mesoblast
the regenerative medicine company

Rexlemestrocel-L for Cardiovascular Diseases

Heart Failure Phase 3 Trial Top Line Results

January 2021

ASX: MSB; Nasdaq: MESO

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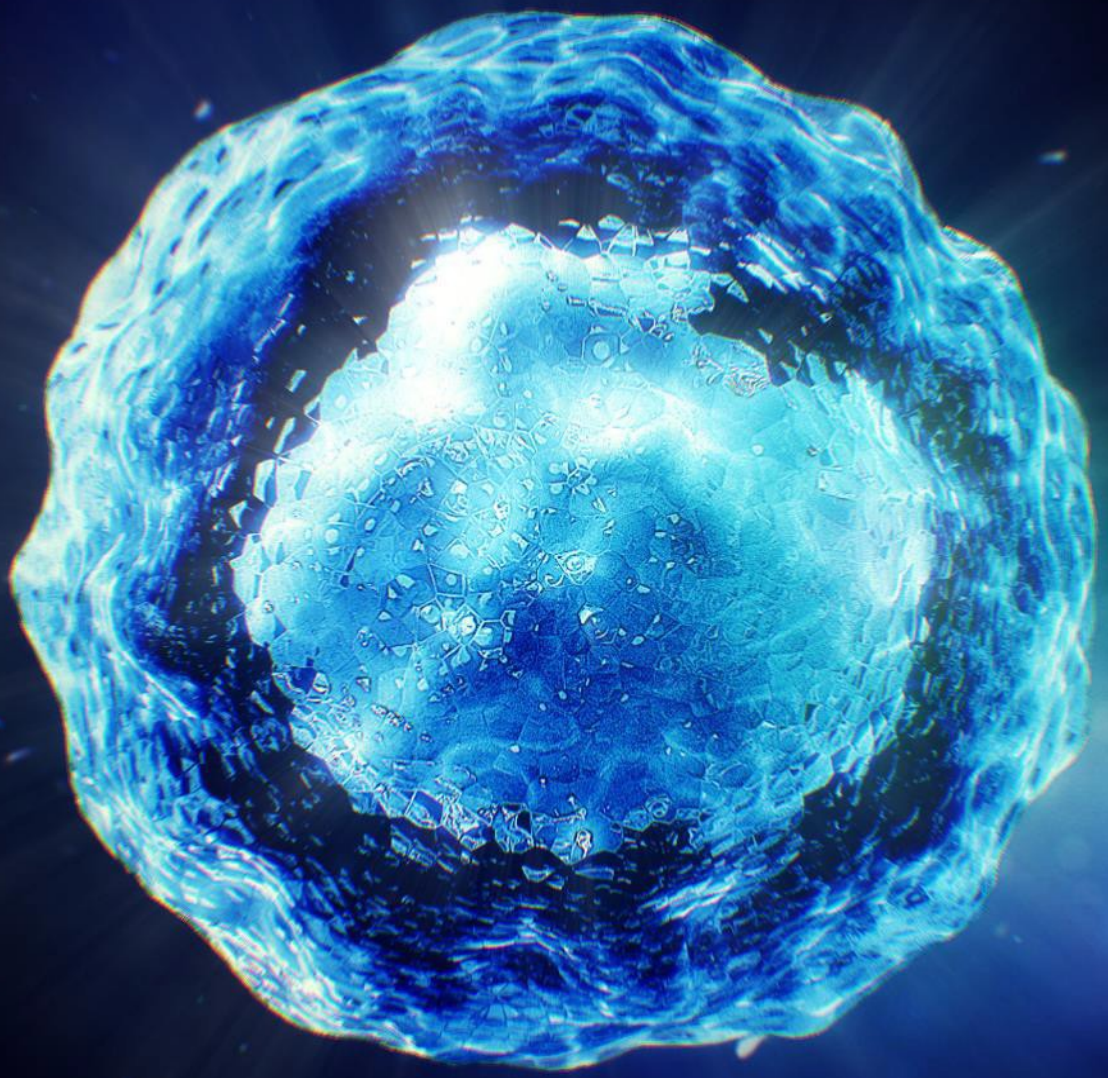
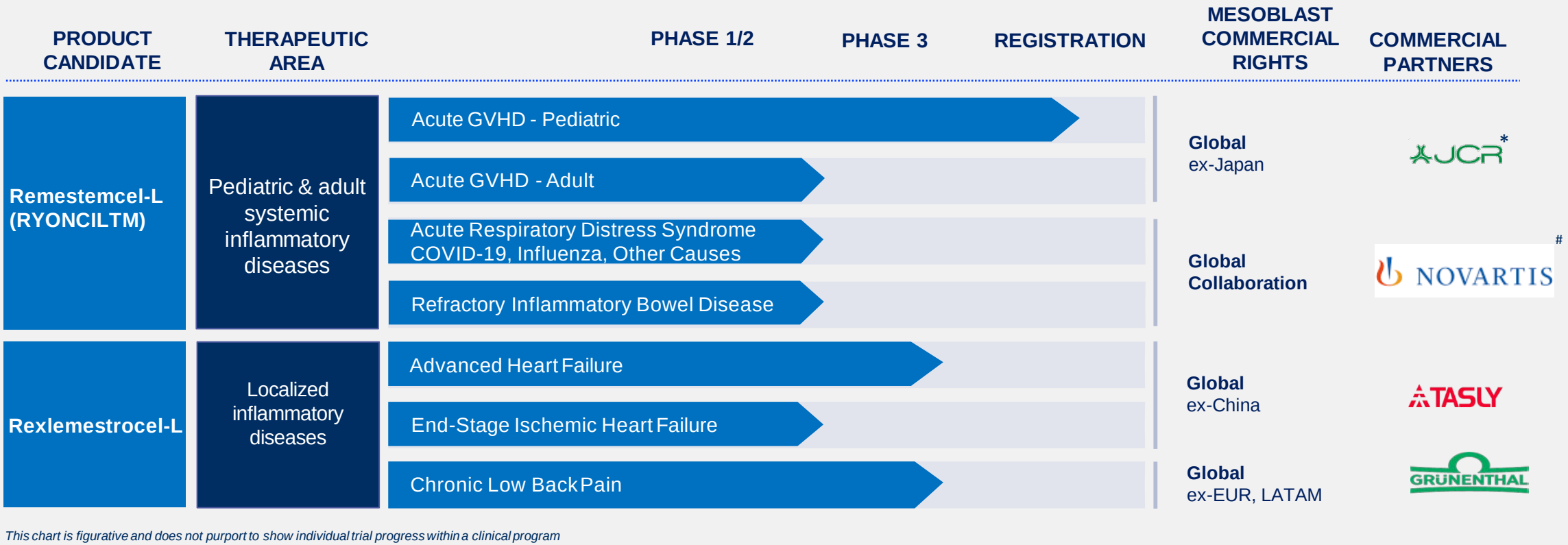
Our Mission

Mesoblast is committed to bringing to market innovative cellular medicines to treat serious and life-threatening illnesses



Product Pipeline



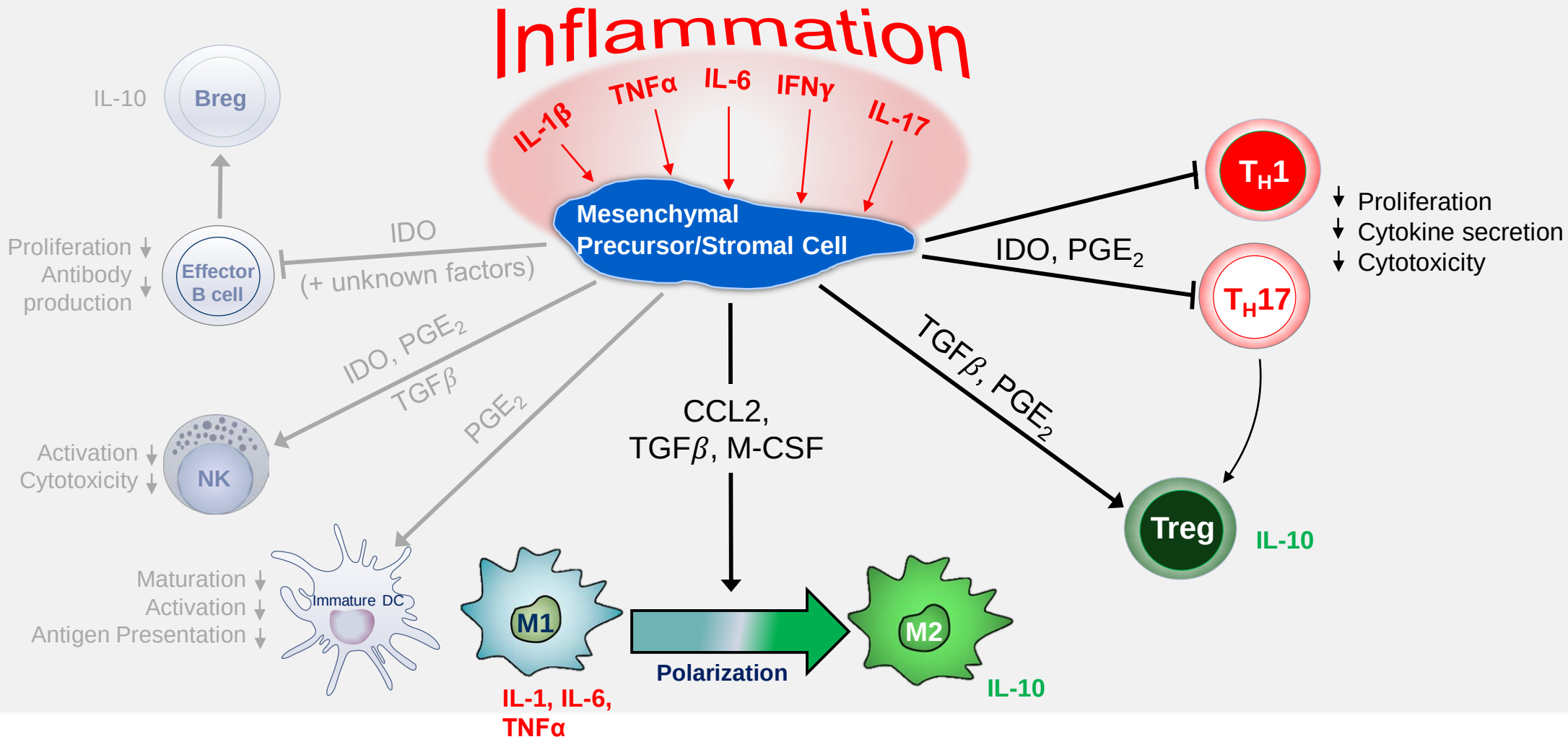
This chart is figurative and does not purport to show individual trial progress within a clinical program

* Mesoblast has the right to use data generated by JCR Pharmaceuticals Co Ltd in Japan to support its development and commercialization plans for remestemcel-L in the US and other major healthcare markets, including for GVHD, Hypoxic Ischemic Encephalopathy and Epidermolysis Bullosa

\# The closing of the license agreement is subject to the expiration or termination of the waiting period under the Hart-Scott-Rodino Antitrust Improvements Act and certain other conditions

Platform Technology – Mechanism of Action

Our mesenchymal precursor/stromal cells respond to and are activated by multiple inflammatory cytokines through surface receptors, resulting in orchestration of an anti-inflammatory cascade



Source: data on file

Global IP Estate Provides Substantial Competitive Advantage

- Extensive patent portfolio with protection extending through 2040 in all major markets
- Over 1,100 patents and patent applications (82 patent families) across all major jurisdictions
- Covers composition of matter, manufacturing, and therapeutic applications of mesenchymal lineage cells
- Provides strong global protection in areas of our core commercial focus against cell-based competitor products
- When outside our core commercial areas, may consider granting rights to third parties who require access to our patent portfolio to commercialize their products
- Mesoblast receives royalty income from its patent licensee TiGenix, S.A.U., a wholly owned subsidiary of Takeda, on its worldwide sales of its product Alofisel® for the treatment of complex perianal fistulas in adult patients with Crohn's disease, as well as milestone payments

Alofisel® is a registered trademark of TiGenix, S.A.U.

Commercial Scale Manufacturing Capability

- Scalable allogeneic “off-the-shelf” cellular platforms
- Manufacturing meets stringent criteria of international regulatory agencies
- Robust quality assurance processes ensure final product with batch-to-batch consistency and reproducibility
- Projected increase in capacity requirements for maturing pipeline

Manufacturing Remestemcel-L

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- ➢ Proprietary xeno-free technologies will increase yields and output
- ➢ Moving to 3D bioreactors will reduce labor and improve manufacturing efficiencies
- ➢ These innovations will significantly reduce cost of goods

Overview of Collaboration with Novartis for Remestemcel-L

- Worldwide license and collaboration agreement with Novartis for the development, manufacture and commercialization of remestemcel-L*
- Initial focus is on the treatment of acute respiratory distress syndrome (ARDS) and other respiratory conditions
- Novartis intends to initiate a Phase 3 study in non-COVID-19-related ARDS after the anticipated closing of the license agreement and outcome of the current COVID-19 ARDS study
- Mesoblast will retain full rights and economics for remestemcel-L for graft versus host disease (GVHD), and Novartis has an option to, if exercised, become the commercial distributor outside of Japan
- For most non-respiratory indications, the parties may co-fund development and commercialization on a 50:50 profit-share basis

* The closing of the license agreement is subject to the expiration or termination of the waiting period under the Hart-Scott-Rodino Antitrust Improvements Act and certain other conditions

SR-aGVHD Regulatory & Commercial Update

- On August 13 2020, results from 309 children with steroid refractory acute graft versus host disease (SR-aGVHD) treated with remestemcel-L were presented to the Oncologic Drugs Advisory Committee (ODAC) of the United States Food and Drug Administration (FDA)
- The ODAC panel voted 9:1 that the available data support the efficacy of remestemcel-L in pediatric patients with SR-aGVHD*
- Despite the overwhelming ODAC vote, on September 30, the FDA provided Mesoblast with a Complete Response Letter
- Mesoblast intends to meet with the FDA during Q1 CY2021 through a well-established process for continuing discussions on the potential for accelerated approval with a post-approval commitment to conduct an additional randomized controlled study

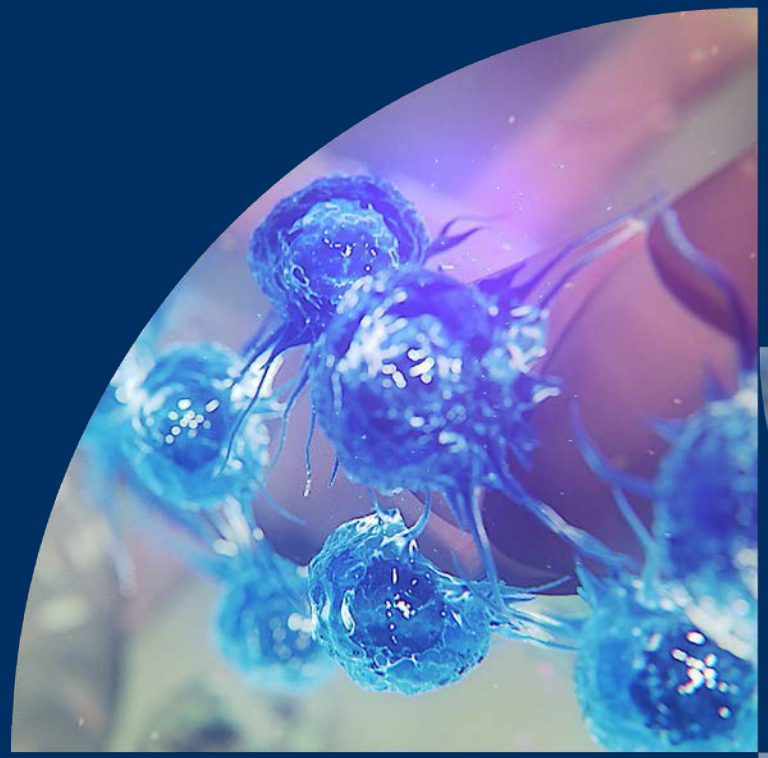
* This vote includes a change to the original vote by one of the ODAC panel members after electronic voting closed

MPC-06-ID for Chronic Low Back Pain

- Phase 3 trial of MPC-06-ID for chronic low back pain in 404 patients:
  - Final study visits for all patients have been completed
  - Ongoing quality review of all data is being completed at the study sites
  - Data readout expected shortly

- Continued operational progress in strategic partnership for chronic lower back pain with Grünenthal in Europe to complete clinical protocol design, obtain regulatory input, and receive clearance from European regulatory authorities to begin European Phase 3 trial

- Results from the Phase 3 trials will be considered pivotal to support regulatory approval in the US, as well as in Europe



DREAM HF

- Phase 3 Trial in Chronic Heart Failure
- Rexlemestrocel-L Mechanism of Action

Chronic Heart Failure: Rising Incidence & High Mortality

- Cardiovascular disease (CVD) remains the leading cause of death in the United States[1]
- Heart failure affects 6.5 million patients in the US and 26 million patients globally. As populations age, the prevalence is increasing[2]
- Chronic heart failure is a progressive disease with a high mortality that approaches 50% at 5 years[2,3], and at least 75% after an initial hospitalization[4]
- Patients with heart failure are also at high risk of recurrent major adverse cardiac events involving large vessels (heart attacks / strokes)
- New therapies for chronic heart failure reduce recurrent hospitalizations due to cardiac decompensation, however they do not materially improve cardiac mortality or major ischemic events (heart attacks/strokes)

1. Muntner BEJ, et al. Heart Disease and Stroke Statistics-2019 Update: A Report From the American Heart Association. *Circulation.* Feb 19, 2019. 2. United States Food & Drug Administration. Treatment for Heart Failure: Endpoints for Drug Development. Draft Guidance. June 2019. 3. Taylor CJ, et al. Trends in survival after a diagnosis of heart failure in the United Kingdom 2000-2017: population based cohort study. *BMJ.* 2019;364:I223. 4. Shah KS, et al. Heart Failure with Preserve, Borderline, and Reduced Ejection Fraction; 5-Year Outcomes. *JACC.* 2017;Nov12.

Myocardial Infarction & Stroke in Chronic Heart Failure: Current Unmet Needs

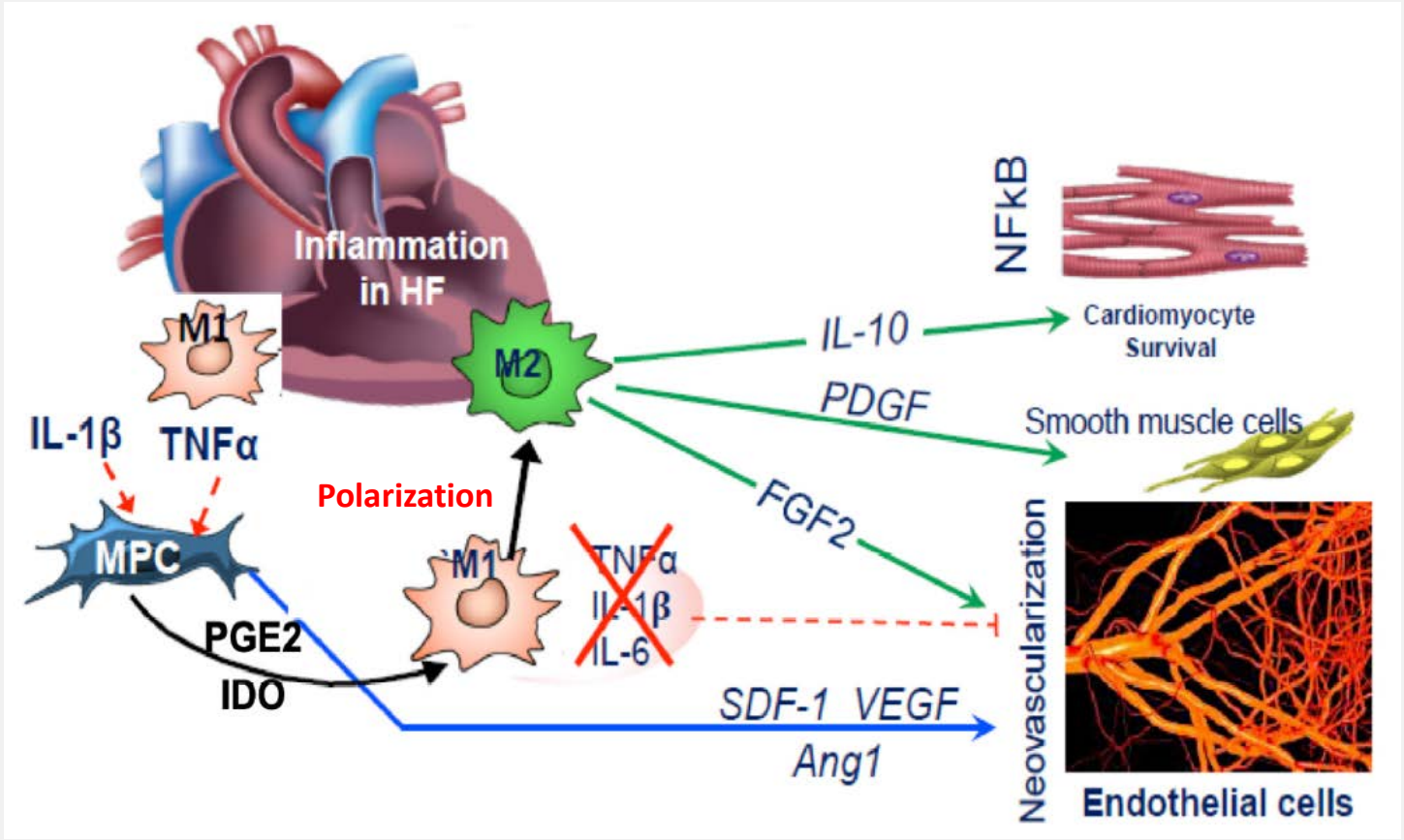
- Each year in the United States approx. 805,000 people suffer from a myocardial infarction (heart attack) and approx. 795,000 people experience a new or recurrent stroke[1]
- A major consequence of a heart attack is chronic heart failure, and patients with chronic heart failure are at higher risk of recurrent heart attacks and strokes[2]
- Atherosclerosis is a chronic inflammatory condition associated with endothelial dysfunction[3]
- Cardiovascular complications associated with atherosclerosis in chronic heart failure patients may respond to potent anti-inflammatory therapeutic approaches

1. Virani ss, et al. Heart Disease and Stroke Statistics-2020 Update: A Report From the American Heart Association. *Circulation.* Jan 29, 2020 2. Kim W, Kim EJ. Heart Failure as a Risk Factor for Stroke. J Stroke. 2018 Jan;20(1):33-45. 3. Frostegard J. Immunity, atherosclerosis and Cardiovascular Disease. *BMC Med*. 2103;11:117.

Proposed Mechanism of Action of Intra-Cardiac MPC Administration in Treatment of both Heart Failure & Large Vessel Atherosclerosis

Mesenchymal precursor cells (MPC) key mechanisms of action thought to beneficially impact the heart and the systemic vasculature:

- Reduction in cardiac and systemic inflammation
- Reversal of endothelial dysfunction
- Induction of microvascular network within viable heart muscle
- Reduction in heart muscle death



Borow KM, Yaroshinsky A, Greenberg B, Perin E. Phase 3 DREAM-HF Trial of Mesenchymal Precursor Cells in Chronic Heart Failure: A Review of Biological Plausibility and Implementation of Flexible Clinical Trial Design. *Circ Res.* 2019;125:265-281

Rexlemestrocel-L for Chronic Heart Failure

Treatment Algorithm in Progressive Heart Failure

Progressive Vascular (Endothelial) Dysfunction and Heart Failure

Early

- ACEI or ARB
- Statins
- Beta blockers
- Re-vascularization or valvular surgery

Mesoblast Target Market
Chronic Heart Failure[1]

↓ ***Cardiac Death / Heart Attack / Stroke***

Class I | **Class II** | **Class III** | **Class IV**

Pharmacological Add-on

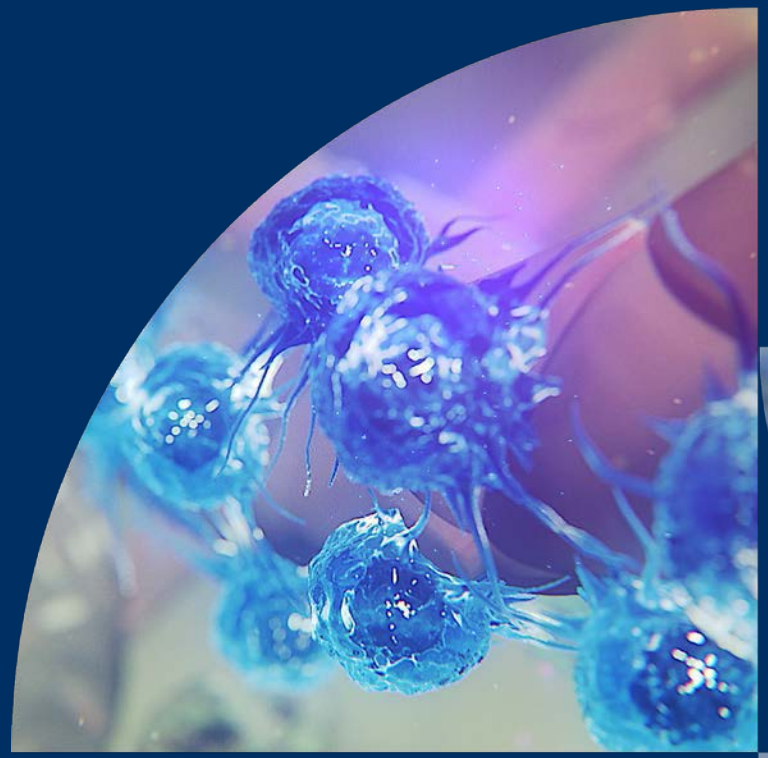
- Diuretics for fluid retention
- Aldosterone antagonists
- Hydralazine / isosorbide dinitrate
- Digitalis

New Oral Therapies for Class II

↓ ***Decompensated Hospitalization Events***

- sacubitril / valsartan
- SGLT2 inhibitors

1. GlobalData-PharmaPoint Heart Failure (2016); McMurray et al., 2012;Yancy et al., 2013, 2016 ACC/AHAHFSA Focused Update on New Pharmacological Therapy for Heart Failure: An Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure.



DREAM HF

- **Phase 3 Trial in Chronic Heart Failure**
- **Rexlemestrocel-L vs Sham Clinical Outcomes**

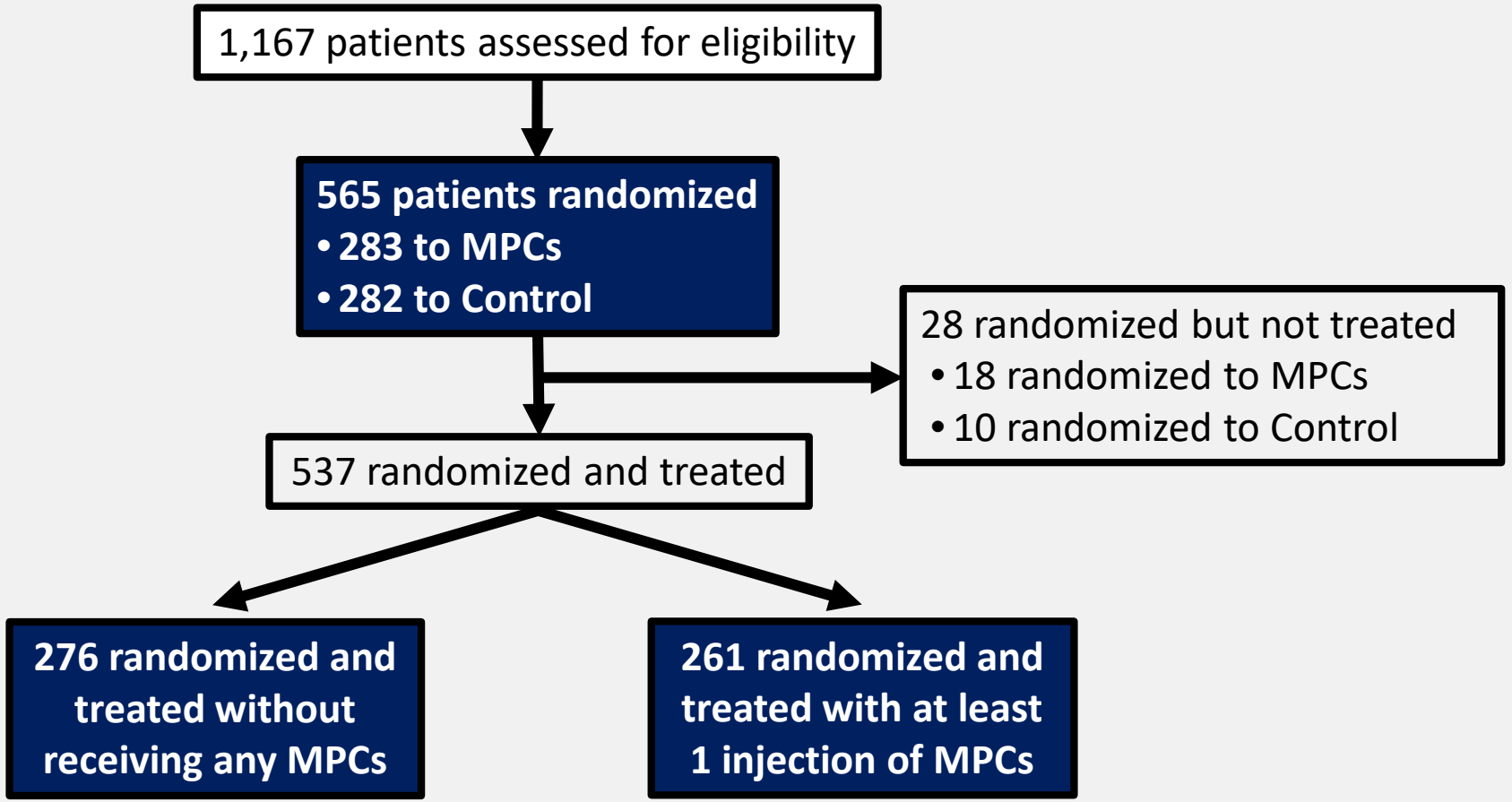
DREAM HF: Overview of Phase 3 Trial

- Mesoblast's allogeneic cell therapy rexlemestrocel-L has a dual mechanism of action that involves immunomodulation and improvement in blood vessel integrity/function
- DREAM-HF Phase 3 trial was designed to evaluate whether rexlemestrocel-L could improve morbidity and mortality in advanced chronic heart failure patients
- Trial design: 1:1 randomized, controlled, double blinded; conducted over 55 sites across North America using 150 million cell dose vs control in 565 patients
- Primary endpoint: reduction in recurrent heart failure-related hospitalizations
- Additional pre-specified key clinical endpoints:
  - Reduction in ischemic cardiovascular events (heart attack / stroke)
  - Reduction in recurrent hospitalizations due to ischemic events (heart attack / stroke)
  - Reduction in death due to cardiac causes
  - Major Adverse Cardiac Events (MACE: heart attack, stroke or cardiac death)

DREAM HF: Patient Flow

Intent-to-Treat (ITT) Randomized Patient Population N = 565 Pts.

Full Analysis Set (FAS) Actual Treatment Patient Population N = 537 Pts.

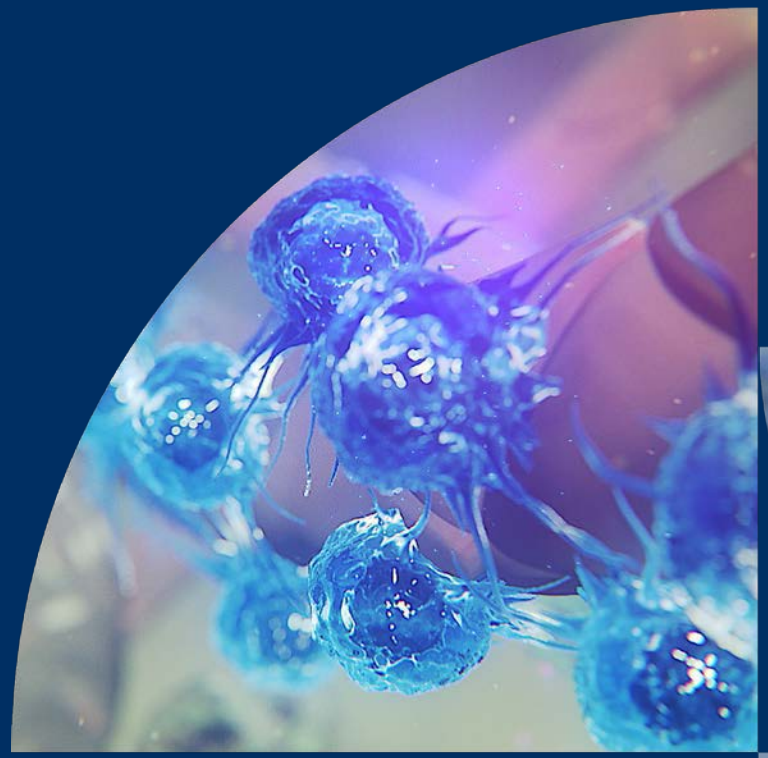


DREAM HF: Baseline FAS Summary Data by NYHA CLASS II or III

Parameter	Units	TOTAL (n=537)		NYHA II		NYHA III	
NYHA Functional Class	Number, %			206	**38.4%**	331	**61.6%**
II	Number, %	206	38.4%				
III	Number, %	331	61.6%				
Age (537 unique subjects)	Yrs (mean)	**62.7**	64.0	**62.2**	63.0	**63.1**	65.0
Sex (537 unique subjects)*							
Males	Number, %	428	**79.7%**	168	**81.6%**	260	**78.5%**
Females	Number, %	109	**20.3%**	38	**18.4%**	71	**21.5%**
Race (537 unique subjects)							
White	Number, %	414	**77.1%**	166	**80.6%**	248	**74.9%**
Black	Number, %	99	**18.4%**	34	**16.5%**	65	**19.6%**
Asian	Number, %	7	1.3%	2	1.0%	5	1.5%
Other	Number, %	17	3.2%	4	1.9%	13	3.9%
Ethnic Group (537 unique subjects)							
Hispanic	Number, %	34	**6.3%**	11	**5.3%**	23	**6.9%**
Blood pressure							
Systolic	mmHg (mean)	**117.1**	114.0	117.2	116	117	113
Diastolic	mmHg (mean)	**70.2**	70.0	71.2	71	69.5	68
Heart rate	Beats/min (mean)	**72.3**	71.0	70.9	70	73.1	71
Body weight	kg (mean, median)	92.8	90.9	91.8	89.2	93.4	92.5

DREAM HF: Baseline FAS Summary Data by NYHA CLASS II or III

Parameter	Units	TOTAL (n=537)		NYHA II		NYHA III	
Non-Ischemic vs Ischemic Cardiomyopathy (per baseline CRF)							
Ischemic	Number, %	303	**56.4%**	111	**53.9%**	192	**58.0%**
Non-ischemic	Number, %	234	**43.6%**	95	**46.1%**	139	**42.0%**
Past Myocardial infarction	Number, %	280	**52.1%**	106	51.5%	174	52.6%
Coronary revascularization							
Previous PCI and/or CABG (unique subjects)	Number, %	307	**57.2%**	119	**57.8%**	188	**56.8%**
Echocardiographic Imaging	(530 unique subjects)						
Left ventricular ejection fraction	% (mean, median)	**28.6**	28.6	**28.6**	29.0	**28.6**	28.5
Left ventricular end-systolic volume	mL (mean, median)	149.8	135.9	155.4	137.4	146.2	135.0
<= 100	number, %	101	18.8%	41	19.9%	60	18.1%
> 100	number, %	429	**79.9%**	163	**79.1%**	266	**80.4%**
missing	number, %	7	1.3%	2	1.0%	5	1.5%
Left ventricular end-diastolic volume	mL (mean, median)	**206.5**	194.0	213.1	193.7	202.3	194.3
6MWT distance (537 unique subjects)	m (mean, median)	**331.5**	340.5	**356.8**	367	**311.7**	329.2
Biomarkers							
NT-proBNP	pg/mL (mean, median)	**2166**	1400	**1809**	1322	**2390**	1458
hsCRP	mg/L (mean, median)	**5.3**	**2.5**	**3.6**	**2**	**6.4**	**3.3**
AICD without CRT	Number, %	245	**84.0%**	99	**81.6%**	146	**85.5%**
CRT-D	Number, %	206		69		137	
Laboratory measurements							
Sodium	mequiv/L (mean)	**139.5**	140.0	139.5	140.0	139.6	140.0
Potassium	mequiv/L (mean)	**4.5**	4.5	4.5	4.5	4.5	4.5
Creatinine	mg/dL (mean)	**1.2**	1.1	1.1	1.1	1.3	1.2
BUN	mg/dL (mean)	24.2	21.0	22.7	20.5	25.2	22.0
HbA1c	% (mean)	**6.4**	6.1	6.3	6.0	6.4	6.2
Hemoglobin	g/dL (mean)	**13.6**	13.7	13.8	13.9	13.5	13.5
Hematocrit	% (mean)	**41.8**	41.8	42.3	42.4	41.5	41.1



DREAM HF

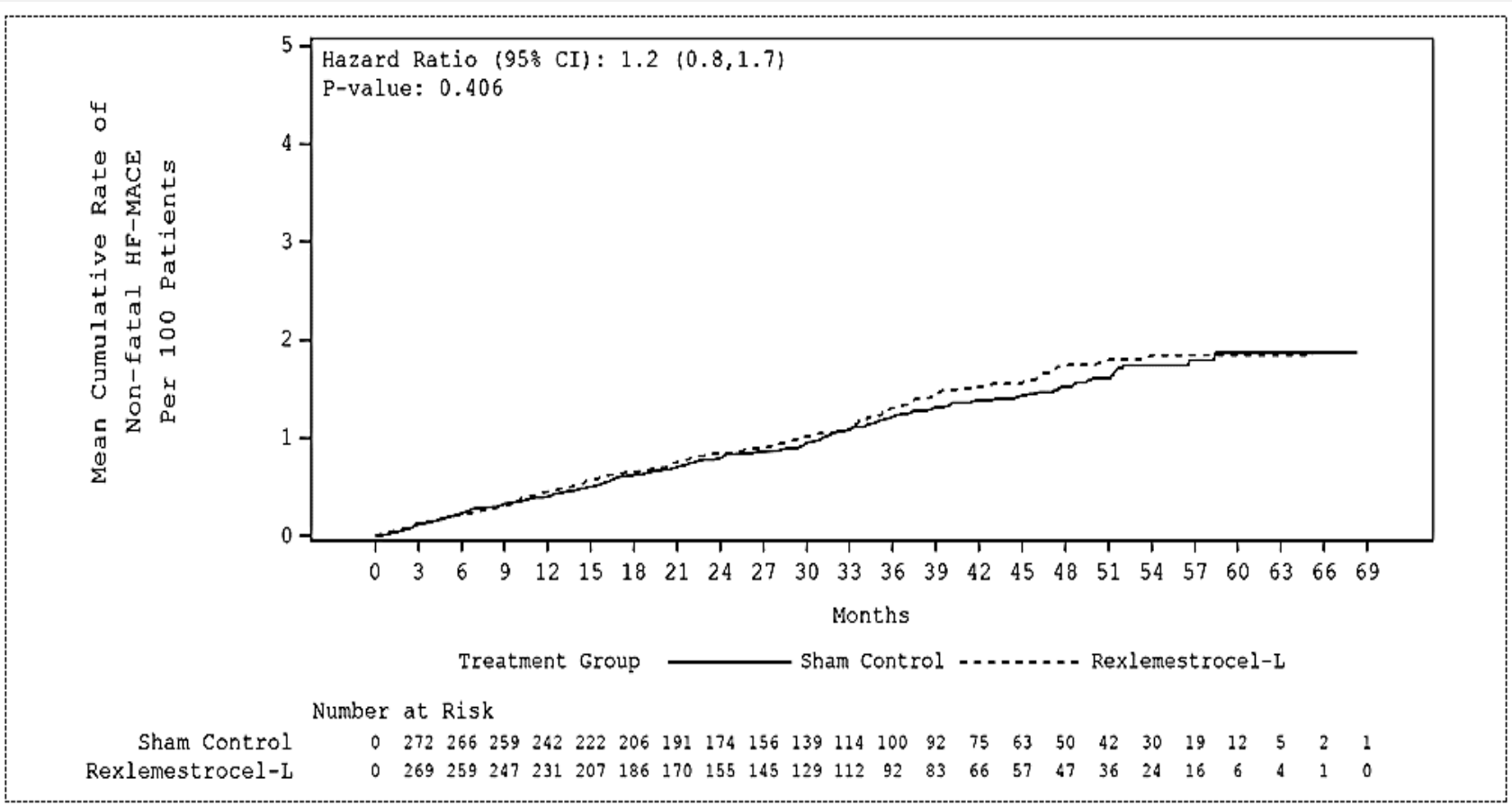
- Recurrent Decompensated Heart Failure Hospitalization Events
- Non-Fatal Ischemic MACE (Heart attacks or Strokes)

Rexlemestrocel-L Did Not Reduce Non-Fatal Heart Failure MACE (Recurrent Decompensated Heart Failure Events or High-Grade Arrhythmias)

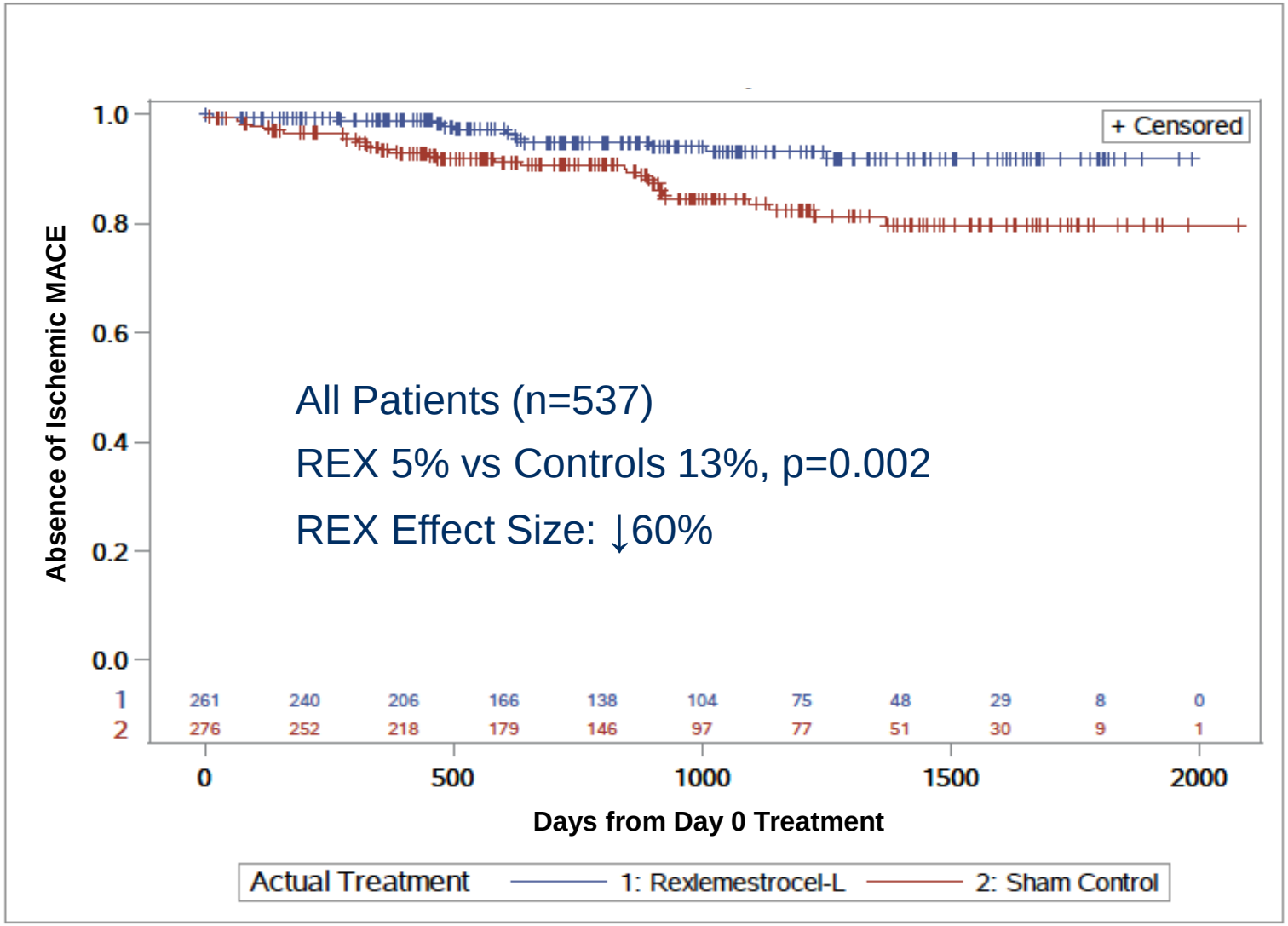
All Patients (n=537)

HR: 1.2

p=0.4



Rexlemestrocel-L Significantly Reduced Incidence of Ischemic MACE (MI, Stroke) by 60% Relative to Controls (n=537 Patients)

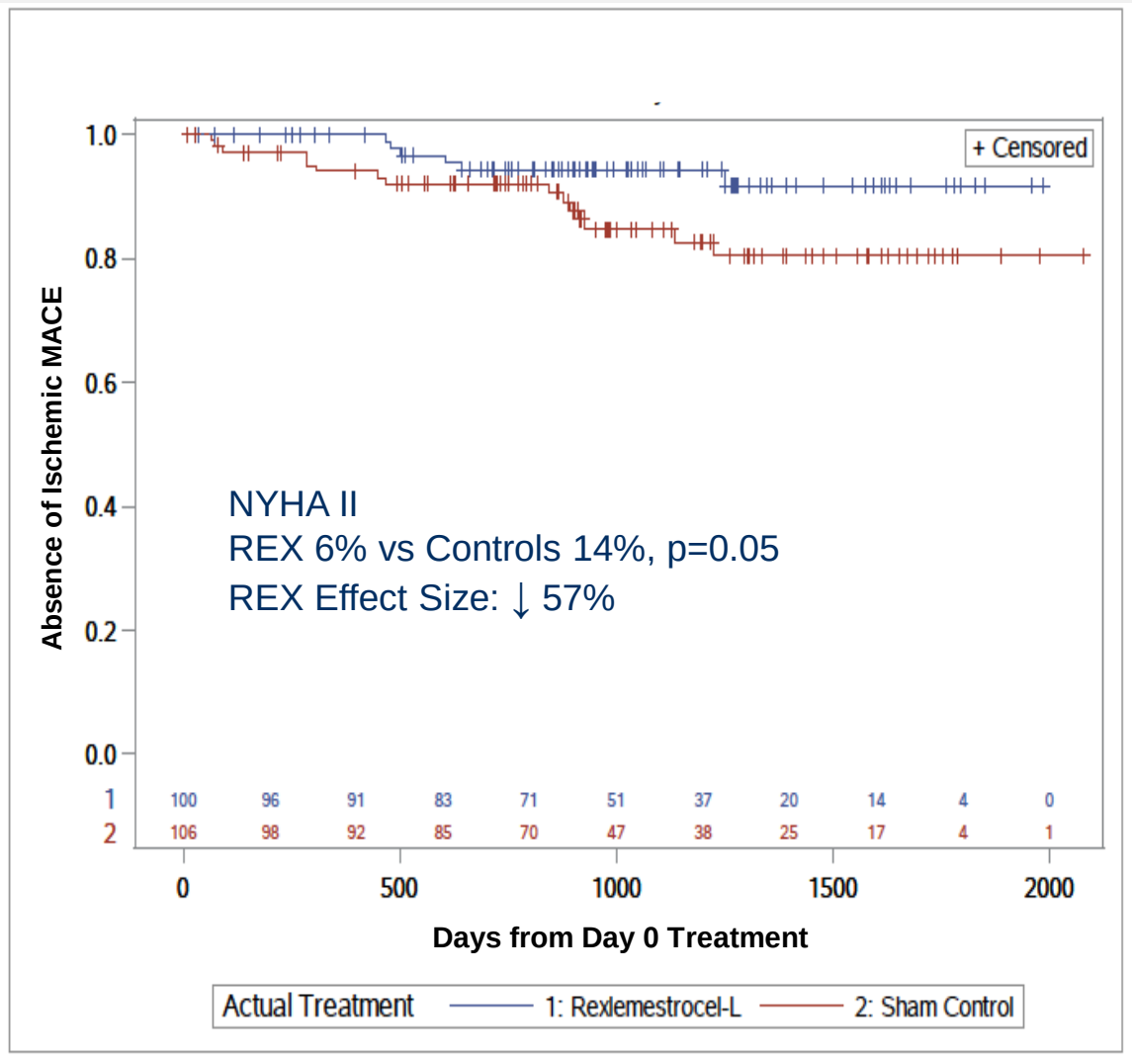


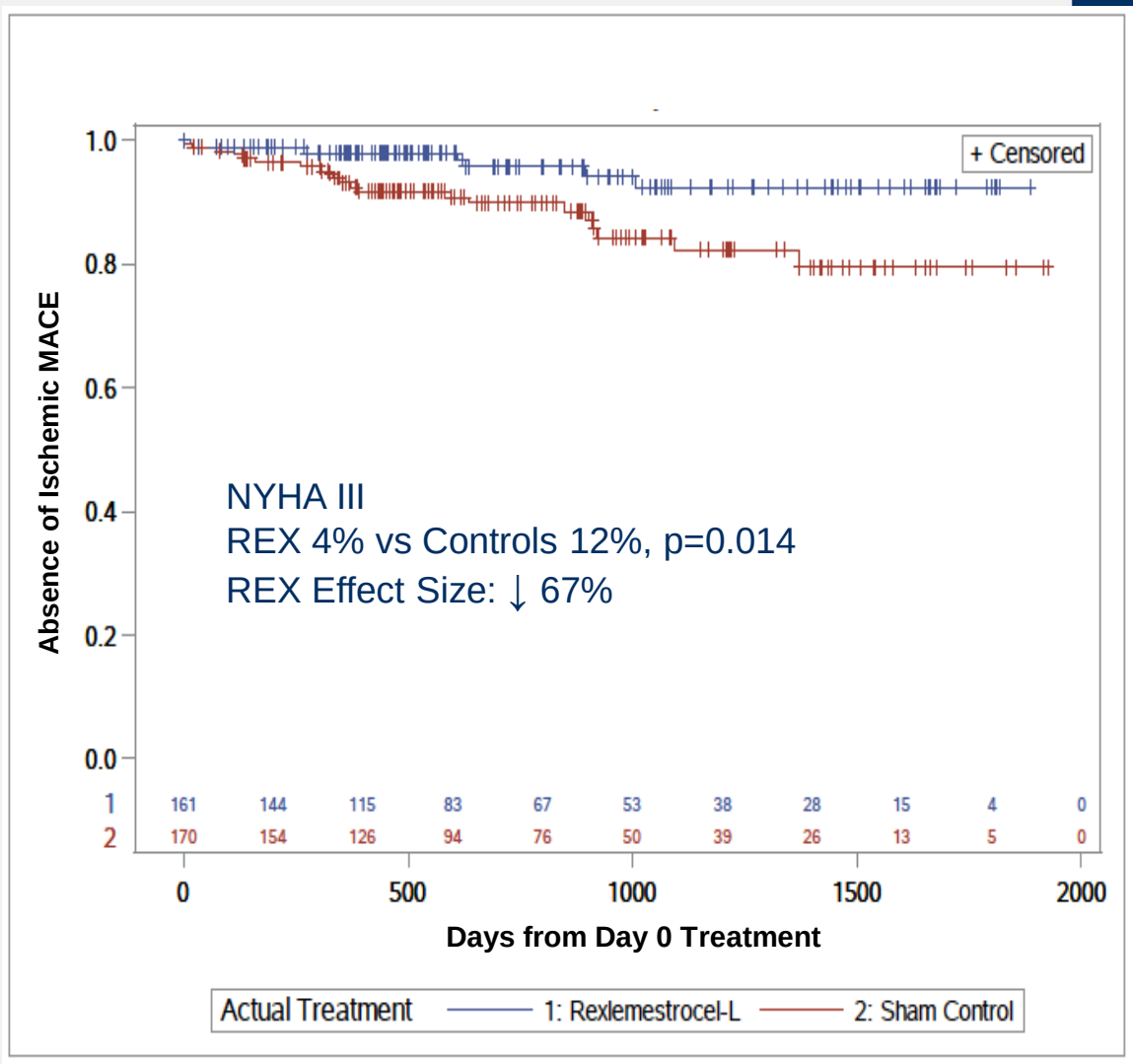
Elevated Baseline CRP Levels Predict Rexlemestrocel-L Benefit on Incident Heart Attacks or Strokes … Consistent with Anti-Inflammatory MOA

Myocardial Infarction or Cerebrovascular Accident

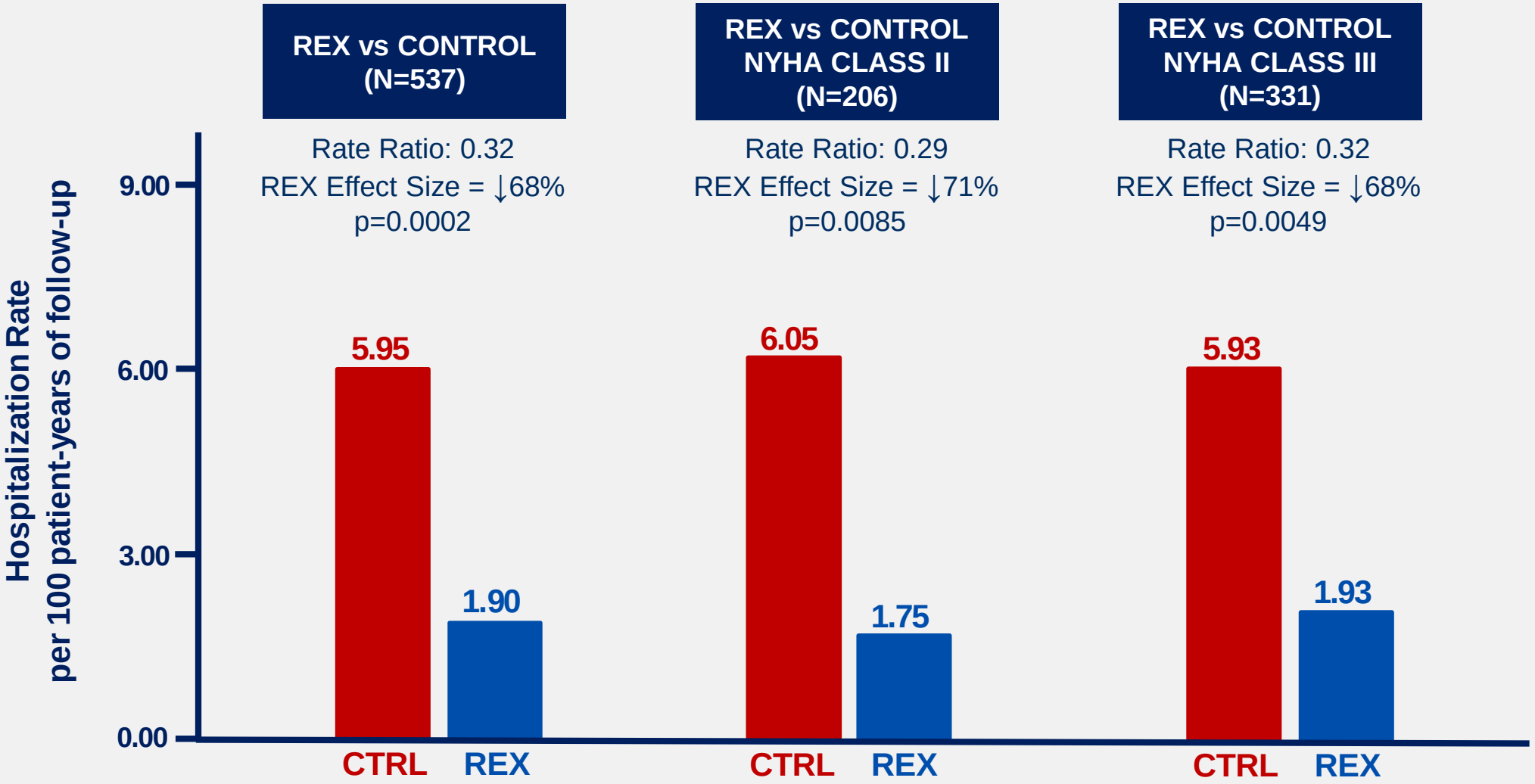
TTFE ANALYSIS	ALL
REX Effect Compared with Controls	↓60%
P-value	0.002
COVARIATES	
Ischemic	P = 0.0098
Non-ischemic	P = 0.0995
hsCRP≥2	P = 0.0045
hsCRP≥3	P = 0.0065
hsCRP≥4	P = 0.0430

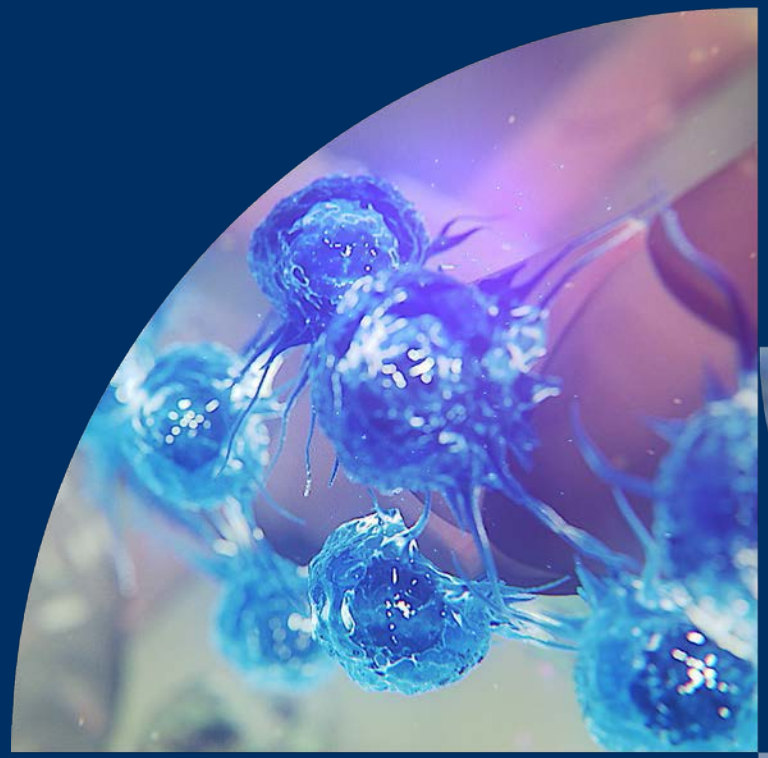
Rexlemestrocel-L Significantly Reduced Incidence of Ischemic MACE (MI, Stroke) by 57% & 67% Relative to Controls In NYHA Class II & III, respectively





Rexlemestrocel-L Significantly Reduced Hospitalization Rates from Non-Fatal MI or Stroke in All Patients, with Similar Effect Size in NYHA Class II and Class III Patients





DREAM HF

- Death From Cardiac Causes (CV Death)

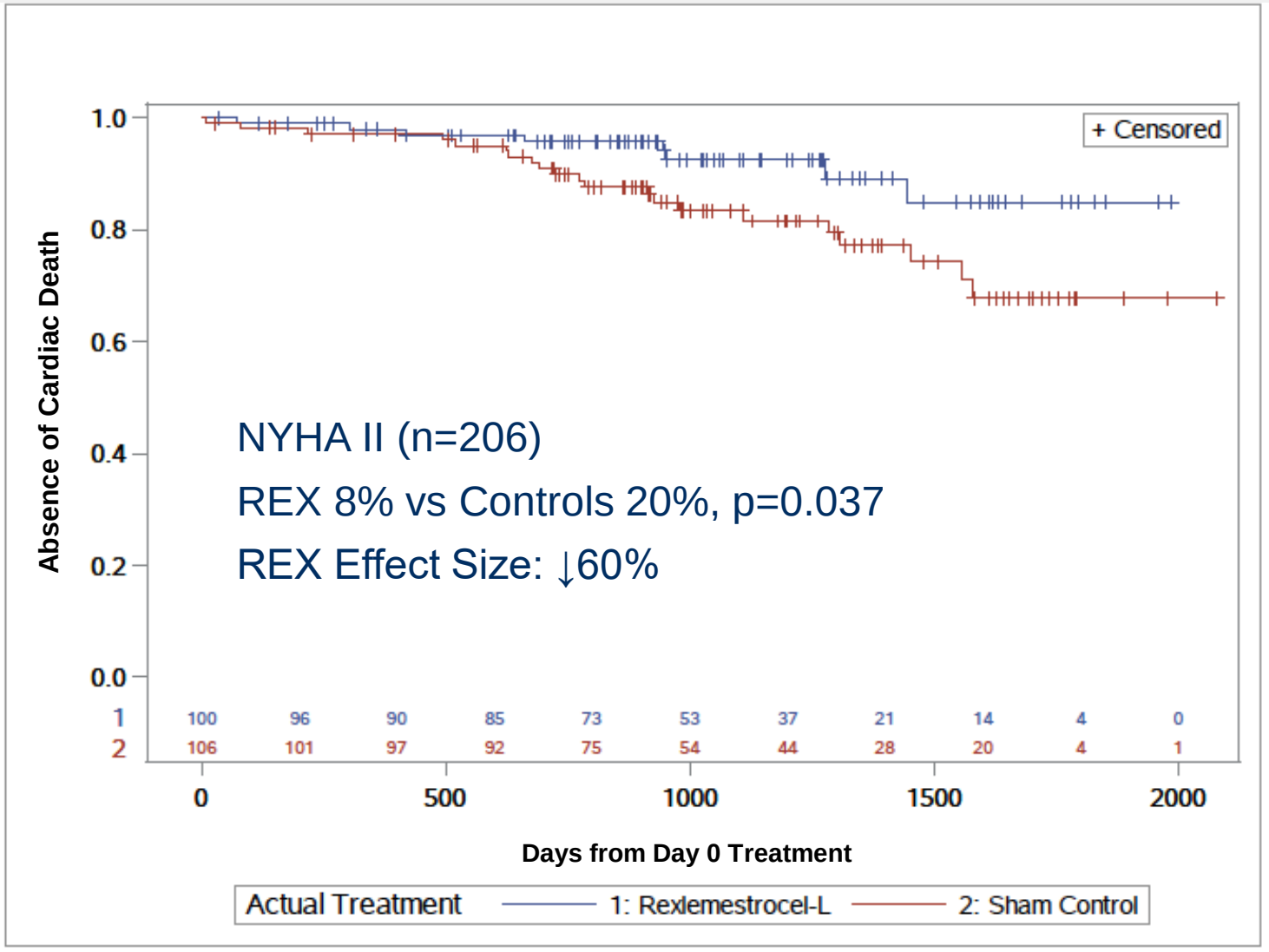
High Baseline CRP and NT-proBNP are Significant Predictors of Rexlemestrocel-L Treatment Benefit on Cardiac Death

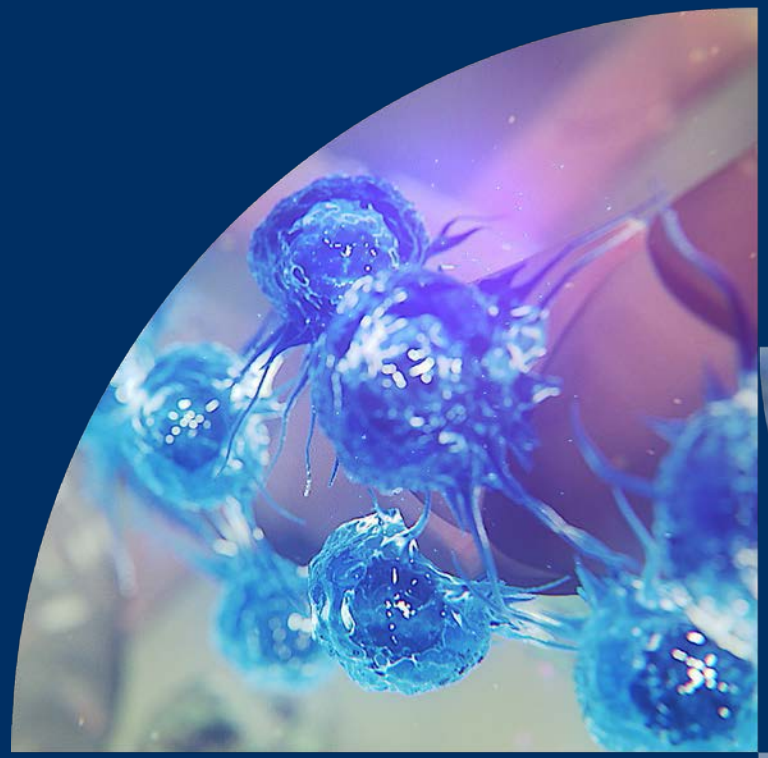
Cardiac Death

	ALL	Class II	Class III
COVARIATES*			
NYHA Class II	P = 0.0430		
NYHA Class III	P = 0.4630		
hsCRP≥2	P = 0.1634	P = 0.0062	
hsCRP≥3		P = 0.0122	
hsCRP≥4		P = 0.0273	
NT-proBNP		P = 0.0139	

* Multi-variate regression analysis using COX proportional hazards

Rexlemestrocel-L Reduced Cardiac Death by 60% in NYHA Class II Patients

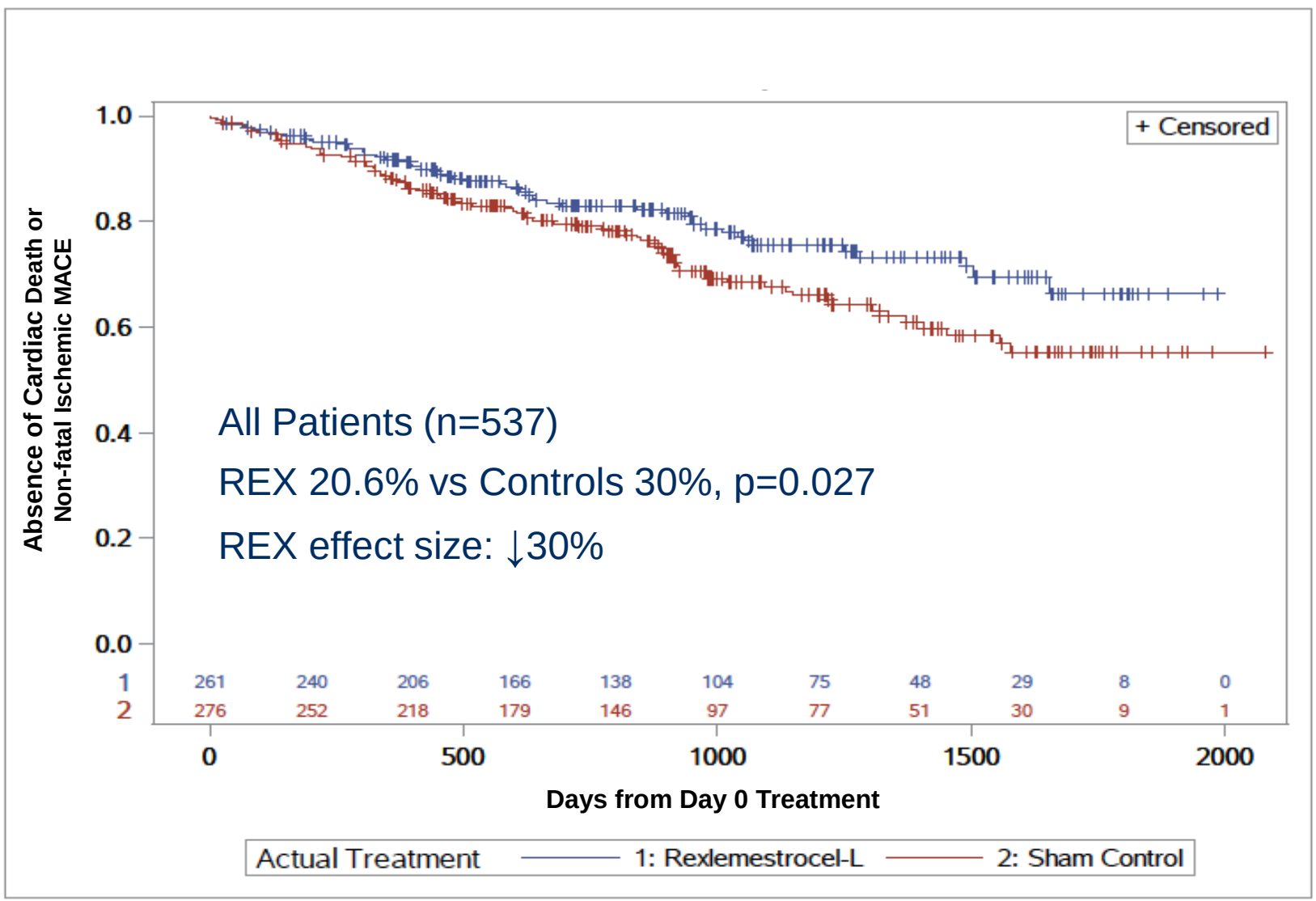




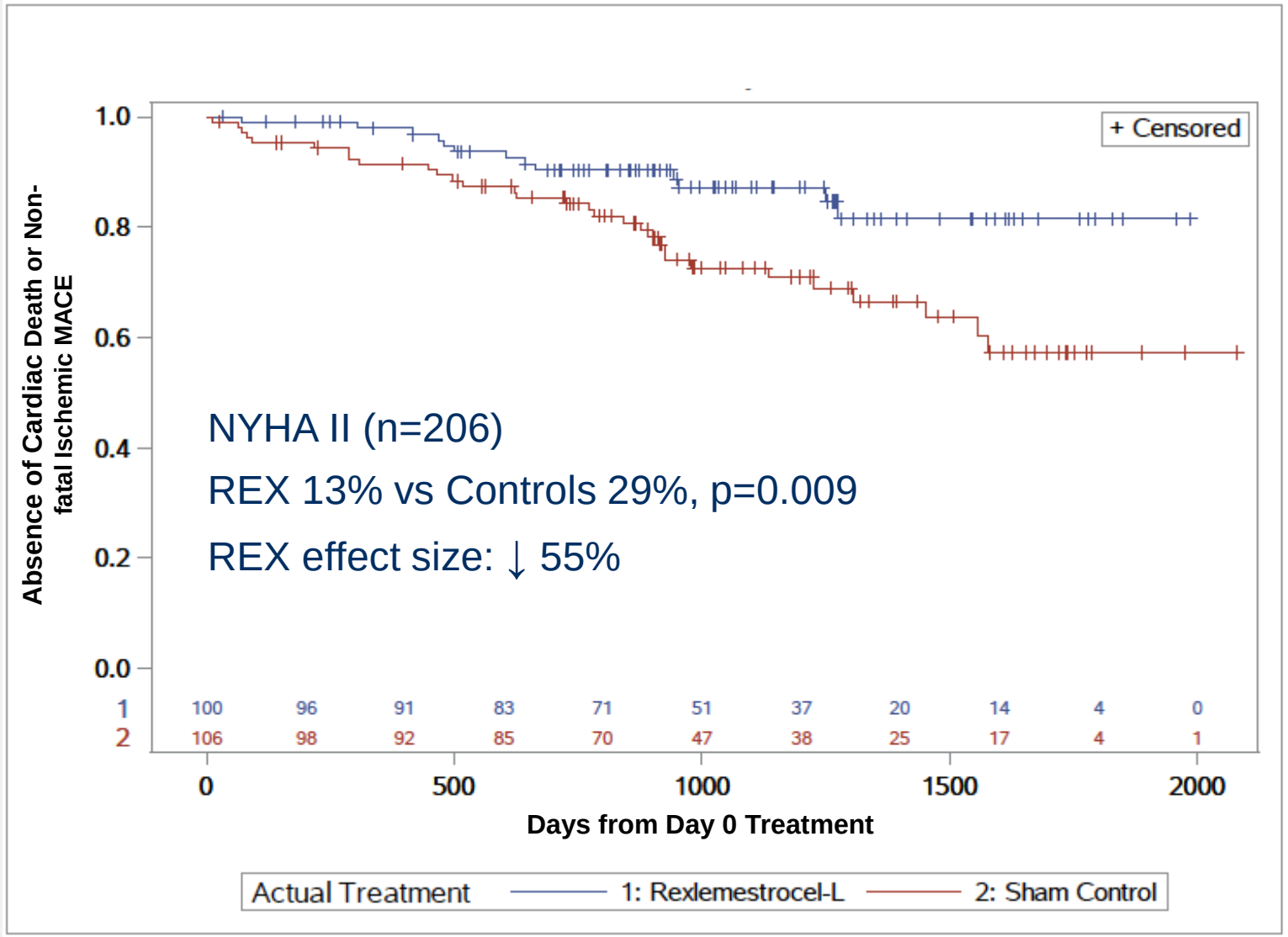
DREAM HF

- Three-Point MACE (CV Death, MI or Stroke)

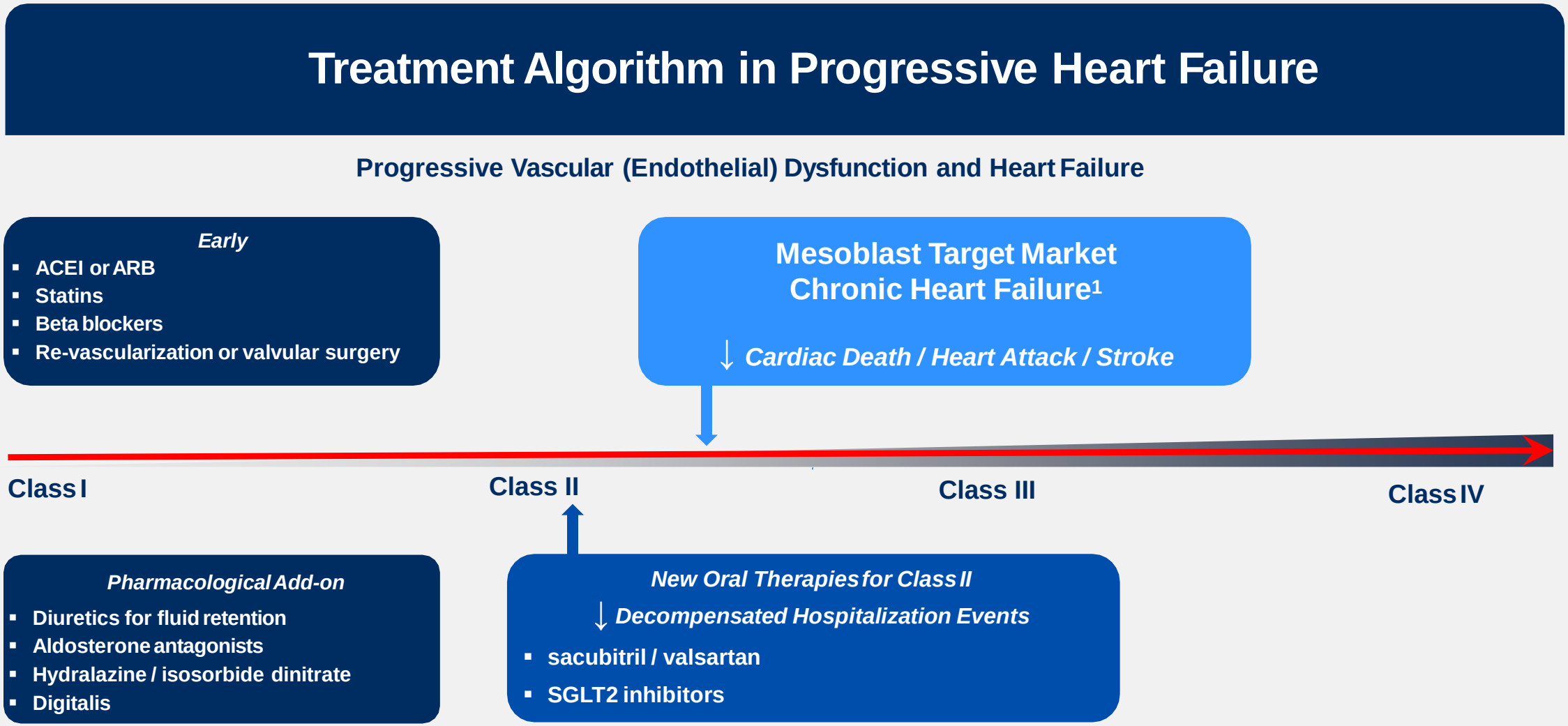
Rexlemestrocel-L Significantly Reduced 3-Point Composite MACE (CV Death, MI or Stroke) Compared to Controls Across All 537 Patients



Rexlemestrocel-L Significantly Reduced 3-Point Composite MACE (CV Death, MI or Stroke) in 206 NYHA Class II Patients



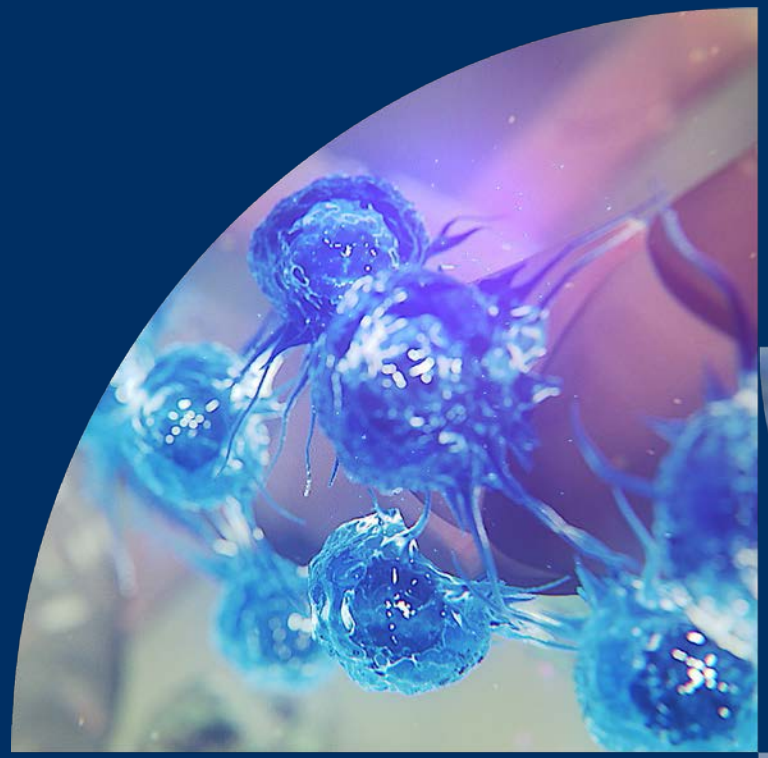
Rexlemestrocel-L for Chronic Heart Failure



1. GlobalData-PharmaPoint Heart Failure (2016); McMurray et al., 2012;Yancy et al., 2013, 2016 ACC/AHAHFSA Focused Update on New Pharmacological Therapy for Heart Failure: An Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure.

Rexlemestrocel-L Phase 3 Trial Conclusions

- Rexlemestrocel-L may provide a major breakthrough in reducing heart failure progression and mortality when used early (class II disease), and may provide durable protection from heart attacks or strokes in high-risk patients
  - 60% reduction in incidence of ischemic MACE (heart attack or stroke) across entire 537 patient study population, irrespective of NYHA class II or III, ischemic or non-ischemic etiology (p=0.002)
  - 30% reduction in incidence of three-point MACE (cardiac death, heart attack or stroke) across entire 537 patient study population (p=0.027)
  - 55% reduction in incidence of three-point MACE (cardiac death, heart attack or stroke) in NYHA class II patients (n=206) (p=0.009)
  - 60% reduction in cardiac death in NYHA class II patients (p=0.037) and prevention of progression to NYHA class III rate of cardiac death
- Based on observed reduction in mortality and morbidity in this Phase 3 trial, Mesoblast intends to meet with the United States Food and Drug Administration (FDA) to discuss potential approval pathways



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