodilator effect

- Aim to be the first therapeutic agent with indication for advanced heart failure in which the heart's pumping ability is severely reduced;
- Address an urgent unmet medical need;
- Provascor's Lead Program MRS2339 initially targets patients with advanced heart failure:
  - Class IIIb and IV (except patients on Ventricular Assist Device or transplant list)
  - IV infusion is for hospitalized patients for acute HF treatment as an indication. SC formulation is for outpatients for as short as a total of 7 days as a separate indication. Rat and dog studies showed efficacy after 7-day treatment.
- 30%-40% of all heart failure patients are Class III or IV;
- 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 with cost projected to reach $70B by 2030 in the U.S. alone

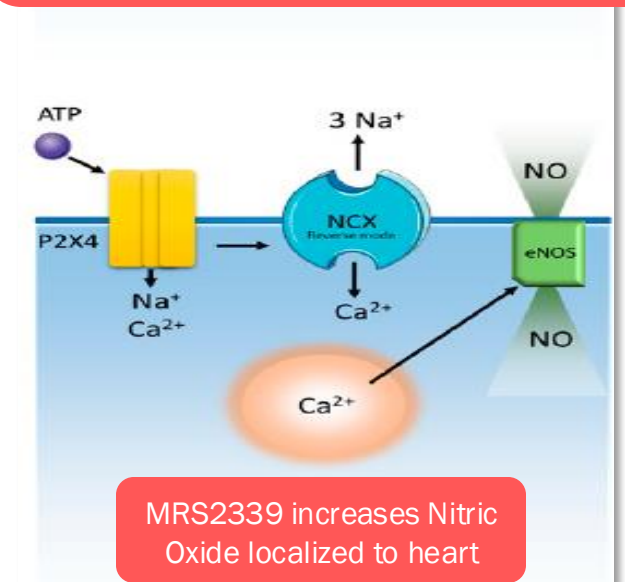
- Provascor has developed IV formulation for inpatients (FDA-approved) & subcutaneous (SC) formulation for outpatients.
- PK and limited bridging study to accelerate development of SC formulation for clinical trial.
- Provascor is developing an oral formulation and plans to expand market into mild to moderate HF.

Provascor's heart failure investigational drug has a unique mechanism of action with cardiac-specific stimulation of cyclic GMP accumulation WITHOUT hypotension

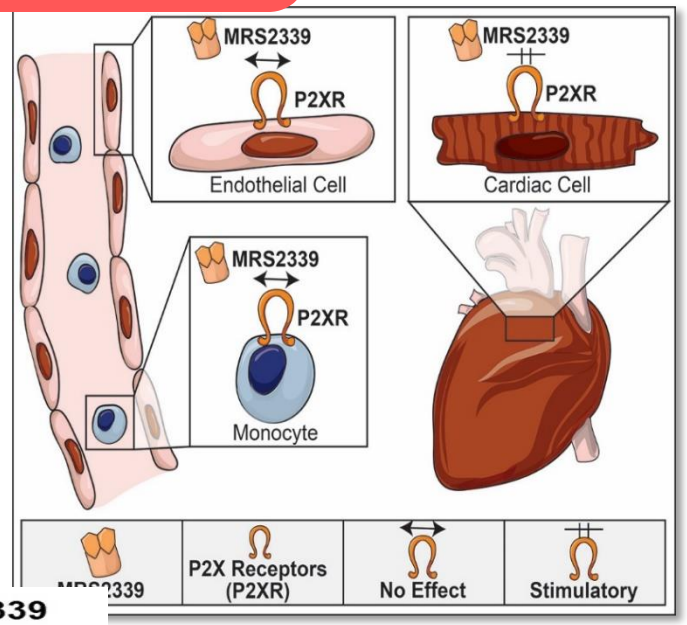
- Heart P2X receptor agonist
  - hydrolysis-resistant adenosine monophosphate derivative

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

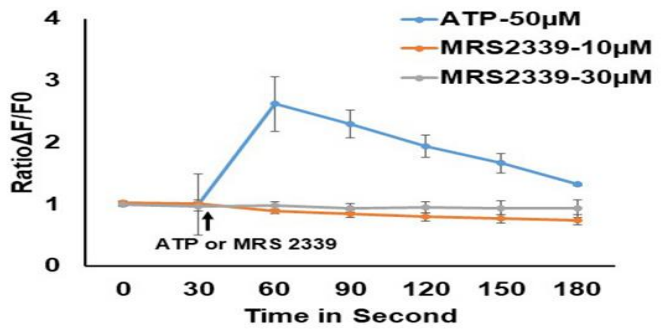
- Physical association of P2X4 receptors with endothelial Nitric Oxide Synthase in the heart;
- Without vasodilatation or immune cell activation;
- Increase stroke volume and cardiac output & reverse the maladaptive remodeling;
- Cardioprotective with benefits lasting for at least one month post-dose;
- Efficacious in multiple animal models of heart failure;
- Can be additive to other heart failure drugs and not replacing them.



MRS2339 increases Nitric Oxide localized to heart



Calcium Influx assay for MRS2339



MRS2339 only is active in cardiac cells where P2XR4 is highly expressed in HF

← 30-36 mouse macrophages

All Current Milestones Are Achieved

Milestone 1
GLP tox/safety done in rat & dog & finished formulation

Milestone 2
GMP manufacturing of drug substance done

Milestone 3
GMP manufacturing drug product & IND "study may proceed", May 2023

Major milestone with Good Lab Practice (GLP) and Good Manufacturing Practice (GMP) is achieved with FDA approval to move to human testing. All non-clinical milestones were achieved with Provascor's funds in obtaining an open Investigational New Drug (IND).

MRS2339 testing is completed in Phase 1a study on healthy human volunteers

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 advanced 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-see next 2 slides.***

A Platform Approach-MRS2339 drug product to span the spectrum of HF

- Three formulations aiming at 3 clinical indications for heart failure:
- - Intravenous (IV) for those with advanced heart failure admitted to hospital for worsening heart failure as an acute therapy indication-IV formulation approved by FDA;
- -Subcutaneous (SC) for those advanced heart failure as an indication for chronic outpatient therapy-SC formulation already developed;
- -An oral formulation would be an indication for chronic therapy in patients with mild heart failure-Several oral formulations have been developed.

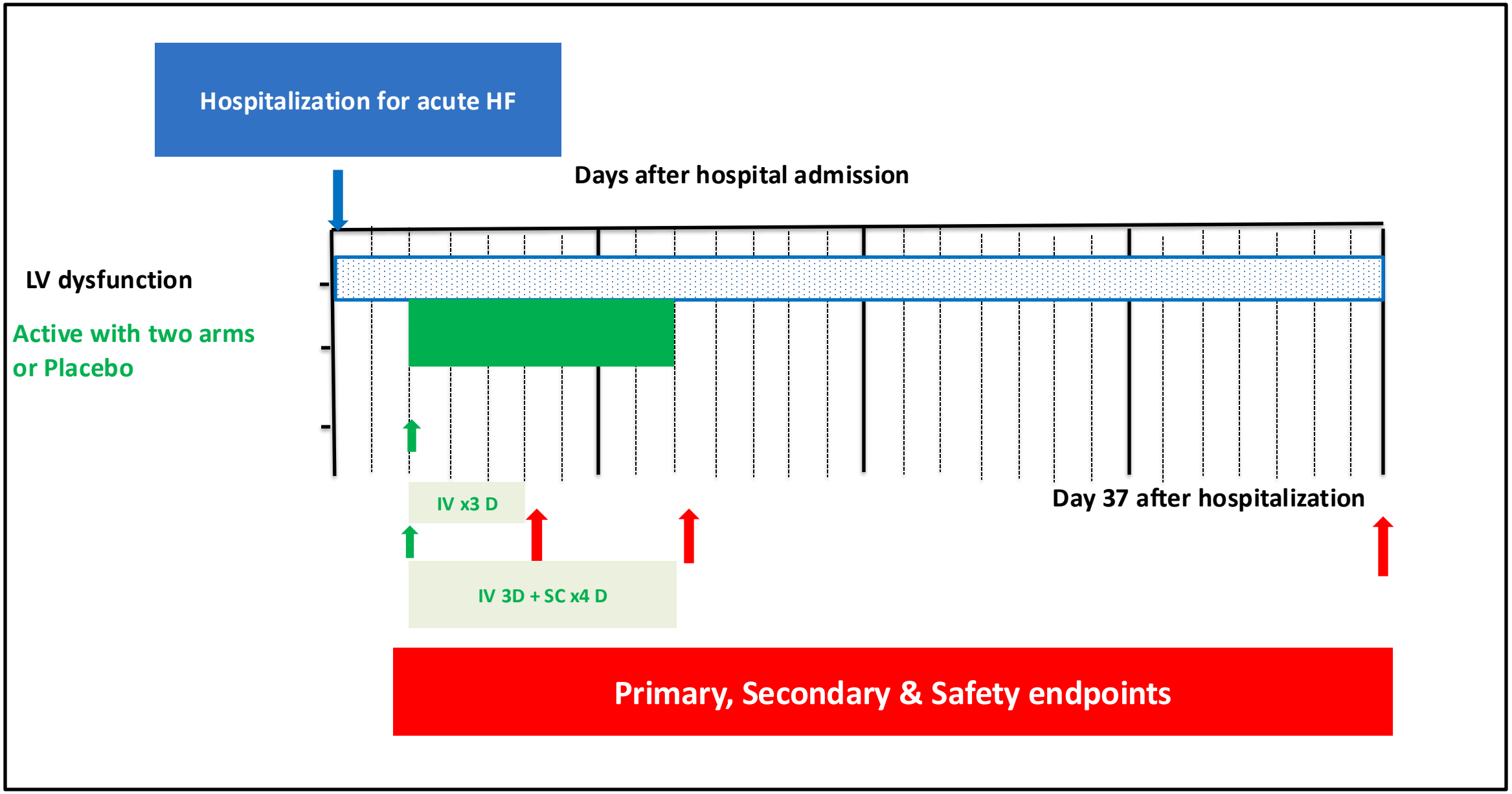
One combined Phase 2 trial using IV & SC therapy

Phase 2 –Efficacy Signal in Class III & IV Systolic HF

- A randomized, open-label, placebo-controlled study in patients admitted for acute HF
- Ascertain efficacy signal using the highest tolerable and safe dosage from Phase 1b. Primary endpoint is a decrease in LVESVI from baseline to day 30. Secondary endpoints are strain & ejection fraction, NT-ProBNP, KCCQ-QS, 6-min walk distance. Safety endpoints such as mortality & SAE are assessed.
- 3-day IV as acute HF therapy and 7-day SC infusion for outpatient therapy.
- Patients-one placebo group for both IV and SC groups

Arm 1: 3-day IV infusion for hospitalized patients with Class III and Class IV admitted due to acute decompensated HF;
Arm 2: 7-day infusion with 3-day IV in hospital and then 4-day SC as bridging to outpatient
Arm 3: placebo: 3-day IV and then 4-day SC
Primary endpoint and secondary endpoint assessed at end of 3-day IV, at end of 7-day infusion, and at 30 days after hospital discharge for all 3 arms
Cost: $2m to prepare and recruit and $15m-$17m for conduct of Phase 2.
Timeline: 2 years after 1b trial completion

Phase 2 design for patients with advanced heart failure



Target Population with aim to treat hospitalized patients-using IV for acute worsening heart failure as the indication

MRS2339, as an IV treatment, will target those in Class IIIB & Class IV minus those who are on assist device or on transplant list. The revenue (not net profit) is based on $5,000 for one infusion cycle of 3 days and 20% market penetration. Repeat cycle can be considered for each episode of acute HF, not unlike the chemo cycle. Repeat of 2 or 3 times per year can result in $1.8B-$2.7B of gross sale.

	Patients US + EU	$ annual sales
	13M	$40B cost (US)
	900,000	$900M

Target Population with SC infusion to treat outpatients with advanced heart failure for chronic therapy as the indication

MRS2339, as SC formulation, will treat those in Class IIIB & Class IV as outpatients. The revenue (not net profit) is based on $7,000 for one infusion cycle of 7 days and 20% market penetration. Repeat cycle can be considered, not unlike the chemo cycle. Repeat of 2 or 3 times per year can result in multiples of 1.26B of gross sale.

	Patients US + EU	$ annual sales
	13M	$40B cost (US)
	900,000	1.26B

Target Population with oral formulation to treat outpatients with mild heart failure as the indication

MRS2339, as an oral formulation, will treat those in Class I, Class II and Class III as an indication for chronic outpatient therapy. The revenue (not net profit) is estimated to price at $7,000 for one year and 20% market penetration with an estimated 16.8B of gross sale.

Patients US + EU	$ annual gross sales
12M	$16.8B

IP Portfolio and Market Exclusivity

- Polymorphs as new compositions and key manufacturing steps are filed as new patent applications with US/PCT;
- Patent filed in July 2023 on novel IV formulations;
- SC formulation is developed and will be filed in US/PCT;
- Oral formulations will be filed in US/PCT
- Method of use patent issued in US and 5 countries in EU through 2031;
- Patent term extension in which half of time from open IND to NDA filing and all of the time from NDA filing to approval can be applied;
- Patent application on clinical method of use of the drug product-to be filed in US/PCT;
- Qualifies for five-year period of NCE exclusivity under Hatch-Waxman Act with additional 30 months exclusivity if there is a case with the generics