Interim Results of a Phase 2 Study With RBT-1 Evaluating Postoperative Course in Patients Undergoing Elective CABG/Valve Surgery on Cardiopulmonary Bypass

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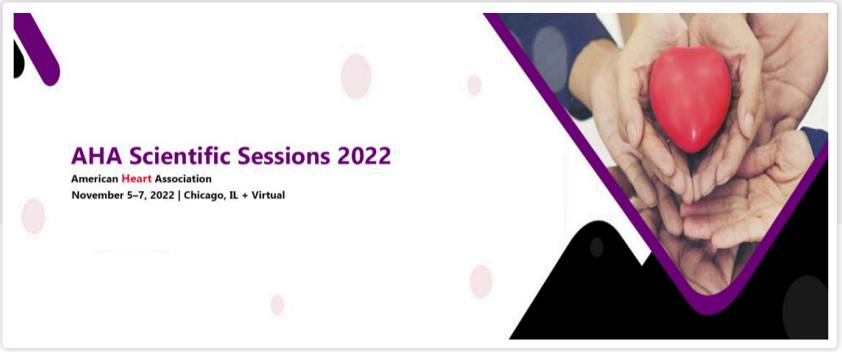
on behalf of START investigators

renibus therapeutics



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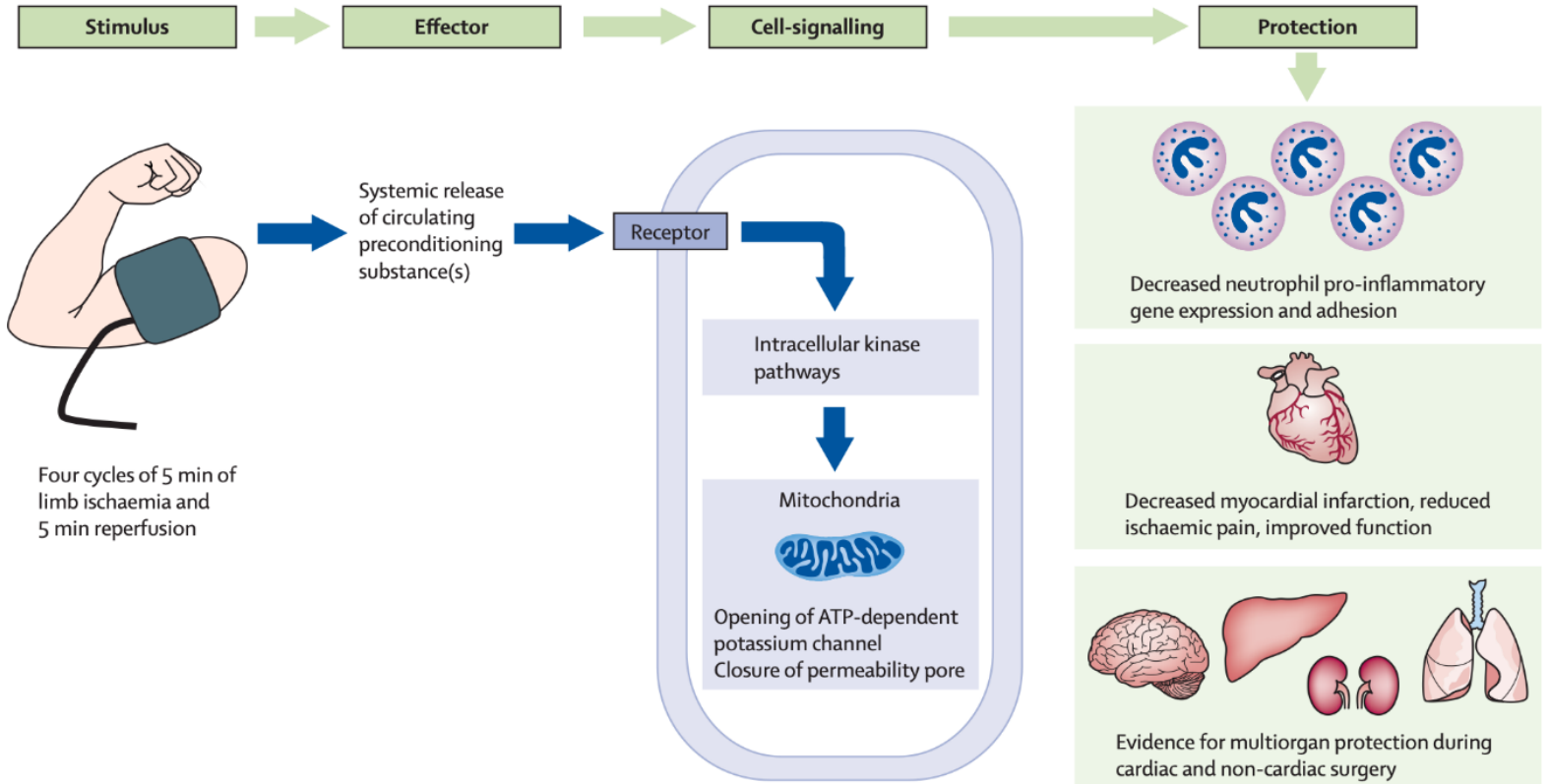
Preconditioning as a Means for Multiorgan Protection

- **Preconditioning** involves **priming a stress response** to **elicit protection against subsequent injury**
- **As early as 1929**, it was observed that the **kidneys of animals** previously exposed to (**preconditioned** by) various minor stressors **acquired resistance to organ failure**
- **In the early 1990s**, **remote ischemic preconditioning** (**RIPC**), which involves a brief induction of ischemia and reperfusion to distal tissues using a sphygmomanometer in the upper arm or leg, was introduced



Sources: Nath M and Agarwal A, 2020 Kidney Res Clin Pract; Honda N et al, 1987 Kidney Int; Jacob KA and Leaf DE, 2019 Anesthesiol Clin; Kharbanda RK et al, 2009 Lancet

RBT-1 – Pharmacologic Approach to Preconditioning

The **mechanism of action of RBT-1** is applicable to **multiorgan protection, beyond the kidneys**

RBT-1

(Stannous Protoporphyrin [SnPP]/Iron Sucrose[FeS])

Antioxidants (eg, HO-1)

Inhibition of Oxidative Stress

Anti-inflammatory (eg, IL-10)

Inhibition of Inflammation

Iron Scavengers (eg, Ferritin)

Sequestration of Free Catalytic Iron, Free Hemoglobin, Free Heme

Prevention of Organ Failure

Brain **Heart** **Lungs** **Kidneys** **Liver** **Intestines**

Phase 2 Study of RBT-1 In Subjects Undergoing CABG and/or Valve Surgery on Cardiopulmonary Bypass

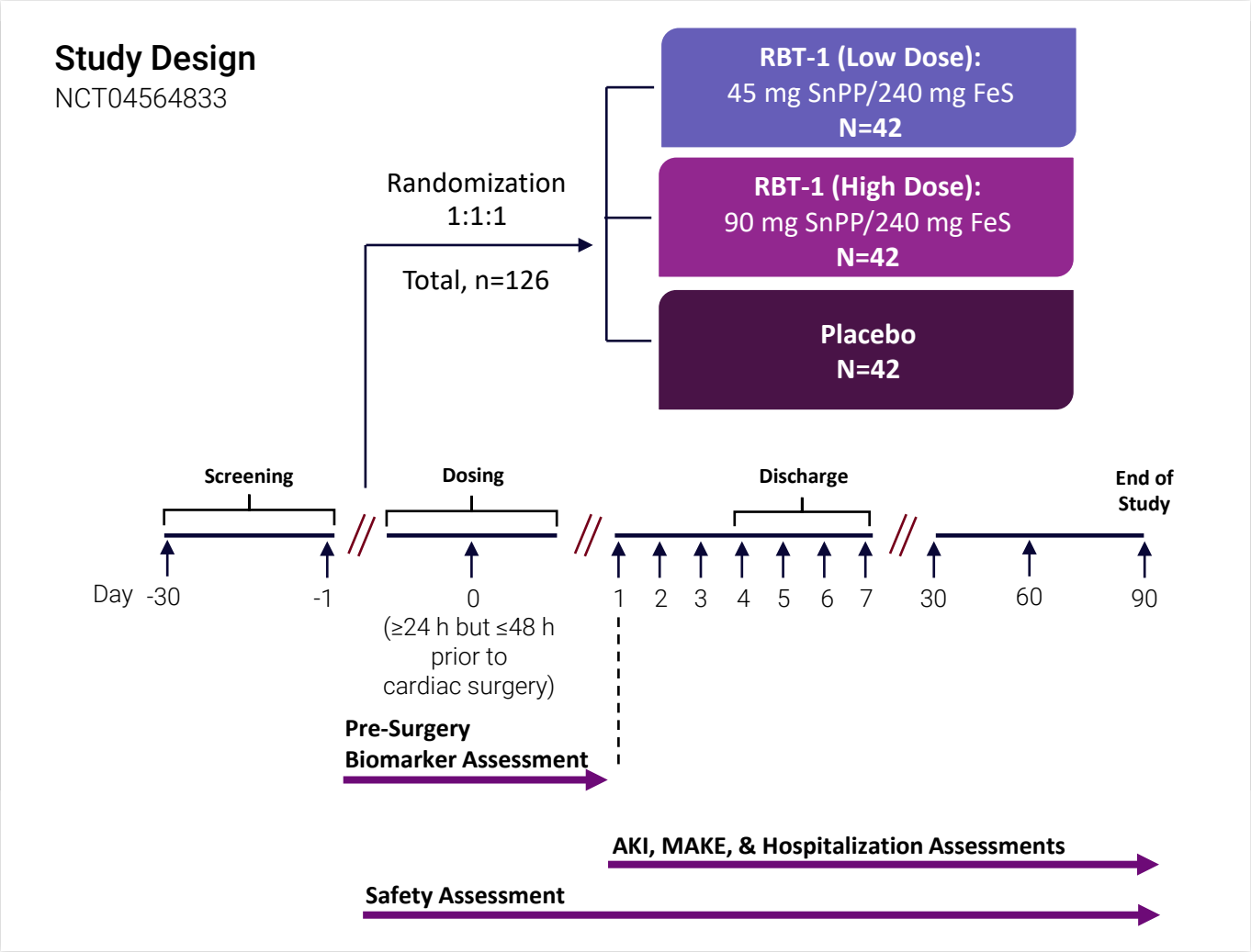
Randomized, double-blind, placebo-controlled, multi-center (US, Canada, Australia)

Primary Objective

Effect of RBT-1 in generating a **preconditioning response**, measured by a **composite of plasma biomarkers** (heme oxygenase-1 [**HO-1**], **ferritin**, and interleukin-10 [**IL-10**]) from Baseline (pre-dose)

Key Secondary and Exploratory Objectives

- Days on **ventilator**
- Days in intensive care unit (**ICU**)
- **Hospital length of stay**
- Incidence of acute kidney injury (**AKI**)
- Incidence of Major Adverse Kidney Events (**MAKE**)
- **Readmission rate**
- Safety



Phase 2 Interim Analysis Population

- The overall study population was **not** enriched for events
- The **efficacy population** included:
  - Subjects who **received study drug** and **underwent surgery without delay**
  - The **first 60 subjects** who **completed the Day 30 evaluation**
    - Placebo: N=22
    - Low Dose: N=18
    - High Dose: N=20
- The **safety population** included **all subjects who received study drug** (n=63)
    - Placebo, N=23
    - Low Dose, N=20
    - High Dose, N=20

Baseline Demographics

DEMOGRAPHICS	Placebo (N=23)	RBT-1 (N=40)
Mean Age (yrs)	66.5	66.3
Sex		
Female, N (%)	6 (26.1)	9 (22.5)
Male, N (%)	17 (73.9)	31 (77.5)
Race		
Black, N (%)	1 (4.3)	0
Asian, N (%)	1 (4.3)	2 (5.0)
White, N (%)	21 (91.3)	38 (95.0)
Time of Infusion Before Surgery		
N	22	39
Mean (hrs)	38.2	40.48
Surgery Type		
CABG Alone, N (%)	12 (52.2)	19 (47.5)
Valve Alone, N (%)	4 (17.4)	12 (30.0)
CABG + Valve, N (%)	7 (30.4)	9 (22.5)
Duration of Surgery		
N	22	39
Mean (hrs)	4.866	4.80
Time on Pump		
N	22	39
Mean (hrs)	1.842	1.95

Baseline Risk Factors

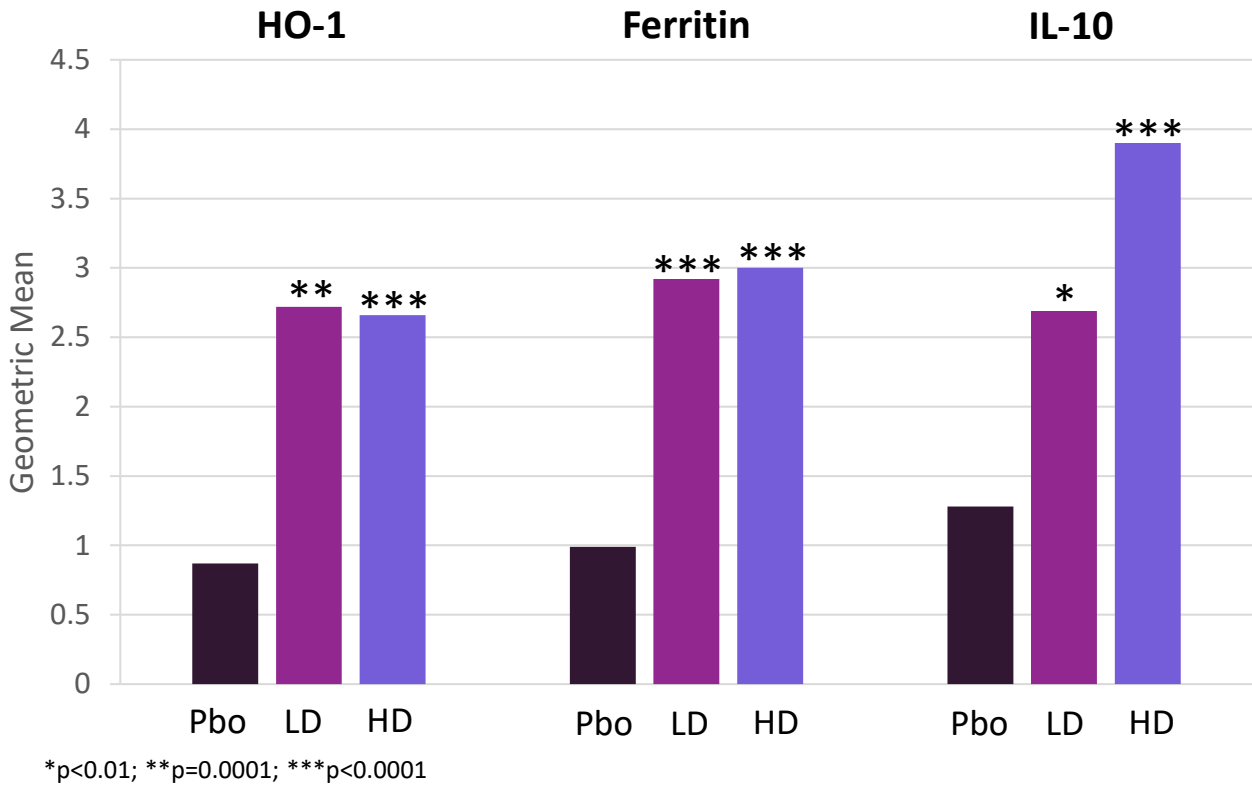
RISK FACTORS	Placebo (N=22)	RBT-1 (N=38)
Age ≥65 years	12 (54.5)	26 (68.4)
Combined CABG and valve surgery	7 (31.8)	9 (23.7)
Previous cardiac surgery with sternotomy	0 (0.0)	0 (0.0)
Documented heart failure (NHYA III/IV) within 1 year prior to surgery	0 (0.0)	3 (7.9)
LVEF ≤35%	1 (4.5)	4 (10.5)
Congestive heart failure	5 (22.7)	7 (18.4)
Diabetes mellitus requiring insulin	1 (4.5)	5 (13.2)
Pre-operative anemia (hemoglobin <10 g/dL upon screening)	1 (4.5)	0 (0.0)
Currently hospitalized for management of cardiac or pulmonary disease	4 (18.2)	5 (13.2)
eGFR ≥20 to <60 mL/min/1.73m^2	4 (18.2)	10 (26.3)

Statistically Significant Increase in Cytoprotective Response Biomarkers with Both Low Dose and High Dose RBT-1

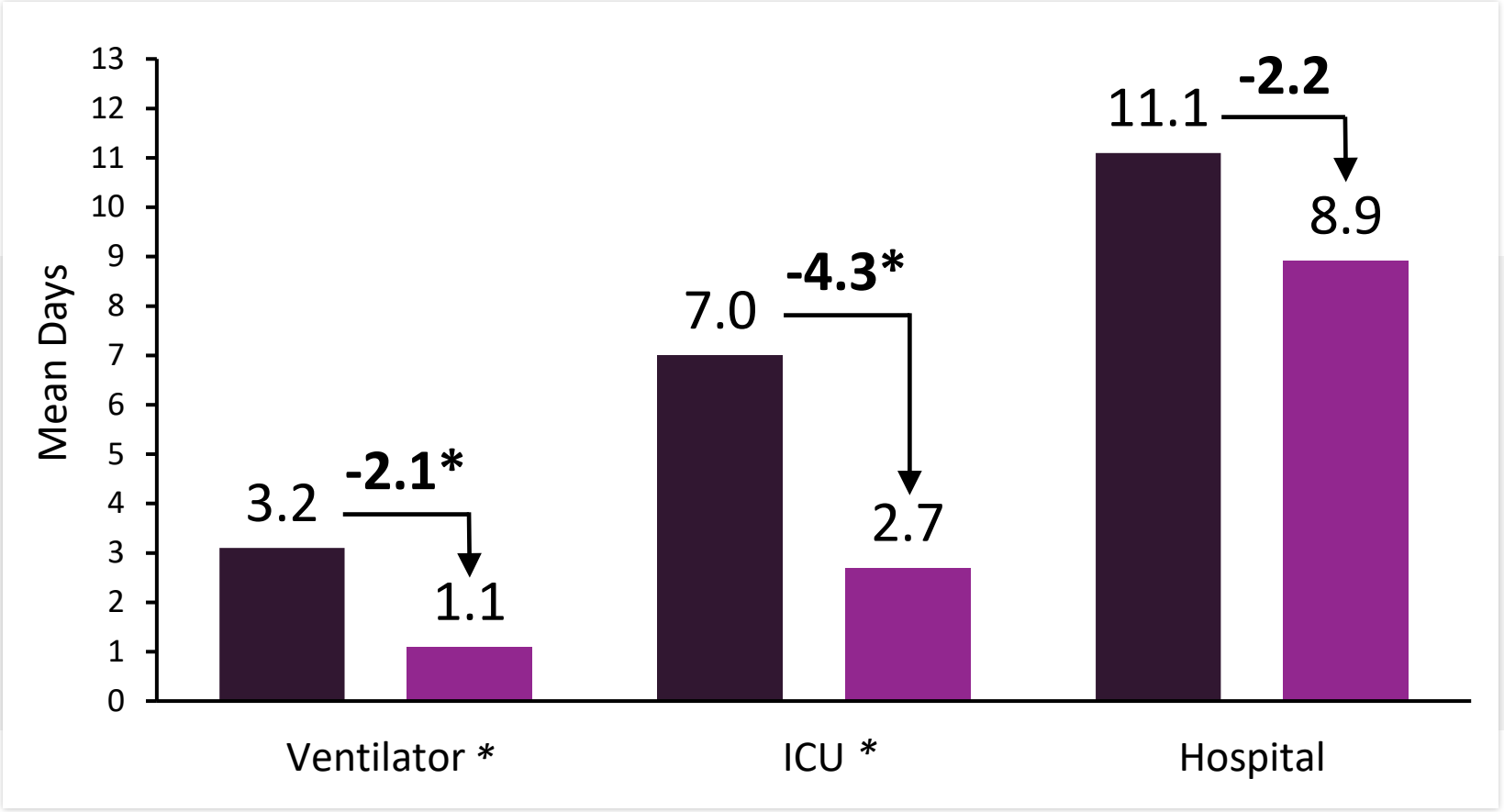
Primary Endpoint Met

Composite Biomarker Response

	Placebo (N=22)	Low Dose (N=18)	High Dose (N=20)
Mean	1.04	2.75	3.15
P-value vs Pbo		<0.0001	<0.0001

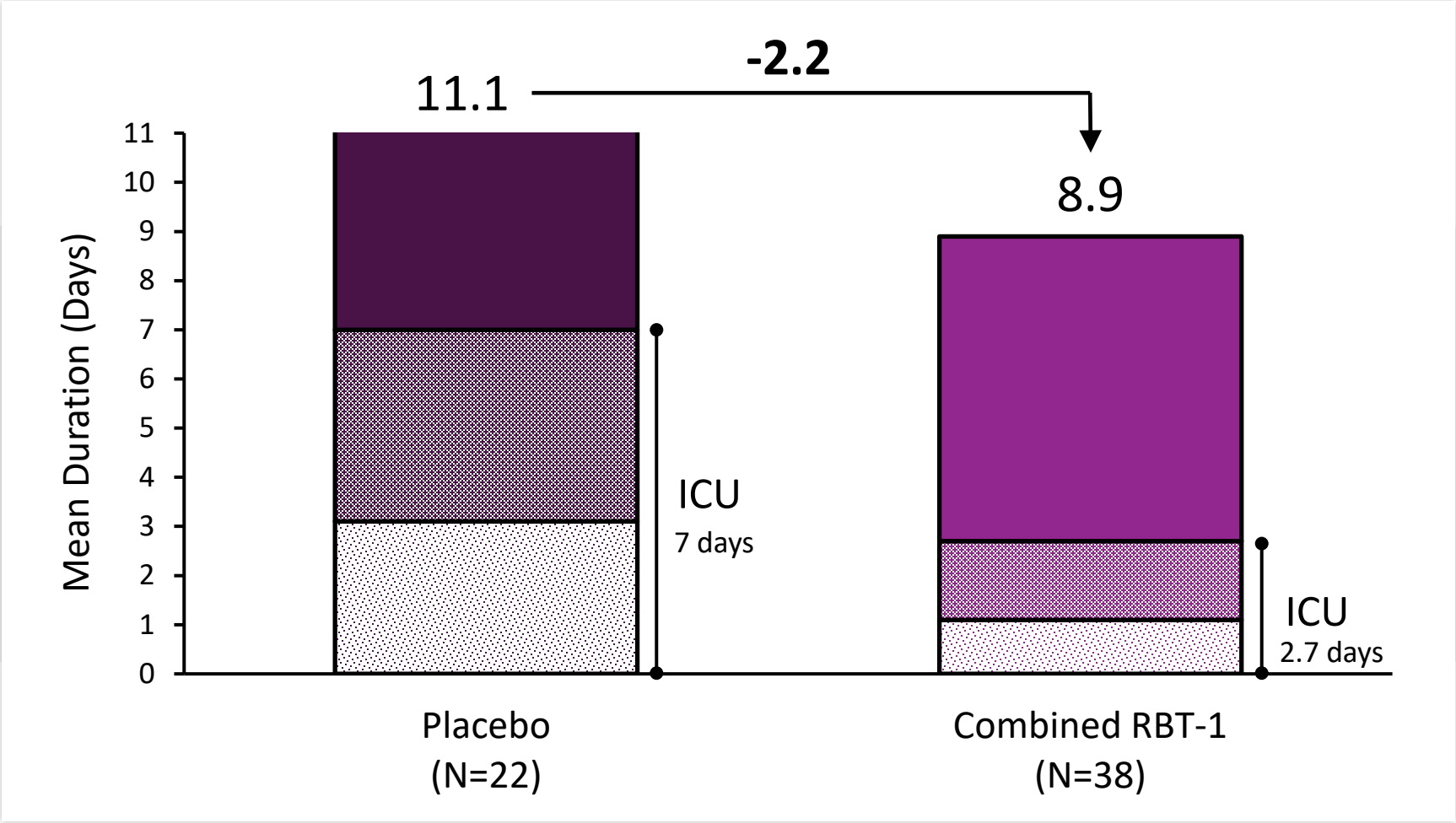


Statistically Significant Reduction in Ventilator and ICU Time in Patients Treated with RBT-1

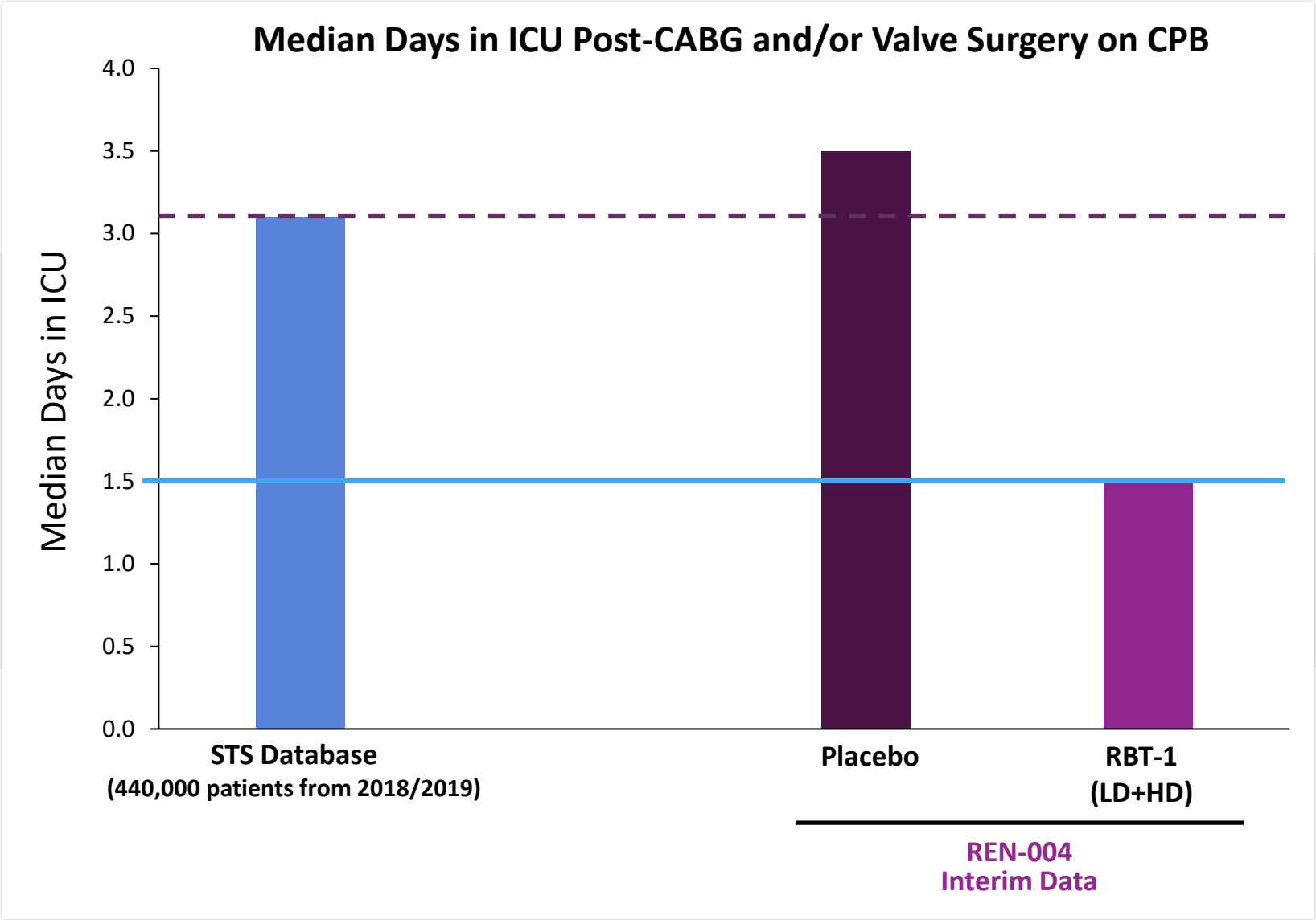


*p<0.05 vs placebo

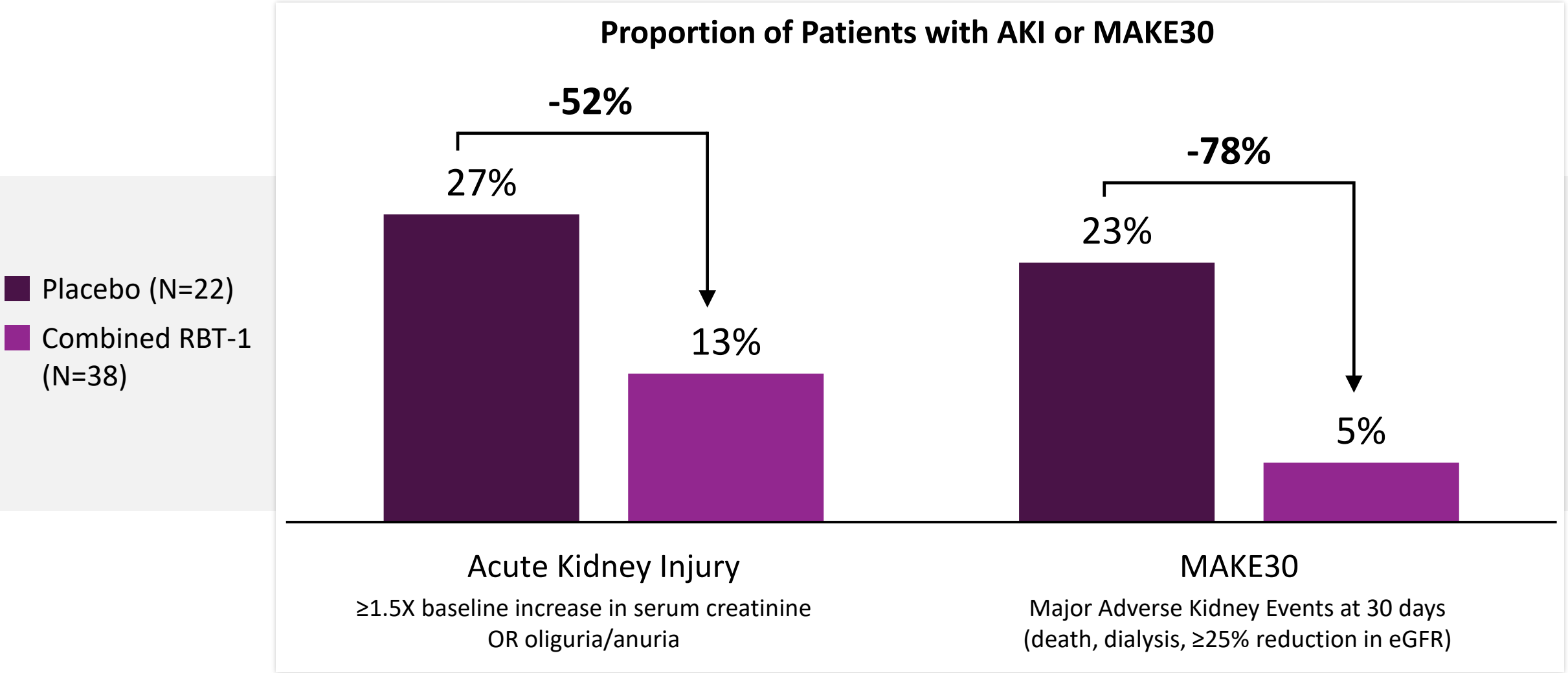
Improvement in Mean Duration and Composition of Hospitalization in Patients Treated with RBT-1



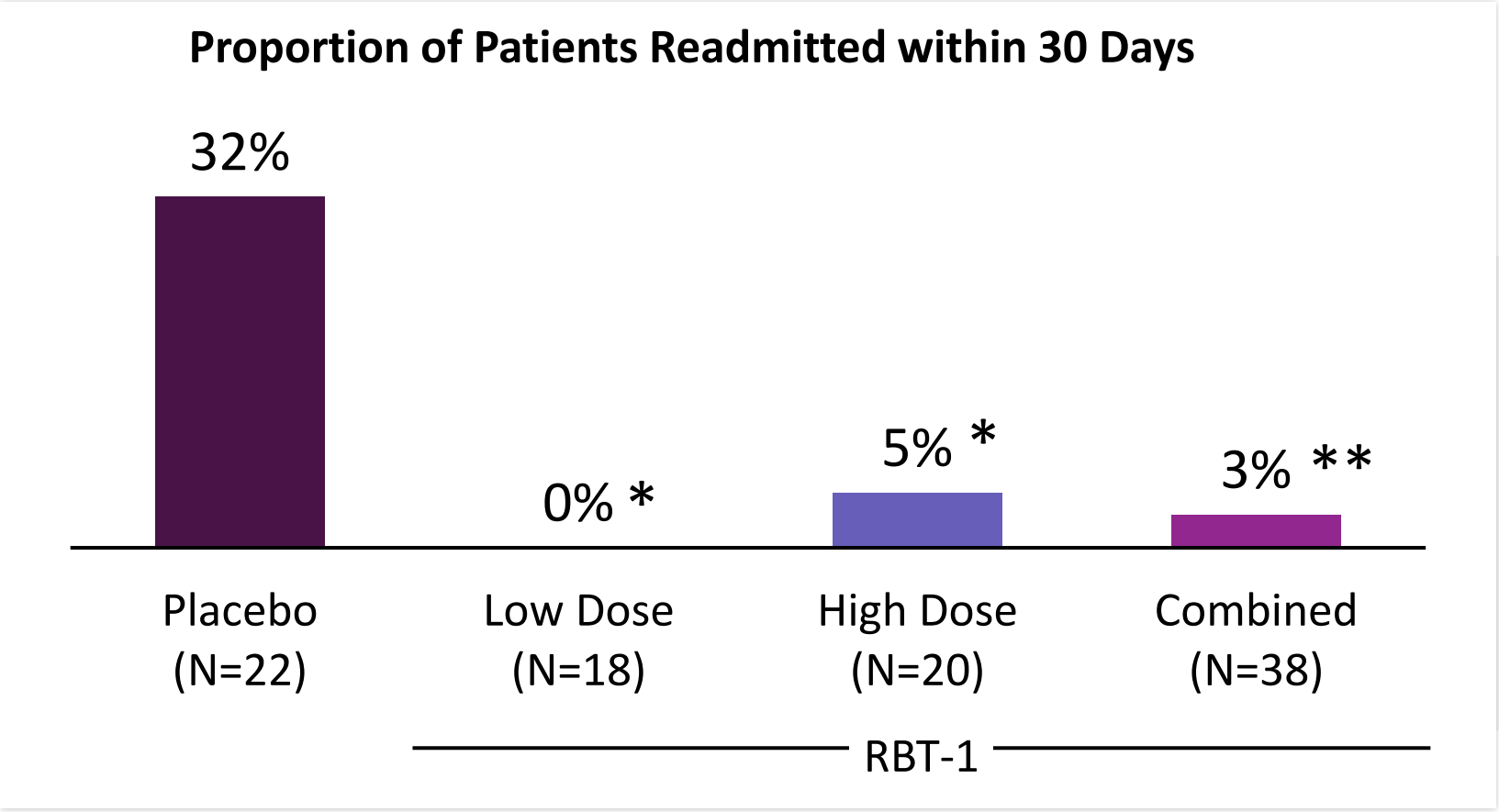
Median ICU Days in Placebo Group is Similar to Historical Control from STS Database



Clinically Meaningful Decrease in Rates of AKI and MAKE30 in Patients Treated with RBT-1



Statistically Significant Decrease in 30-Day Readmission Rates in Patients Treated with RBT-1



Readmissions were primarily due to cardiopulmonary reasons:

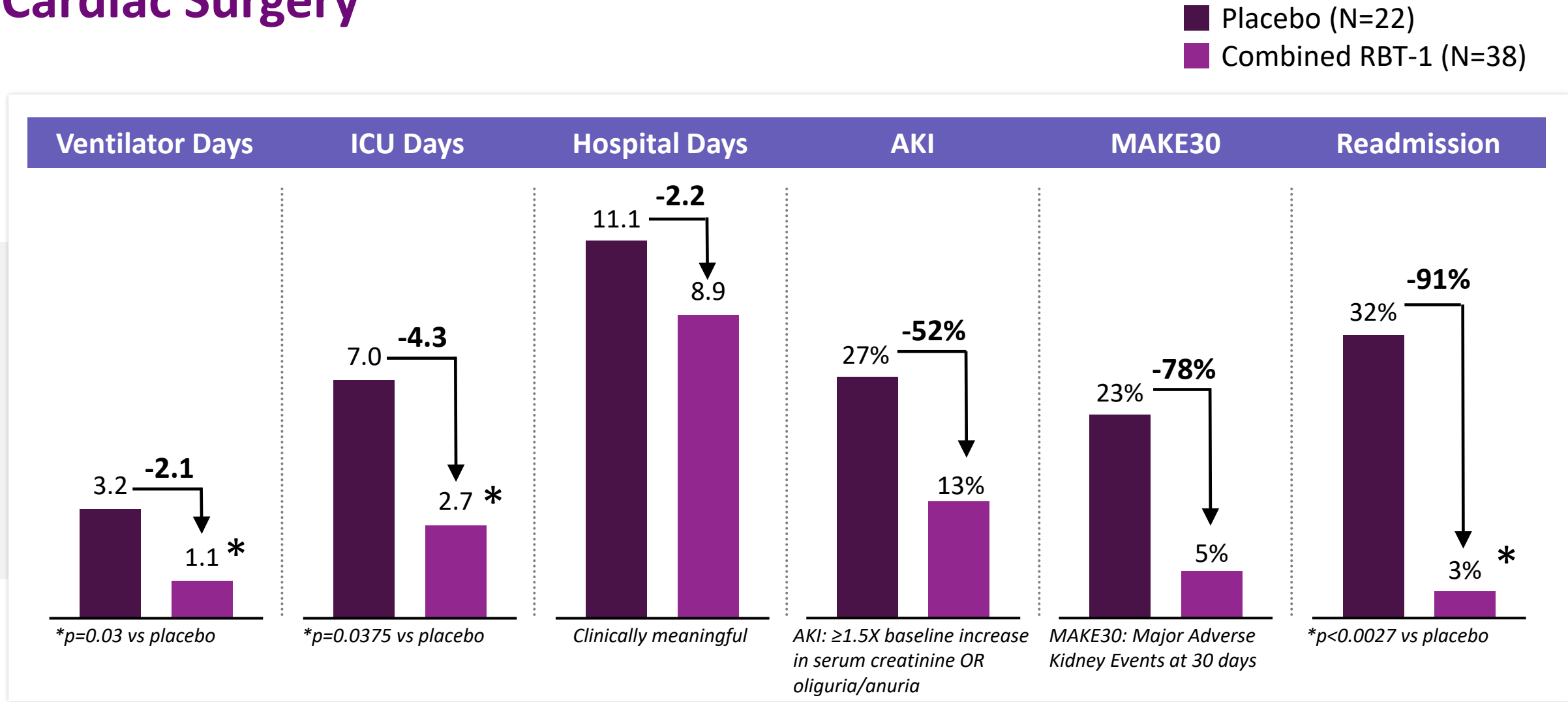
- *CHF/Worsening CHF*
- *Worsening pulmonary hypertension*
- *Pleural effusion*
- *Pericardial effusion*
- *Post-cardiotomy syndrome*
- *Left groin hematoma*

* *p<0.05 vs placebo*
** *p<0.003 vs placebo*

RBT-1 Safety Profile Demonstrates It Is Well Tolerated

- Related adverse events (AEs) **limited to photosensitivity**
  - Generally mild to moderate
  - Transient
  - Manifests primarily as pruritus and erythema (similar to a sunburn)
  - Resolves without the need for intervention
- **No treatment discontinuations** have occurred as a result of photosensitivity
- **Photosensitivity can be avoided** with proper use of sunscreen (SPF 30+) and avoidance of direct exposure to the sun, especially when sun rays are strongest

RBT-1 Improves Postoperative Outcomes in Patients Undergoing Cardiac Surgery



RBT-1 was recently granted Fast Track Designation from the FDA

Summary of RBT-1 Interim Phase 2 Study Data (N=60)

Statistically **significant increase in biomarkers** of cytoprotective preconditioning (primary endpoint; p<0.0001)

Statistically significant **reduction in ICU days and ventilator days** (p<0.05)

Clinically meaningful **reduction in hospital length of stay** (2-day reduction)

Clinically meaningful **decrease in rates of AKI** (-52%) and **MAKE30** (-78%)

Statistically significant **decrease in 30-day hospital readmission rates** (p<0.003)