

A photograph of a female doctor with grey hair in a ponytail, wearing a white lab coat, smiling warmly at a young girl. The girl is wearing a light blue surgical cap and a pink t-shirt, and is holding a brown teddy bear. They are in a hospital setting with a window in the background. A large blue curved graphic is overlaid on the left side of the image.

# Welcome to **R&D Day**

ASX: MSB; Nasdaq: MESO. | April 8, 2026

# Cautionary Note Regarding Forward Looking Statements

This presentation includes forward-looking statements and forecasts that relate to future events or our future financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to differ materially from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements. We make such forward-looking statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. All statements other than statements of historical facts contained in this presentation are forward-looking statements. Words such as, but not limited to, “believe,” “expect,” “anticipate,” “estimate,” “intend,” “plan,” “targets,” “likely,” “will,” “would,” “could,” and similar expressions or phrases identify forward-looking statements. We have based these forward-looking statements largely on our current expectations and future events, recent changes in regulatory laws, and financial trends that we believe may affect our financial condition, results of operation, business strategy and financial needs. These statements may relate to, but are not limited to: expectations with respect to sales and revenue, expectations regarding the safety or efficacy of, or potential applications for, Mesoblast's adult stem cell technologies; expectations regarding the strength of Mesoblast's intellectual property, the timeline for Mesoblast's regulatory approval process, and the scalability and efficiency of manufacturing processes; expectations about Mesoblast's ability to grow its business and statements regarding its relationships with current and potential future business partners and future benefits of those relationships; statements concerning Mesoblast's share price or potential market capitalization; and statements concerning Mesoblast's capital requirements and ability to raise future capital, among others. Forward-looking statements should not be read as a guarantee of future performance or results, and actual results may differ from the results anticipated in these forward-looking statements, and the differences may be material and adverse. You should read this presentation together with our financial statements and the notes related thereto, as well as the risk factors, in our most recently filed reports with the SEC or on our website. Uncertainties and risks that may cause Mesoblast's actual results, performance or achievements to be materially different from those which may be expressed or implied by such statements, include, without limitation: risks inherent in the development and commercialization of potential products; uncertainty of clinical trial results or regulatory approvals or clearances; government regulation; the need for future capital; dependence upon collaborators; and protection of our intellectual property rights, among others. Accordingly, you should not place undue reliance on these forward-looking statements. We do not undertake any obligations to publicly update or revise any forward-looking statements, whether as a result of new information, future developments or otherwise.

# Agenda

	<u>Presenting</u>	<u>KOL Perspective</u>
● Welcome	Paul Hughes	
● Overview	Silviu Itescu, MD	
● Ryonicil® Flagship Growth Adult SR-aGvHD	Marcelo Santoro, DBA Michael Schuster, MBA, MS	Joanne Kurtzberg, MD Susan Prockop, MD
● Chronic Lower Back Pain	Roger Brown	Doug Beall, MD
● Inflammatory Heart Failure	Ken Borow, MD	Emerson Perin, MD Eric Rose, MD
● Pediatric Label Extension	Michael Schuster, MBA, MS	
● Next Generation Platforms	Dan Devine, JD, MBA	Saad Kenderian, MB
● Financial and Manufacturing	James O'Brien / Justin Horst	
● Wrap-up and Closing Remarks	Silviu Itescu, MD	
● Audience Q&A		



# Meet Today's Invited Experts – Key Opinion Leaders



**Joanne Kurtzberg, MD**

Jerome Harris Distinguished Professor  
of Pediatrics  
Professor of Pathology  
Duke University School of Medicine



**Emerson C. Perin, MD, PhD**

Medical Director of The Texas Heart  
Institute  
Professor of Medicine, Baylor College  
of Medicine



**Douglas P. Beall, MD**

Chief of Services, Comprehensive  
Specialty Care; Director of Research  
Clinical Investigations LLC



**Susan Prockop, MD**

Director, Clinical and Translational  
Research  
(Stem Cell Transplant Program, DFCI/BCH  
Cancer and Blood Disorders Center)



**Eric Rose, MD**, Chief Medical Officer  
World-renowned heart surgeon and  
scientist made history when he performed  
the first successful pediatric heart  
transplant



**Saad Kenderian, MD, ChB**

Assistant Professor of Oncology,  
Medicine and Immunology at Mayo  
Clinic

# Strategic Overview

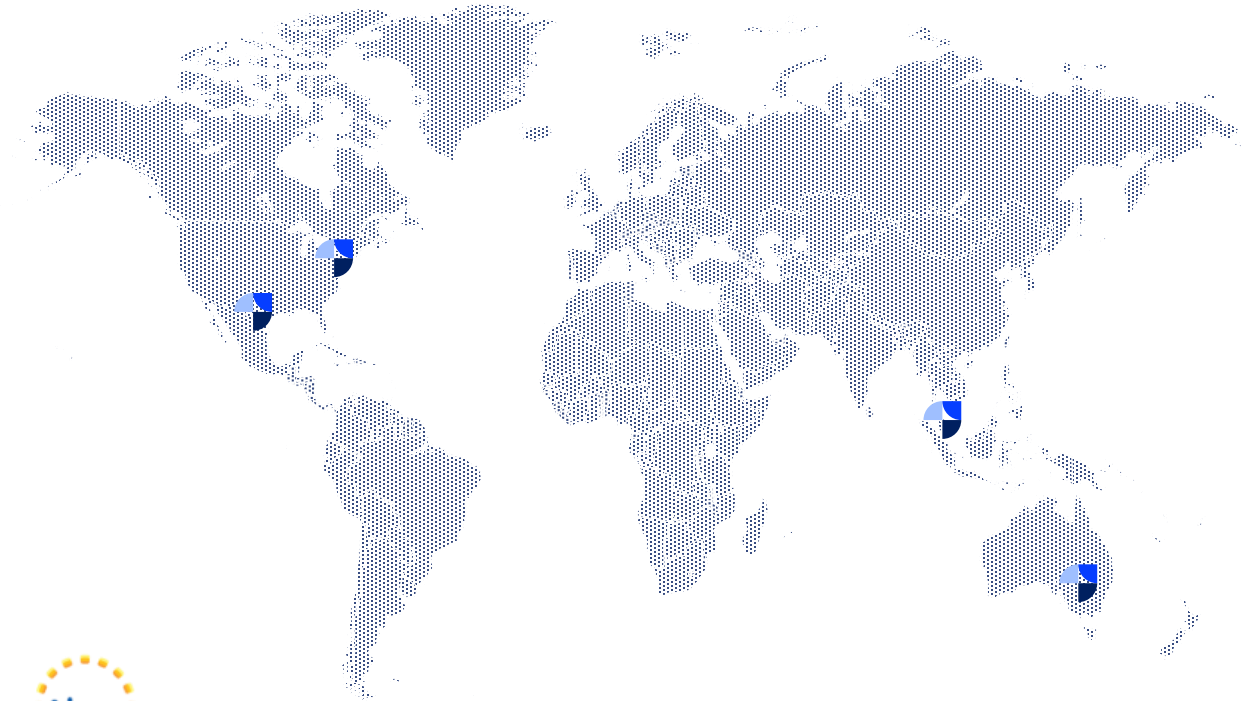
**Silviu Itescu**

Chief Executive



# Mesoblast: Global Leader in Allogeneic (Off-the-Shelf) Cellular Medicines

- World leader in developing allogeneic (off-the-shelf) cellular medicines for the treatment of severe and life-threatening inflammatory conditions
- Locations in United States, Australia, and Singapore
- Listed on NASDAQ (MESO) and ASX (MSB)
- Developing product candidates for distinct indications based on its remestemcel-L and rexlemestrocil-L stromal cell technology platforms
- First FDA-approved product launched successfully
- Extensive global intellectual property portfolio with protection extending through to at least 2044 in all major markets
- FDA-inspected commercial scale manufacturing process and facilities



**Ryoncil**  
(remestemcel-L-rknd)

**First FDA approval**

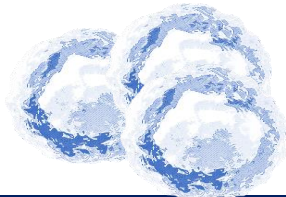
**THREE**  
Additional Major  
Phase 3  
Assets

**Robust  
Pipeline**

**more than  
1,100  
patents &  
applications**

# Proprietary Stromal Cell Technology Positions Mesoblast First-in-Class

Based on mesenchymal lineage adult stromal cells (MLCs)



## MLCs: Unique Cells Fighting Inflammation

- Derived from healthy donors
- Home to inflamed tissue and respond to inflammatory signals
- Secrete factors that target multiple inflammatory pathways, inert in the absence of inflammation
- Reduction in inflammation and tissue repair



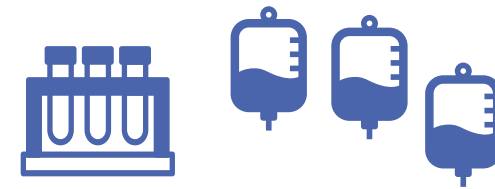
## Proven 1<sup>st</sup> and 2<sup>nd</sup> Gen Technology Platforms

- **Remestemcel-L:** first generation, FDA-approved, focused on rare orphan diseases
- **Rexlemestrocel-L:** second generation, immunoselected for precision, greater potency for blockbuster high volume diseases



## Unique Off-the-Shelf (Allogeneic) Properties Underpin Business

- No expression of cell surface co-stimulatory molecules
- Do not induce immune reaction, no need for immunosuppression
- From a single donor product made for thousands of unrelated recipients

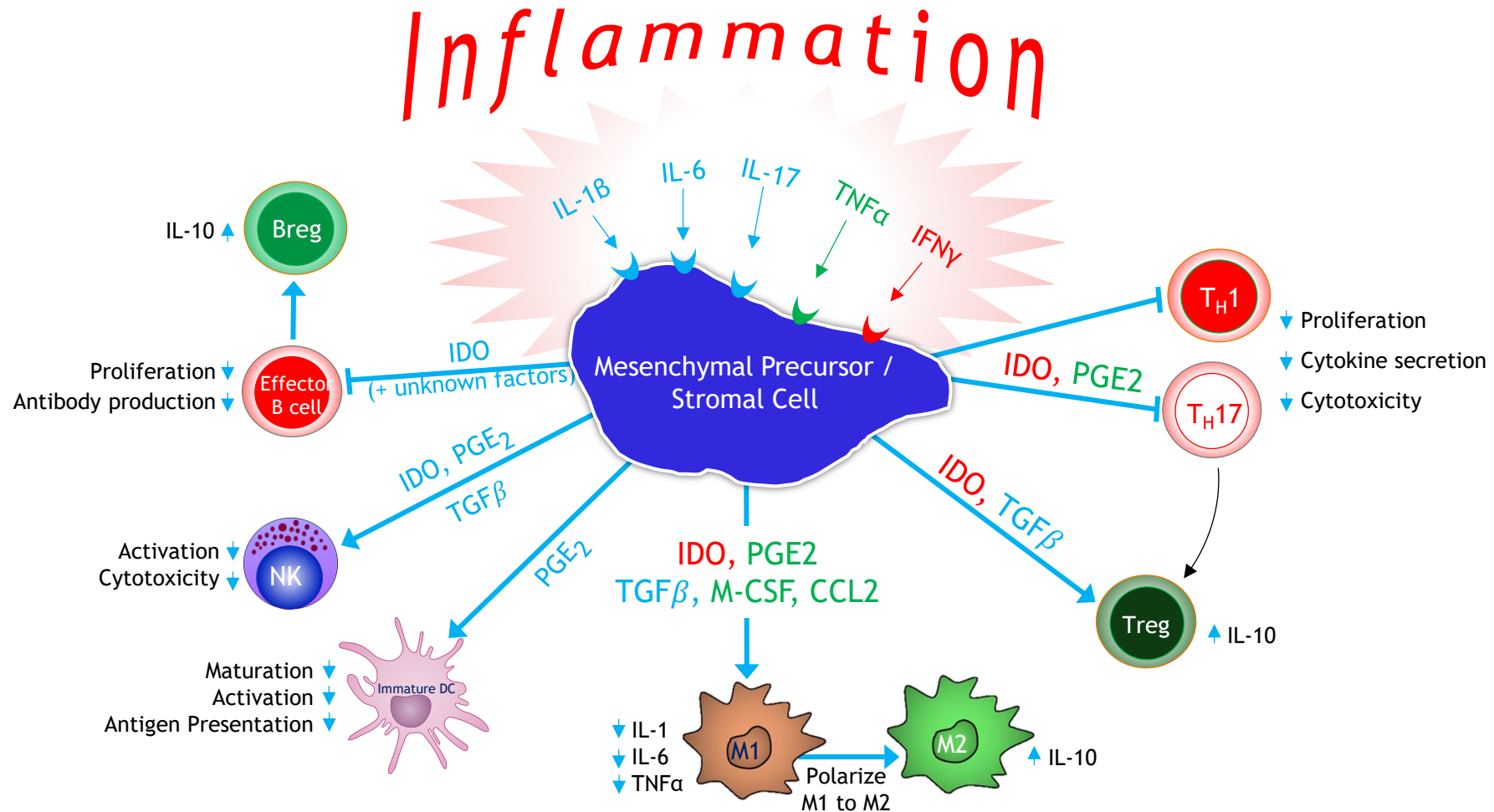


## Proprietary Scalable Production

- Scalable “off-the-shelf” cellular platforms
- Expansion without differentiation
- Validated potency assays ensure batch-to-batch consistency
- Proprietary media formulations and bioreactors for scale-up

# MLCs Orchestrate Potent Anti-Inflammatory Cascade

Activation Via Multiple Surface Receptors Results In Powerful Multi-Modal Response That Cannot Be Achieved By Agents Targeting Single Pathways



Source: data on file

# Mesoblast First-In-Class Leader in Allogeneic Cellular Therapies



## **Ryoncil® Only FDA Approved MSC, Successful First US Launch**

Net revenue approaching  
US\$100M since launch last year

Highly profitable single product on  
stand-alone basis

Proceeds from revenue generated  
is being re-invested in label  
extensions studies and  
blockbuster opportunities



## **Commercial Capability Established**

Infrastructure to support product  
launches across multiple  
expansion indications

Built specialized sales team  
focused on hospitals, transplant  
centers, and specialists



## **Pipeline with Multiple Blockbuster Opportunities**

Phase 3 programs position  
rexlemestrocel-L to transform the  
treatment of low back pain with  
degenerative disc disease, and  
inflammatory heart failure

Phase 3 programs to extend  
Ryoncil® label to adult aGvHD and  
pediatric rare diseases such as  
Duchenne Muscular Dystrophy

# RYONCIL Profitability to Fund Growth Pipeline

## Successful U.S. commercial launch of RYONCIL

- Q3 FY26 gross revenue US\$35.3M, net revenue US\$30.3M
- RYONCIL net revenue approaching US\$100 million since launch last year
- RYONCIL gross profit 1H FY26, excluding amortization expense, was US\$44.2M. Direct selling costs were US\$7.7M

## Strong operating performance in the period allowed us to invest in:

- R&D, including to support the Phase 3 trial on the blockbuster chronic low back pain indication
- Clinical programs for lifecycle extension
- Commercial manufacturing of Ryoncil® inventory as well as for launch of second-generation product



**Ryoncil**®  
(remestemcel-L-rknd)

# What We Have Built - Commercial Capability

- ✓ Established **commercial infrastructure** to support product launches
- ✓ Built **specialized sales and marketing teams** focused on hospitals and transplant centers
- ✓ Implemented **market access and payer engagement** strategies to support reimbursement and adoption
- ✓ Established strong **manufacturing and supply chain capabilities** ensuring scalable, consistent cell therapy production and delivery
- ✓ Leveraged **clinical data and real-world evidence** to support product positioning and physician uptake
- ✓ Established **medical affairs and education programs** to drive clinician awareness and training
- ✓ Ensured leadership position is maintained by continued access to **cutting-edge technology**

# Pipeline with Multiple Blockbuster Opportunities

## **RYONCIL** **Remestemcel-L**

### **Adult SR-aGvHD**

Pivotal trial as part of second-line regimen

**TAM**

children & adults

**~US\$1B**

### **Pediatric Inflammatory Rare Diseases**

(e.g. DMD,

**TAM >US\$1B)**

## **Rexlemestrocel-L**

### **Cardiac HFrEF**

Ischemic chronic heart failure with inflammation

**TAM**

**>US\$10B**

**CLBP** with degenerative disc disease; confirmatory Phase 3 topline results in mid-CY2027

**TAM**

**>US\$10B**

SR-aGvHD: steroid-refractory acute graft versus host disease | TAM: total addressable market | DMD: Duchenne Muscular Dystrophy | HFrEF: heart failure reduced ejection fraction | CLBP: chronic low back pain

# Mesoblast Allogeneic Mesenchymal Stromal Cell Portfolio

Product	Indication	Phase 2	Phase 3	Approved
<b>RYONCIL®</b> <b>remestemcel-L</b>	Pediatric SR-aGvHD			
	Adult SR-aGvHD			
<b>RYONCIL®</b> <b>remestemcel-L</b>	Duchenne's			
<b>REVASCOR®</b> <b>rexlemestrocel-L</b> <b>(STRO3+)</b>	Adult HFrEF Class II/III			
	Adult HFrEF End-stage			
<b>Rexlemestrocel-L</b> <b>(STRO3+)</b>	CLBP			

SR-aGvHD = Steroid-Refractory Acute Graft versus Host Disease; HFrEF = Heart Failure with Reduced Ejection Fraction; CLBP = Chronic Low Back Pain

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

#### Notes:

- JCR Pharmaceuticals Co., Ltd. (JCR), has the right to develop mesenchymal stromal cells (MSCs) in certain fields for the Japanese market, including for the treatment of hematological malignancies, such as Graft vs Host Disease, and for hypoxic ischemic encephalopathy (HIE).
- Grünenthal has an exclusive license to develop and commercialize rexlemestrocel-L for chronic low back pain in Europe and Latin America/Caribbean.
- Tasly Pharmaceuticals has exclusive rights for rexlemestrocel-L for the treatment or prevention of chronic heart failure in China.

# Anticipated Major Upcoming Milestones



## **Blockbuster CLBP**

- Complete enrollment of pivotal trial end of April
- Top-line primary endpoint mid-CY2027
- BLA filing for FDA approval Q3 CY2027
- Potential FDA approval and US launch Q2 CY2028



## **CHF: regulatory strategy to gain approval for blockbuster indication**

- File BLA with FDA for end-stage heart failure patients on LVADs this quarter
- Leverage approval to initiate confirmatory trial in NYHA II/III HFrEF

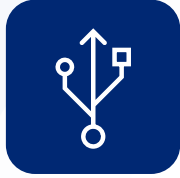


## **Label extension for RYONCIL**

- Adult SR-aGvHD partnered with BMT-CTN network, trial initiated, to complete in 12-18 months
- Pediatric Duchenne's partnered with PPMD advocacy group, Phase 3 IND cleared by FDA

SR-aGvHD: steroid-refractory acute graft versus host disease | CHF: chronic heart failure | BLA: Biologics License Application | LVAD: left ventricular assist device | HFrEF: heart failure reduced ejection fraction | NYHA: New York Heart Association | CLBP: chronic low back pain | PPMD: Parent Project Muscular Dystrophy

# Innovation in Technology & Manufacturing Drives Next Generation Products



## New technologies Genetically Modifying Our MLCs

- Chimeric antigen receptors (CAR) expressed for precision targeting and enhanced potency
- Delivery of Oncolytic Viruses encoded with immunostimulatory factors for treating cancer



## Multiple New Blockbuster Opportunities

- Ulcerative colitis and Crohn's Disease (IBD)
- Lupus nephritis / other B cell autoimmune disorders
- Alzheimer's Disease / Parkinson's
- Cancer applications



## Manufacturing Efficiencies

- Second generation media with growth factors for increased yield
- Automation for larger volume production and demand
- Bioreactors for COGS and footprint reduction

MLC: mesenchymal lineage cell | IBD: inflammatory bowel disease | COGS: cost of goods sold

# Key Takeaways

- MSCs safe and effective treatments to transform outcomes
- First-in-class platform technology approved by FDA, unlocks many opportunities
- Massive barriers to entry include dominant IP, clinical trial outcomes, robust manufacturing, proprietary potency assays and FDA approval
- Well cashed-up, profits from RYONCIL being re-invested into follow-on opportunities
- Blockbuster potential with major near-term milestones with back pain and heart failure products
- Innovative next generation technologies to genetically modify our cells provide potential for even greater efficacy

**Ryoncil**<sup>®</sup>  
(remestemcel-L-rknd) Suspension  
for IV infusion

# Pediatric Steroid Refractory Acute Graft versus Host Disease

**Marcelo Santoro**  
Chief Commercial Officer



# Redefining What's Possible for SR-aGvHD Children and Their Loved Ones

Ryonicil<sup>®</sup>  
(remestemcel-L-rknd) Suspension  
for IV infusion



## Successful First Year of RYONCIL

- Ryoncil is transforming outcomes in pediatric SR-aGvHD, with strong positive feedback from treating physicians
- Commercial uptake has exceeded expectations, outperforming benchmarks from comparable successful launches
- We have established the capability to scale, with a clear path to doubling our US revenue from RYONCIL
- Adult indication represents a major opportunity, representing a 3-fold increase in TAM and revenue potential

# Key Accomplishments So Far

Initial real  
world  
experience

84% survival  
outcomes all  
with Grade  
III/IV disease\*

Net revenue  
approaching  
US\$100M  
since launch  
last year

50  
centers  
onboarded

30  
formulary  
approvals  
(13 accounts  
using  
specialty  
pharmacy)

98% US lives  
covered

Medicaid in  
place

J-Code  
received  
October 2025

Expansion  
into adult  
market (phase  
3 underway)

\*Children with steroid refractory active graft versus host disease after completing 28 days of treatment

# Customer Centric Model – Key Account Executives as Quarterbacks

Supported By MSLs, Field Reimbursement and Digital Ecosystem



**Key Account Executives (8)**



**TC quarterback – fully accountable for transplant centers assigned**



**Medical Science Liaisons (3)**



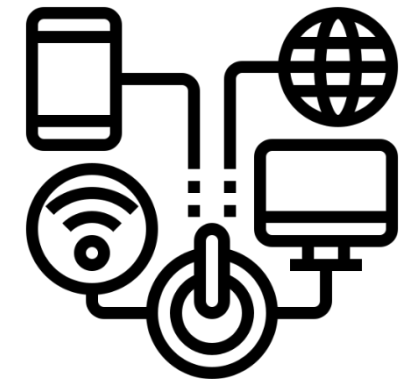
**Scientific exchange - support KAEs as required**



**Field Reimbursement (3)**



**Reimbursement (Commercial and Medicaid/Medicare) support**



**Digital Ecosystem**



**Digital CRM hub providing omnichannel capabilities and performance tracking**

# Revenue Growth Plan

**Next target:  
Doubling net revenue**

Broader Ryoncil utilization in first  
line after steroids

Ryoncil available at the site of care for  
immediate dispensing

Expand Ryoncil utilization across all 64 targeted  
centers, driving breadth and depth

**Approaching US\$100M net  
revenue since launch**

# Three Strategic Priorities for Continued Growth in FY 2027



**Proactively identify  
and prioritize  
appropriate  
patients**



**Reinforce superior  
patient outcomes  
in first-line**



**Empower caregivers to  
demand Ryoncil<sup>®</sup> for  
their children**

## Key Takeaways

- Approaching US\$100M in net revenues since launch last year, strategy in place to double revenue
- TAM for children and adults in SR-aGvHD alone is >US\$1.0 billion
- Leveraging the commercial capability to support RYONCIL label extensions
- Opportunity to expand ex-US at US Most Favored Nation pricing

# Ryoncil in Adult GvHD

**Michael Schuster**

Head of Business Development



## Beyond 2027, First-line Treatment in Adult SR-aGvHD is a Huge Opportunity for RYONCIL Growth

Approx. 50%  
of all SR-  
aGvHD are  
Grade III/IV

Market size in  
adults is ~3x  
larger than  
pediatric

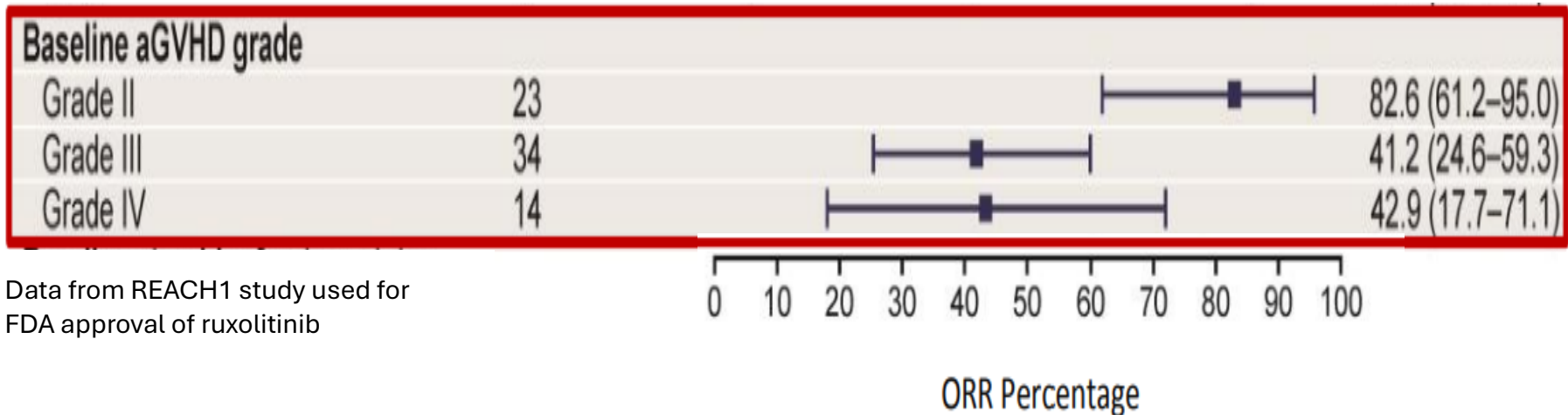
~50% overlap  
Adult and  
pediatric centers

Existing  
pediatric  
KAM/MSLs and  
infrastructure  
can be  
leveraged and  
expanded to  
commercialize  
adult GVHD

Pricing structure  
maintained  
given high  
mortality risk  
and orphan  
population

# Grade III/IV Adult SR-aGvHD is a Major Unmet Need

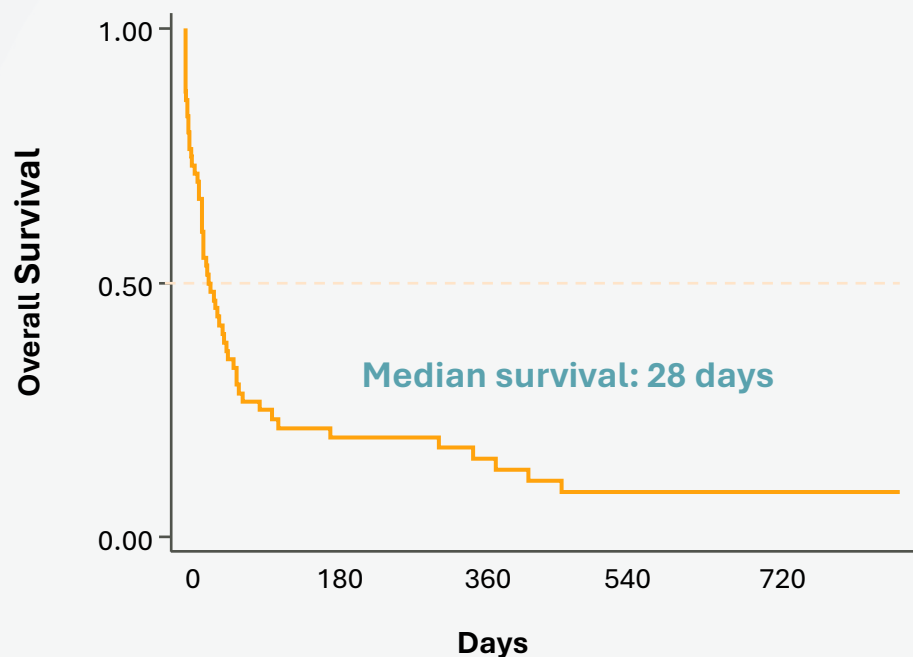
Only ~42% of Grade III/IV GVHD patients achieve Day 28  
ORR with the existing FDA-approved treatment<sup>1</sup>



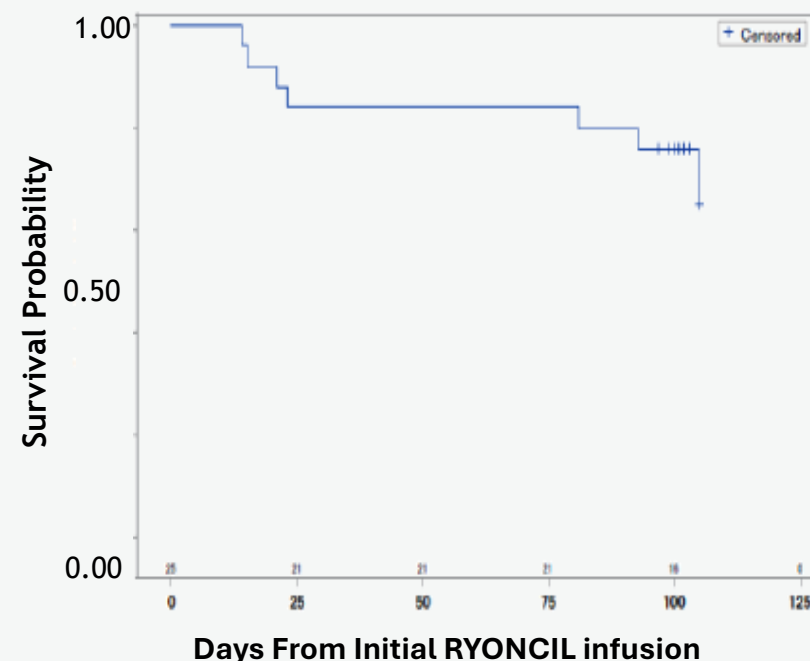
1. Jagasia M et al. *Blood*. 2020;135(20):1739-1749.
2. Abedin S et al. *Br J Haematol*. 2021;195(3):429-432.

# Ryonicil is Effective in Grade III/IV SR-aGvHD

Survival is a dismal ~25% at Day 100 for adults with SR-aGvHD who have failed ruxolitinib and are treated with other agents



Day 100 Survival with RYONCIL is 76% when used after ruxolitinib or other second-line failure In Adults with SR-aGvHD



***Single-site pilot study has shown additive benefit when MSCs are used concurrently with ruxolitinib in severe SR-aGvHD immediately after steroids***

# Registrational Adult Steroid Refractory Acute GVHD Trial In Partnership With NIH-Funded Blood & Marrow Transplant Clinical Trial Network (BMT-CTN)

**180 Grade III/IV SR-aGvHD Adults  
will be Randomized 1:1**



RUX + RYONCIL ( $2 \times 10^6/\text{kg}$ ) 8 doses over 4 weeks vs RUX alone

**Trial Primary Endpoint**



Assess Overall Response @ Day 28

**Trial Key Secondary Endpoint**

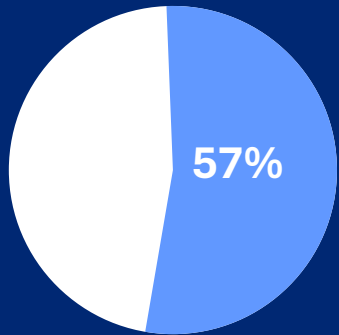


Overall Survival at Day 180

RUX: ruxolitinib

# Adult SR-aGvHD Trial Timelines

- Mesoblast will oversee trial execution using NIH-sponsored BMT-CTN network of major hospitals
- DSMB approval and NMDP Central IRB clearance
- Patients to be recruited across 45 U.S. centers (representing  $\approx$ 5,000 annual allo transplants)
- First sites to be activated this quarter
- Expected duration 18 months, with interim analysis at 12 months



Interim analysis planned for early success when first 102 patients (57% enrolled) have reached Day 28 (primary endpoint)

# Label Expansion into Adult GvHD Provides Significant Revenue Upside

- Partnership with the BMT-CTN consortium will subsidize cost and create end-user awareness for market adoption
- Potential to shorten time to launch by six months through successful interim analysis
- Label extension in adult SR-aGvHD maintains existing Ryoncil pricing structure
- Leverages existing commercial infrastructure for pediatric
- Adult SR-aGvHD represents a market opportunity 3x that of pediatric SR-aGVHD

## **KOL Perspective**

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### **Joanne Kurtzberg, MD**

**Duke University School of Medicine**

Jerome Harris Distinguished Professor of Pediatrics

Professor of Pathology

Duke University School of Medicine



## **Adult aGvHD KOL Perspective**

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### **Susan Prockop, MD**

**Dana Farber Cancer Institute/Boston Children's Hospital**

Director, Clinical and Translational Research

Stem Cell Transplant Program, DFCI/BCH Cancer and Blood Disorders Center



# Rexlemestrocel-L for Chronic Lower Back Pain

**Roger Brown**

Head of Musculoskeletal



# Rexlemestrocel-L for CLBP: Huge Commercial Opportunity

## Substantial Unmet Need

~35M patients in US suffer from CLBP of which ~60% is due to degenerative disc disease (DDD)

~7M US patients have moderate / severe DDD within 5 years of diagnosis that is refractory to medical therapies including opioids

10% of prevalent market penetration represents US\$14B per year in product sales

## Timelines to CLBP Commercial Launch

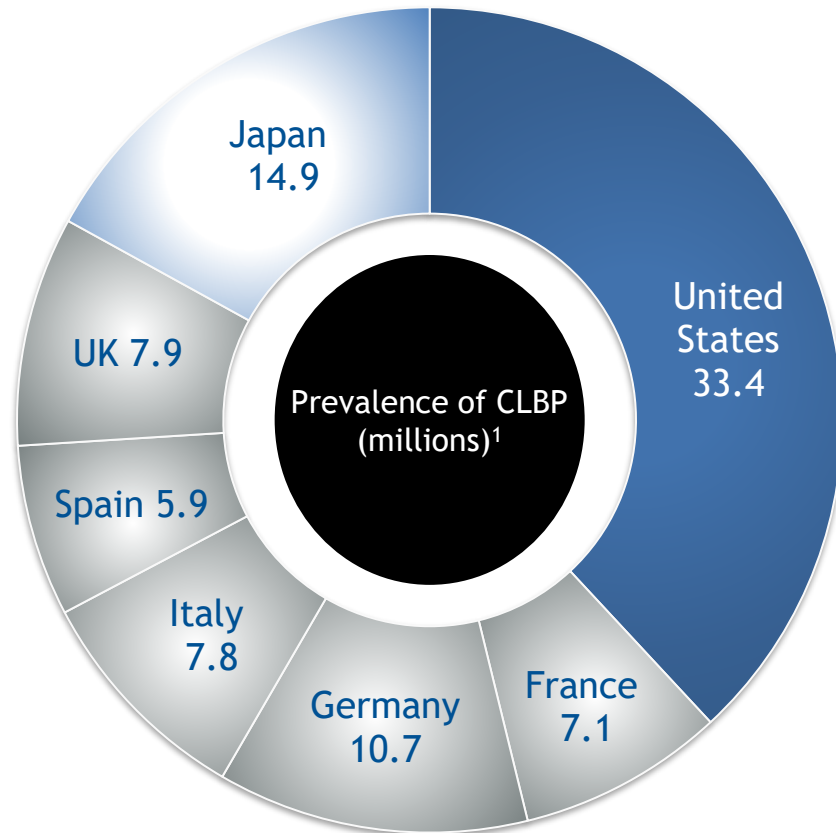
P3 trial results to confirm first trial pain reduction at 12 months expected mid-CY2027

Filing BLA with FDA in Q3 CY2027

Potential approval following Priority Review Q2 CY2028

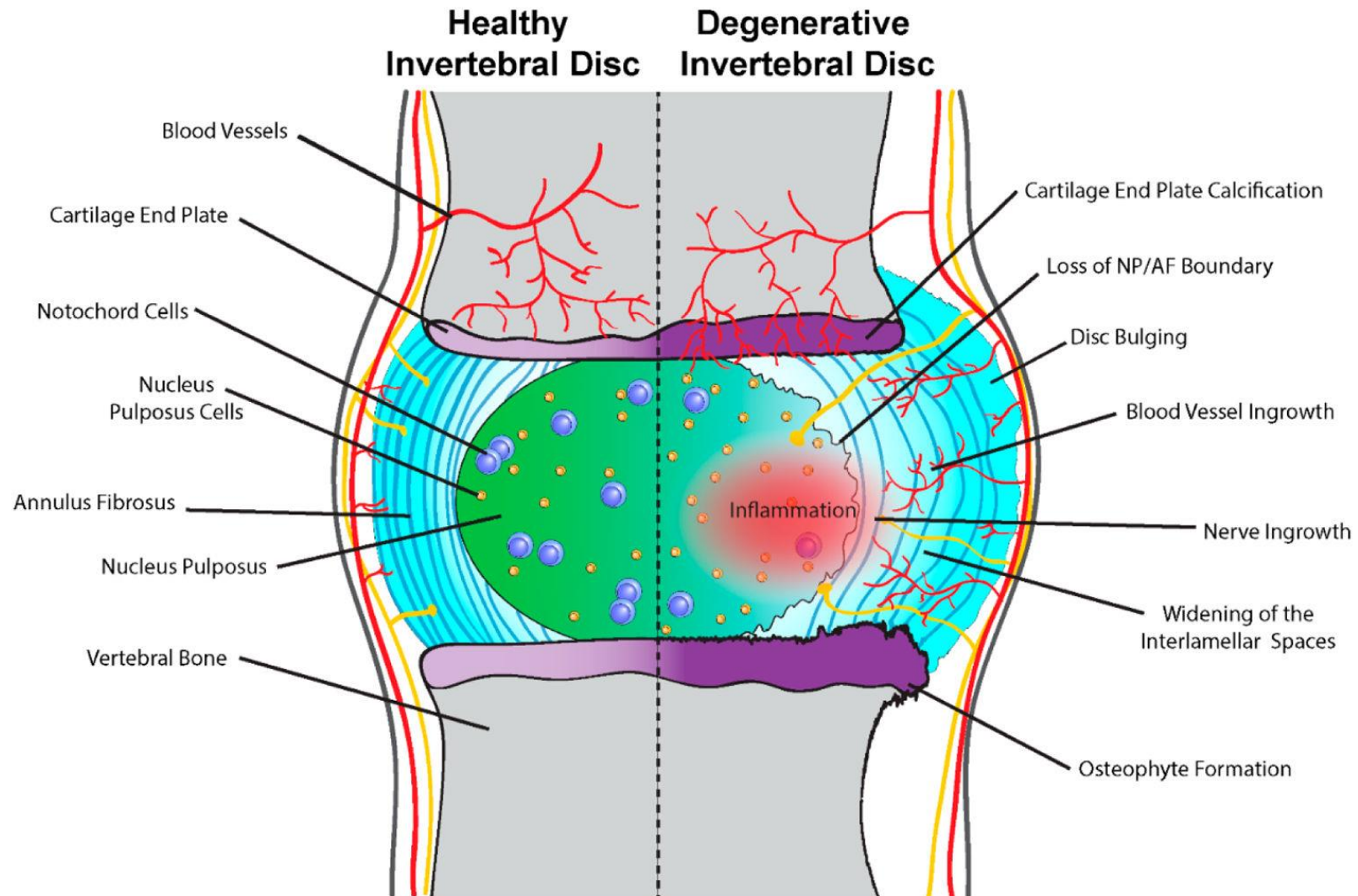
# Transformational Market Opportunity in US, EU & Japan

Approx. 10–15% of Adult Population Suffers from Chronic Lower Back Pain



- US prevalence 33.4M, Japan 14.9M  
Mesoblast to commercialize with or without strategic partner
- EU5 prevalence 39.4M
  - To be commercialized by Grunenthal, Mesoblast to receive milestone payments & royalties

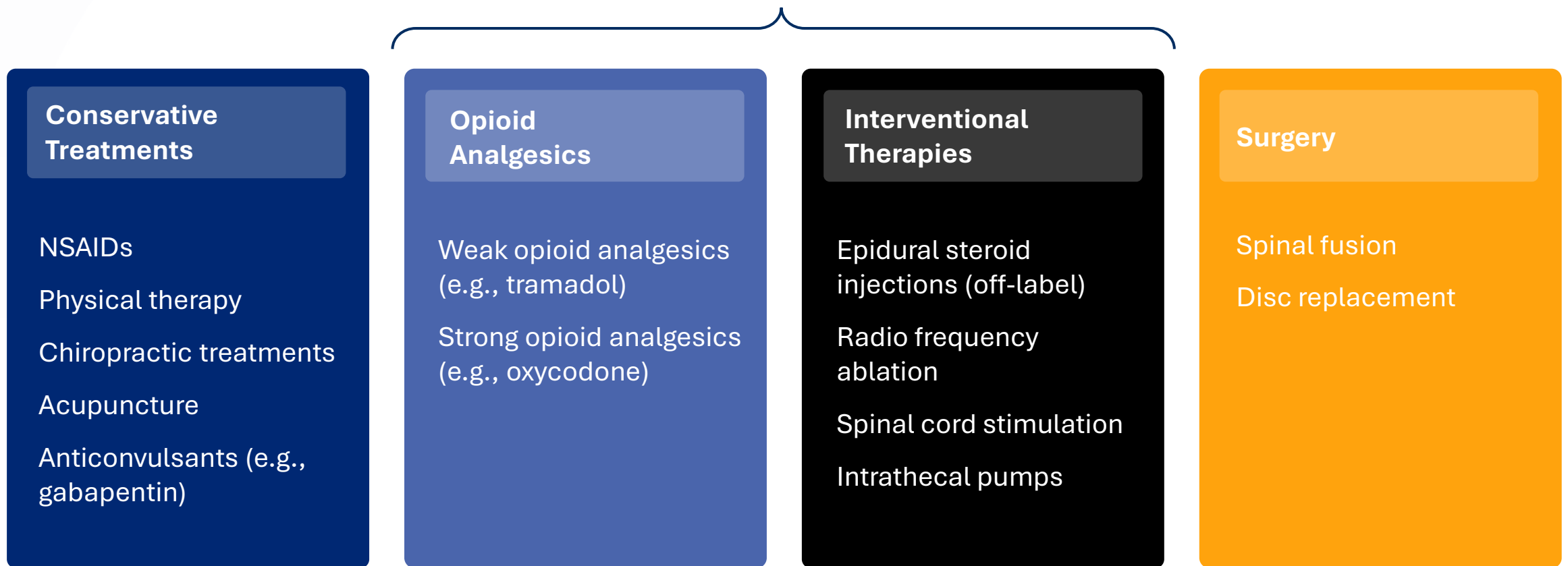
# Inflammation is at the Core of Pain in Degenerative Disc Disease



# The Patient Treatment Journey

## Rexlemestrocel-L has Potential to be First-Line in Choice for Treatment of CLBP with DDD Refractory to Conservative Treatment

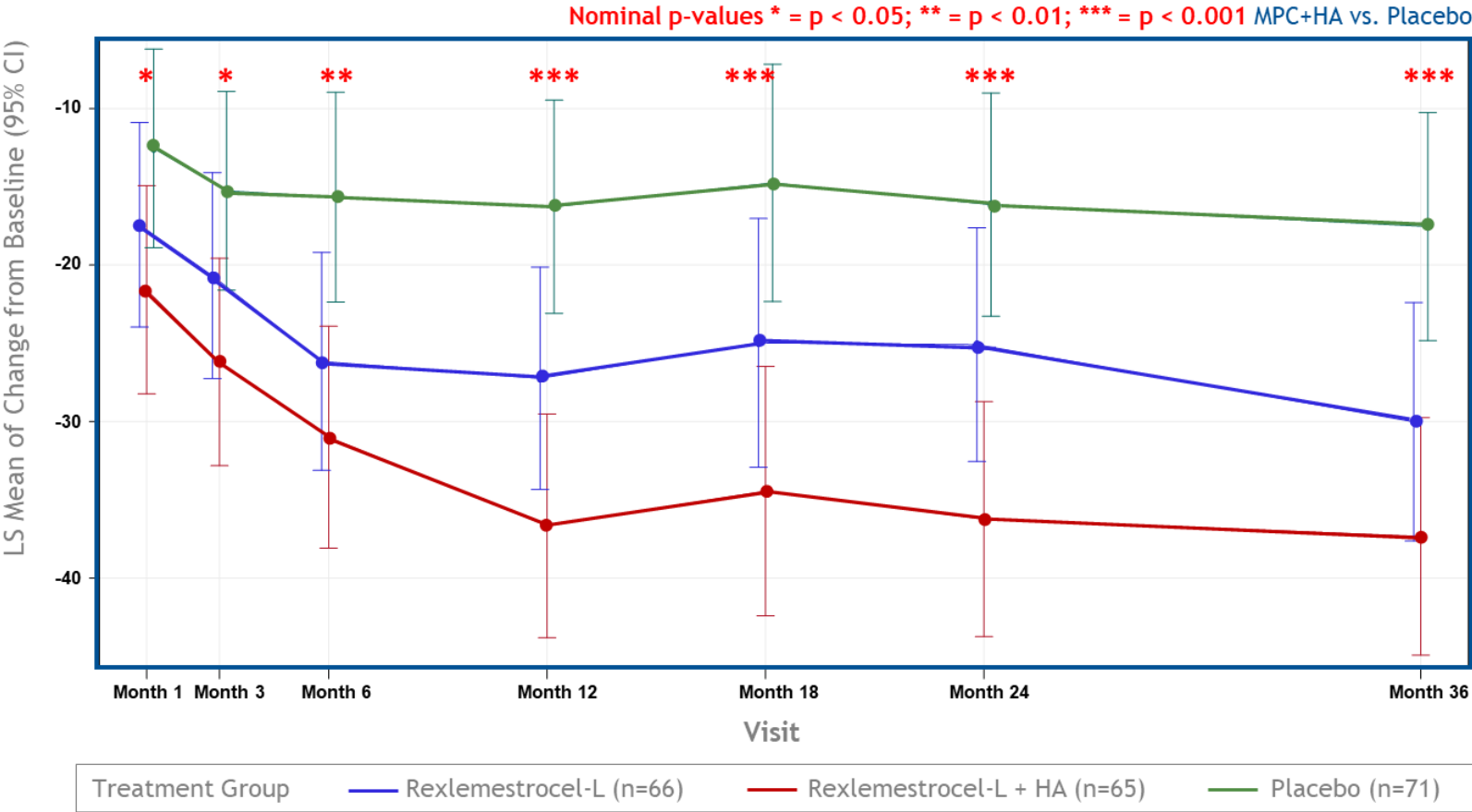
Rexlemestrocel-L targeting moderate-to-severe CLBP



# Phase 3 Trial Key Outcome Pain Reduction

## Rexlemestrocel-L+HA Demonstrated Significant Pain Reduction Through 36 Months

LS Mean VAS Change From Baseline, CLBP < 68 Months (n=202)

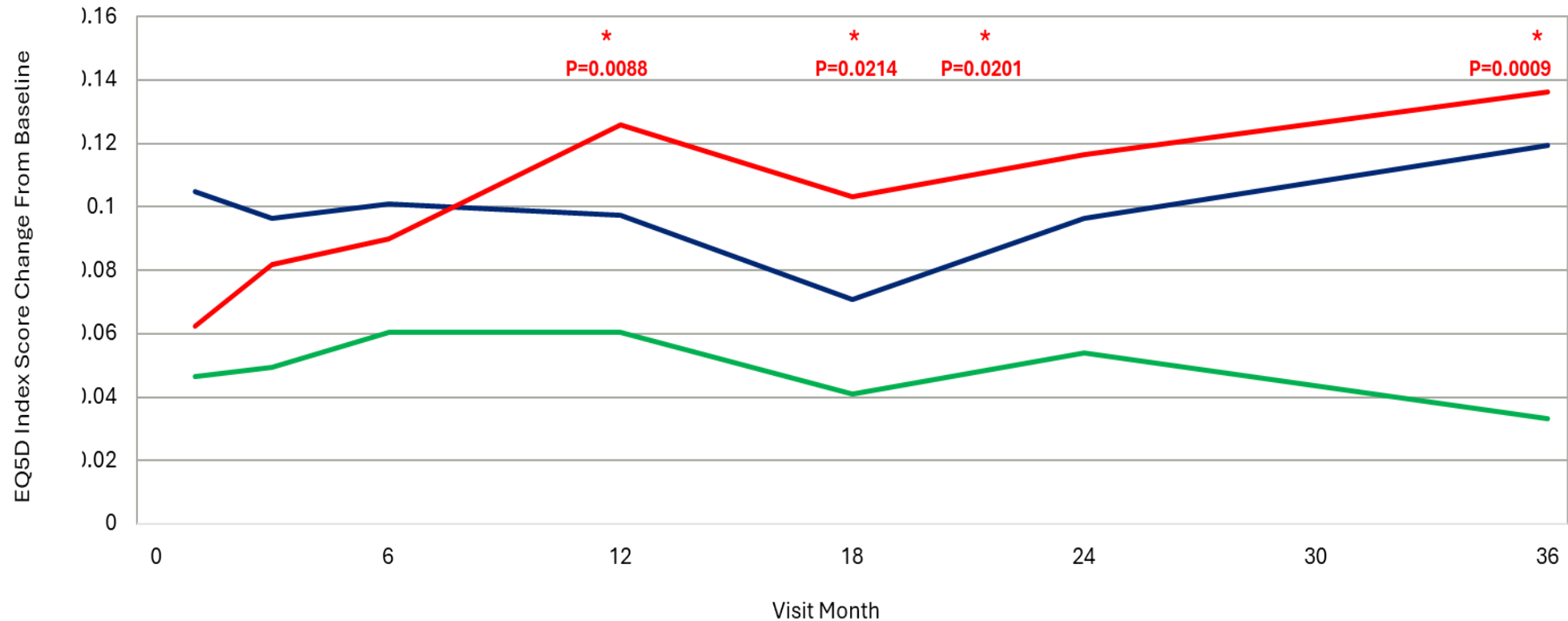


**Duration < Median  
Rexlemestrocel-L +HA**  
Demonstrated significant  
reductions in pain over 36-months

# Phase 3 Trial Quality of Life (QOL) Outcomes:

**Rexlemestrocel-L+HA significantly improved QOL (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) through 36 months**

EQ-5D Index Score Change From Baseline –CLBP < 68 Months (n=202)

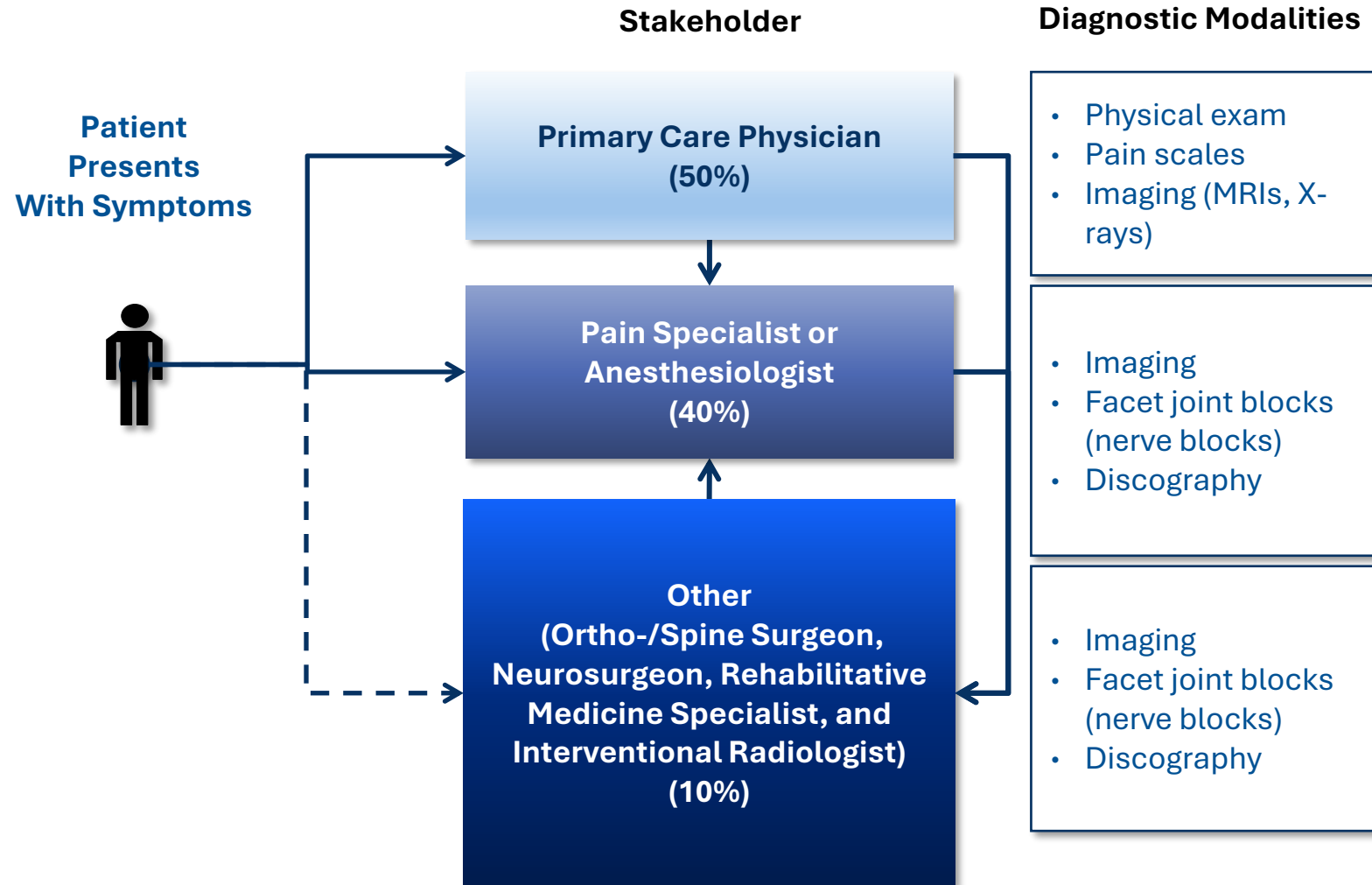


\* = nominal p-value  
MPC+HA vs. Placebo

Treatment Group    — Rexlemestrocel-L (n=63)    — Rexlemestrocel-L + HA (n=52)    — Placebo (n=49)

# Pain Specialists are the Primary Caregivers Seen by Patients with CLBP

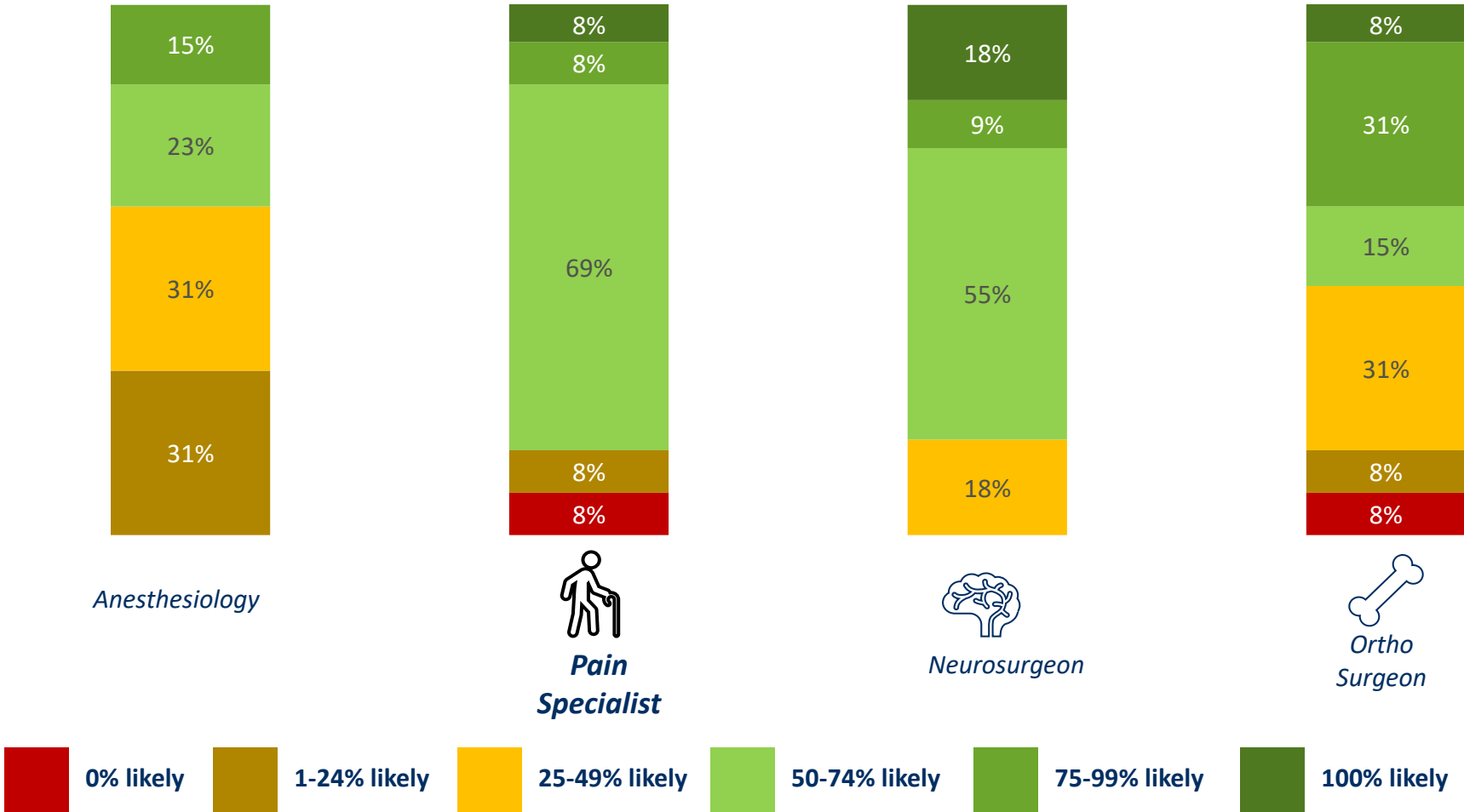
## 50% of Patients With Moderate-to-Severe CLBP Progress to Specialists for Diagnosis & Treatment of Degenerative Disc Cause



# 85% of Pain Specialists are More Likely to Recommend Rexlemestrocel-L for CLBP Based on Observed Clinical Outcomes



## Likelihood of Recommendation Irrespective of Price: Pain and Function Data at 12 Months

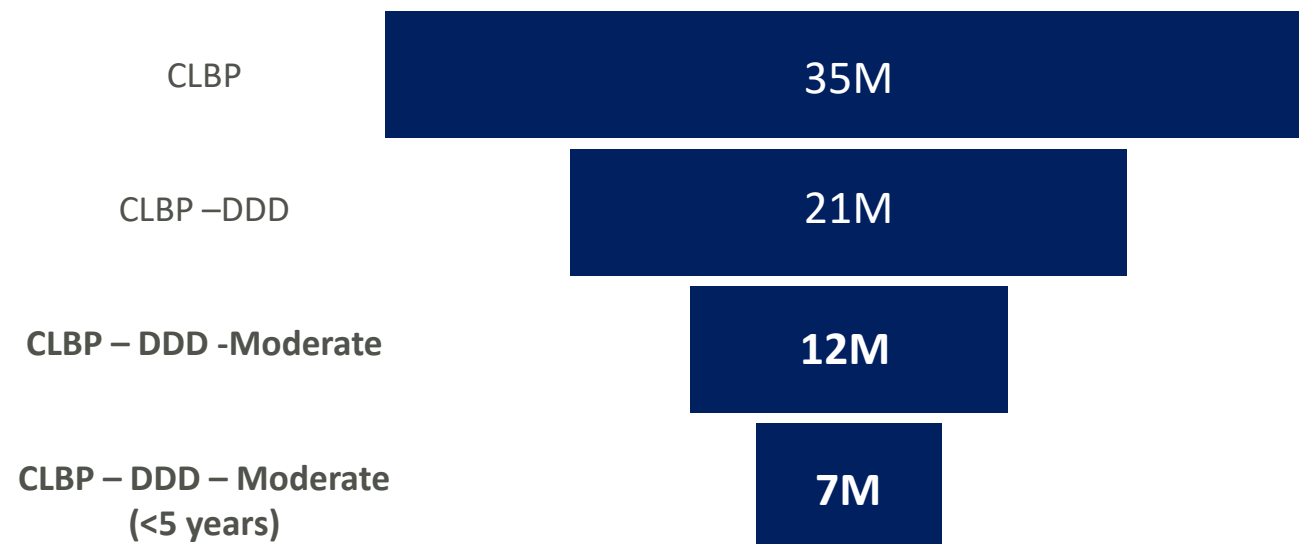


Guidehouse 2021 Study

# Rexlemestrocel-L: Potential Mega-Blockbuster in CLBP in U.S. Alone

- 7M+ Addressable Population
- Price ~\$20,000/patient based on durable pain and function results
- 85% of Pain Specialists are Likely to Recommend Rexlemestrocel-L for CLBP Based on Observed Clinical Outcomes<sup>1</sup>
- Potential revenue of \$14B with just 10% market penetration

## Addressable U.S. Market Number of Patients - Millions



# Launch timeline for rexlemestrocel-L in CLBP

**300 Patient 1:1 Placebo-Controlled Phase 3 Pivotal  
Trial in DDD Completes Enrollment**

**APR 2026**

**12 Month Primary Endpoint of Pain Reduction  
Top-Line Results**

**Mid CY2027**

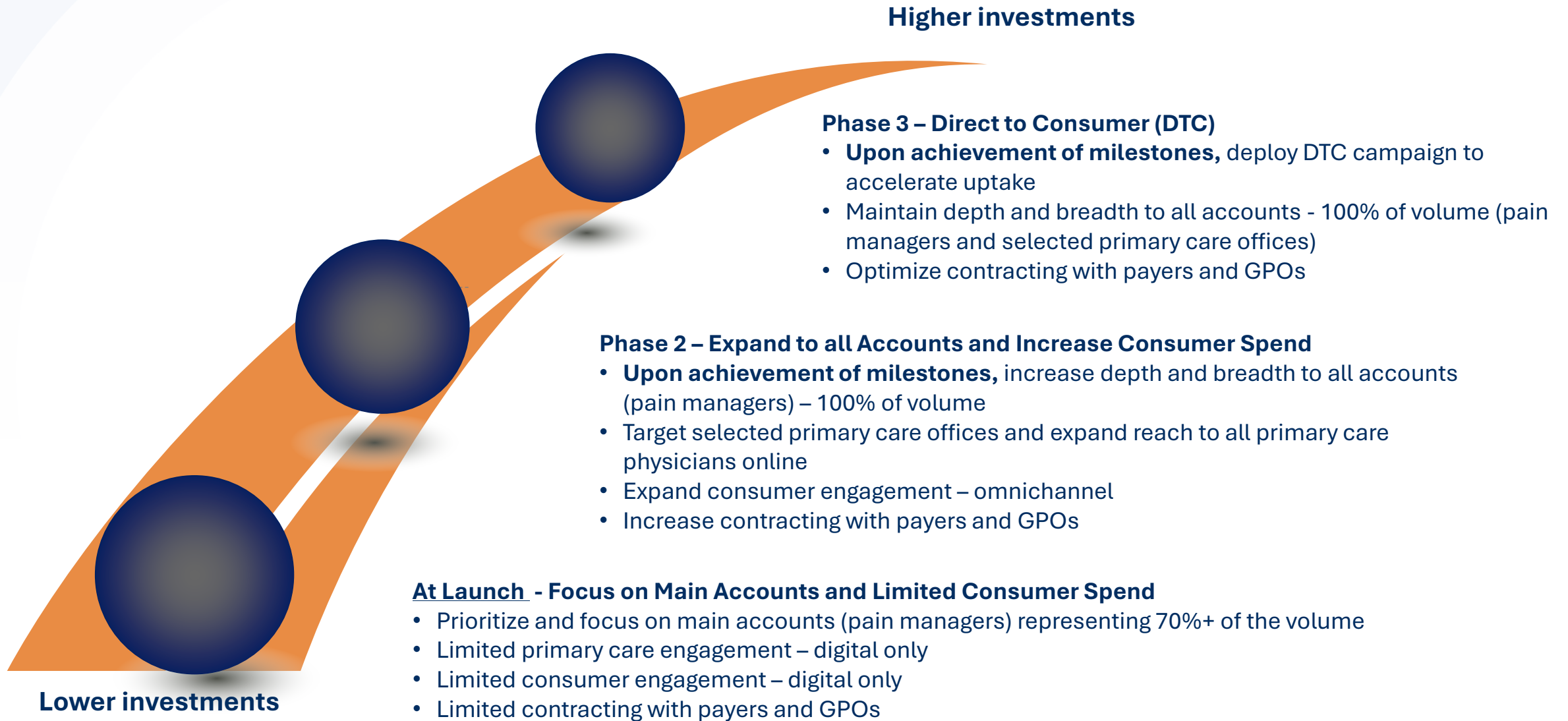
**BLA Submission to FDA**

**Q3 CY2027**

**Potential Approval Following Priority Review**

**Q2 CY2028**

# Go To Market - Phased Launch Based on Milestones Achievement



# Chronic Lower Back Pain KOL Perspective

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**Doug P. Beall, MD**

**Clinical Investigations LLC**

Chief of Services, Comprehensive Specialty Care;  
Director of Research Clinical Investigations LLC



# Chronic Heart Failure/LVAD

**Ken Borow**

Head of Cardiovascular



# Chronic Heart Failure: Rising Incidence with High Morbidity and Mortality

- Cardiovascular (CV) disease associated with inflammation is the leading cause of death in the U.S.<sup>1</sup>
- Heart failure (HF) in the United States is projected to affect >7 million adults by the year 2030. Approximately 50% of these people will have heart failure with reduced ejection fraction (HFrEF)<sup>2</sup>
- Chronic heart failure is a progressive disease with mortality that approaches 50% at 5 years and at least 75% after an initial hospitalization<sup>2-4</sup>

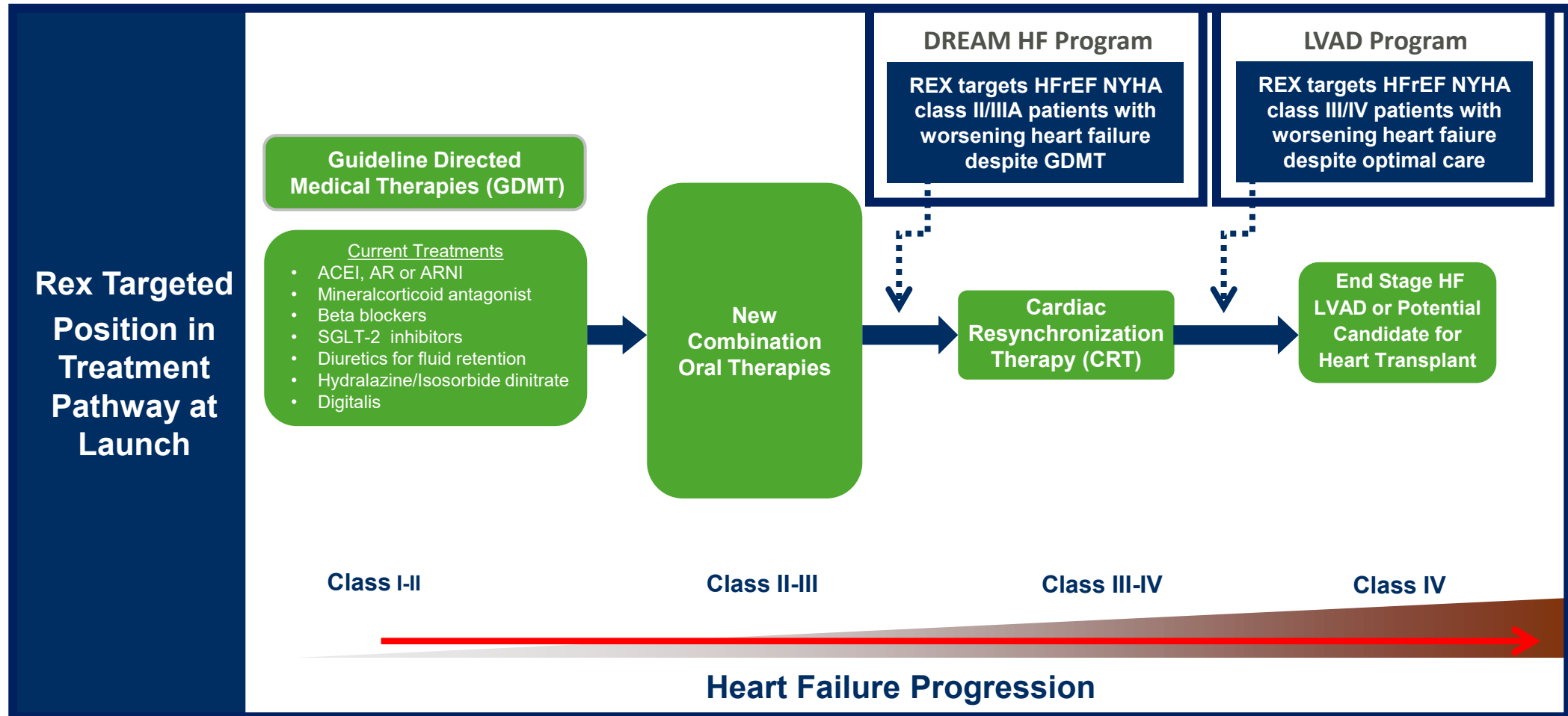
1. Muntner BEJ, et al. Heart Disease and Stroke Statistics-2019 Update: A Report From the American Heart Association. *Circulation*. Feb 19, 2019.

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:l223.

4. Shah KS, et al. Heart Failure with Preserve, Borderline, and Reduced Ejection Fraction; 5-Year Outcomes. *JACC*. 2017;Nov12.

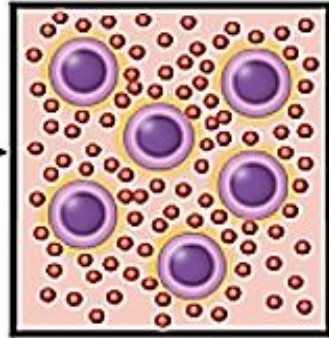
# Mesoblast's Rexamestrocel-L Targets Patients with Worsening HFrEF and Inflammation...A Paradigm Shift In Precision CV Medicine



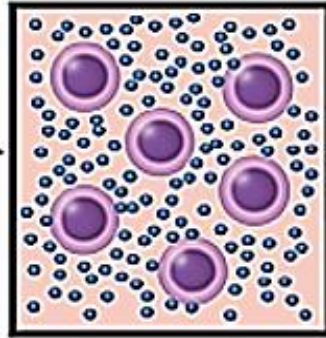
## Same formulation, dose and potency assay for product in both indications



MPCs are injected into viable but dysfunctional myocardium



MPCs are activated by local cytokines in the heart



MPCs exert anti-inflammatory, neovascular, and immunomodulatory effects

### DREAM-HF Trial

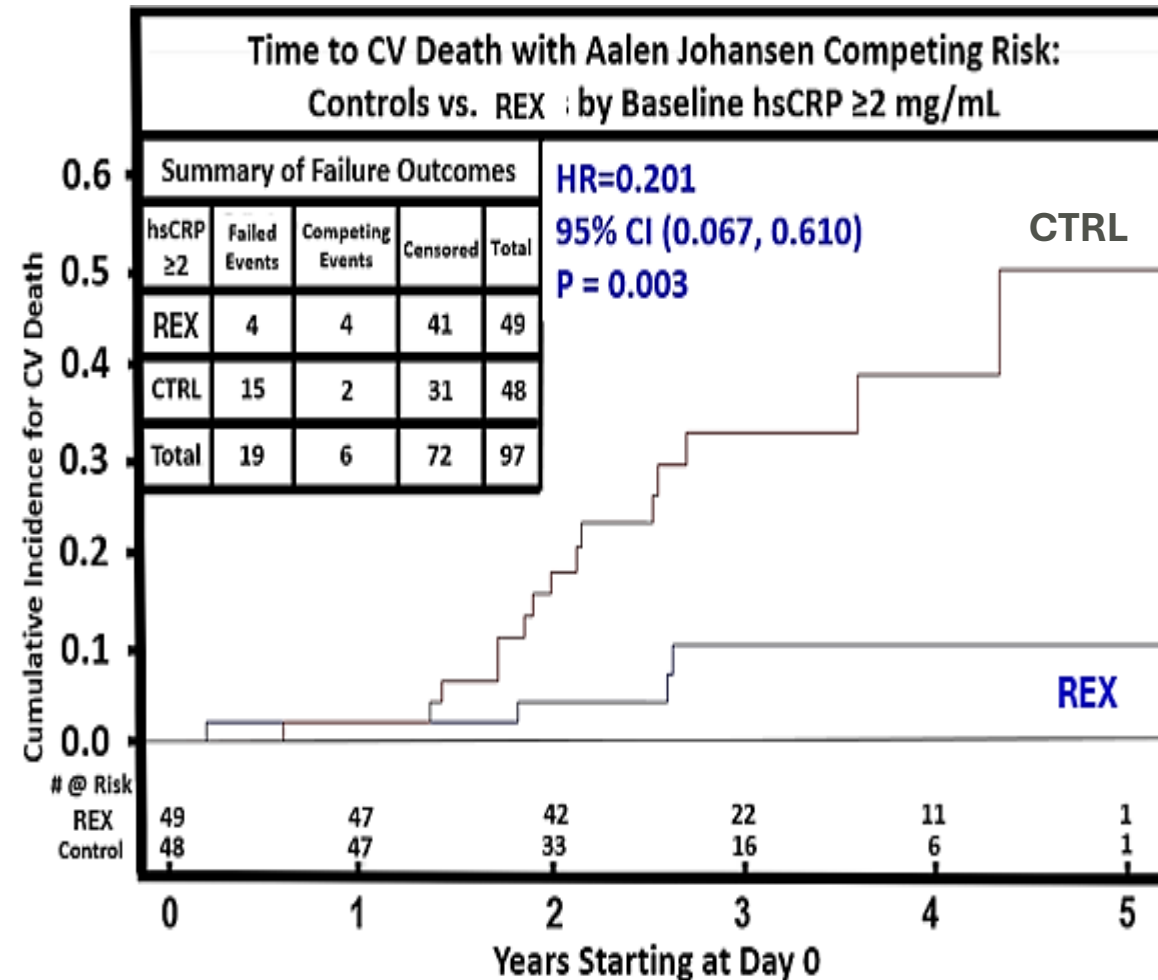
- 565 patient Phase 2b/3 randomized clinical trial (RCT) in NYHA II/III A HFrEF
- Rexlemestrocel-L reduced myocardial infarctions (MIs), strokes and cardiovascular death.

### LVAD Study

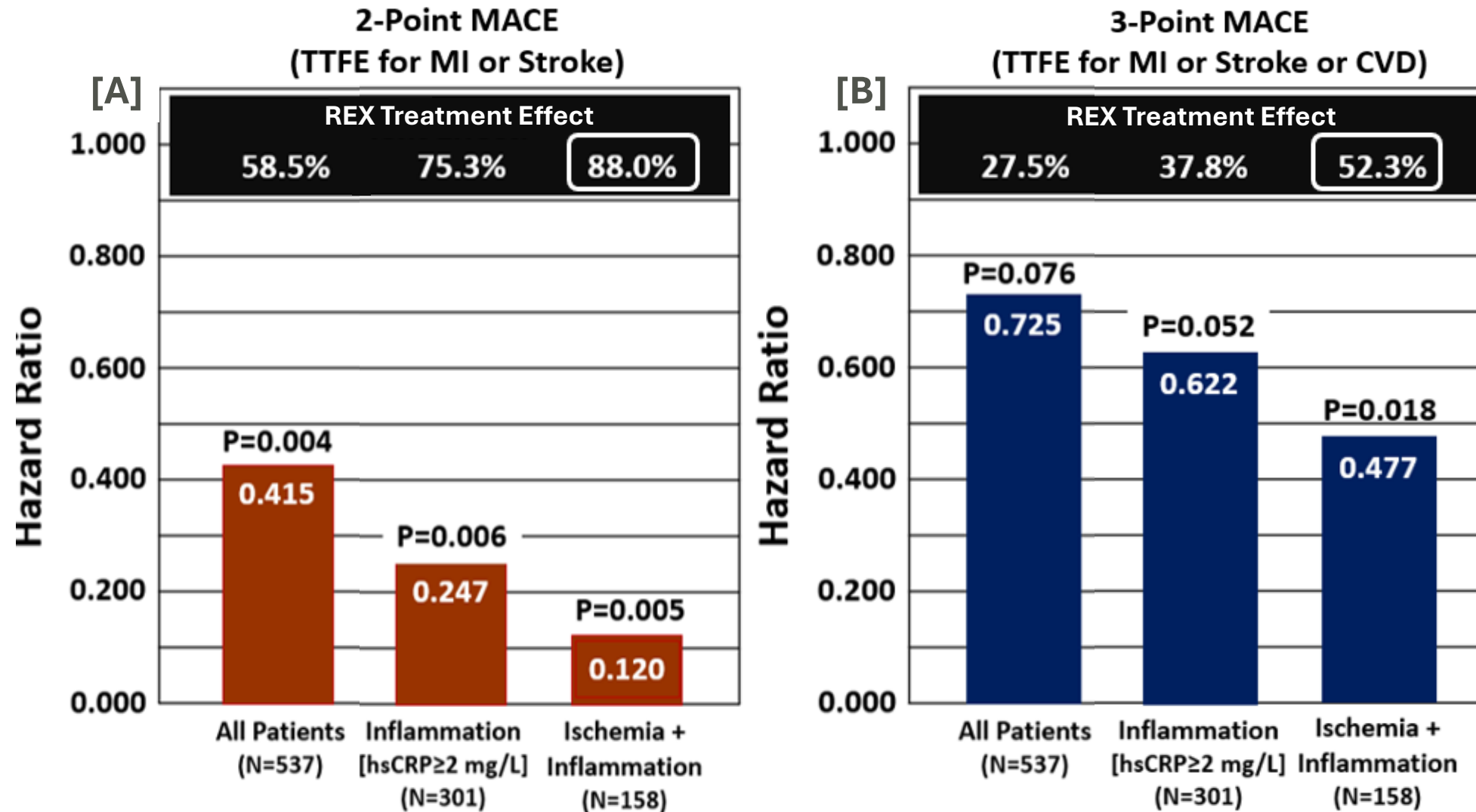
- 159 patient Phase 2b/3 randomized clinical trial in end-stage (NYHA IIIB/IV)
- Rexlemestrocel-L reduced complications of right heart failure (RHF) and GI bleeding

**Successful outcomes of 150M intramyocardial cell dose of rexlemestrocel-L in both RCTs**

# DREAM-HF: Rexlemestrocel-L Significantly Reduced CV Deaths In Patients With Inflammation (p=0.003)



# DREAM-HF Trial: Effect of REX on 2-point MACE (Panel A) and 3-point MACE (Panel B) in all HFrEF Patients and Sub-groups with Inflammation and Ischemia + Inflammation



# Investigational Agents Evaluated for Cardiovascular Risk Reduction Using 3-Point MACE (TTFE for MI or Stroke or CV Death)

## Comparison with Rexamestrocel-L in Patients with Myocardial Ischemia &/or Diabetes

Medication	Drug Class	Clinical Trial	Hazard Ratio	Risk Reduction	95% CI	P-value	# Randomized Patients
Liraglutide	GLP-1 Receptor Agonist (RA)	LEADER	0.87	13%	0.78, 0.97	0.01	9,340
		Heart Failure Sub-group	0.94	6%	0.72, 1.21	-----	1,305
Dulaglutide	GLP-1 Receptor Agonist (RA)	REWIND	0.88	12%	0.79, 0.99	0.03	9,901
Empagliflozin	SGLT-2 Inhibitor	EMPA-REG	0.86	14%	0.74, 0.99	0.04	7,020
Canagliflozin	SGLT-2 Inhibitor	CANVAS + CANVAS-R	0.86	14%	0.75, 0.97	0.02	10,142
		Heart Failure Sub-group	0.80	20%	0.61, 1.05	-----	1,461
Dapagliflozin	SGLT-2 Inhibitor	DECLARE Timi 58	0.93	7%	0.84, 1.03	-----	17,160
		Heart Failure Sub-group	1.01	0%	0.81, 1.27	-----	1,724
Ertugliflozin	SGLT-2 Inhibitor	VERTIS CV	0.99	1%	0.88, 1.12	-----	8,246
Rexamestrocel-L	Mesenchymal Precursor Cells	DREAM HF Ischemics &/or Diabetics	0.63	37%	0.43, 0.93	0.019	385
		Ischemics &/or Diabetics With Baseline hsCRP $\geq$ 2mg/L	0.46	52%	0.27, 0.77	0.003	212

# A Treatment that Reduces 3-Point MACE (Myocardial Infarction, Stroke and CV Death) Represents a Multi-Billion Dollar Opportunity

## Addressable Market in US

Pts. with Heart Failure

6.7M

Pts. with HFrEF

3.3M

Pts. with HFrEF & Ischemia

1.6M

Pts with HFrEF, Ischemia & Inflammation (hsCRP >2mg/L)

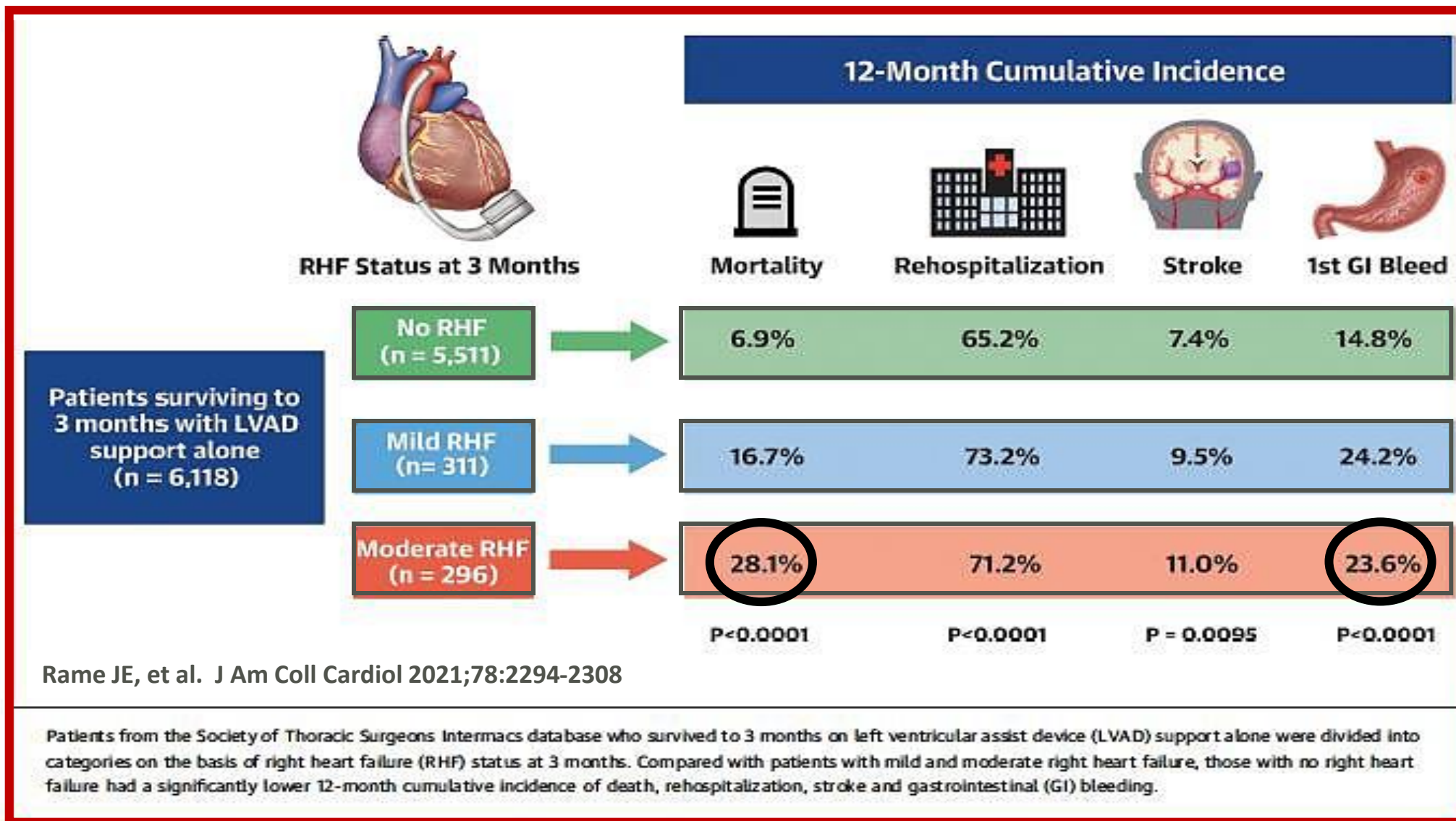
1.0M

- Sales price of \$150,000 would be supported based on phase 3 study results
- Potential annual revenue of >\$15B with just 10% market penetration

# End-stage Chronic HFrEF with LVAD

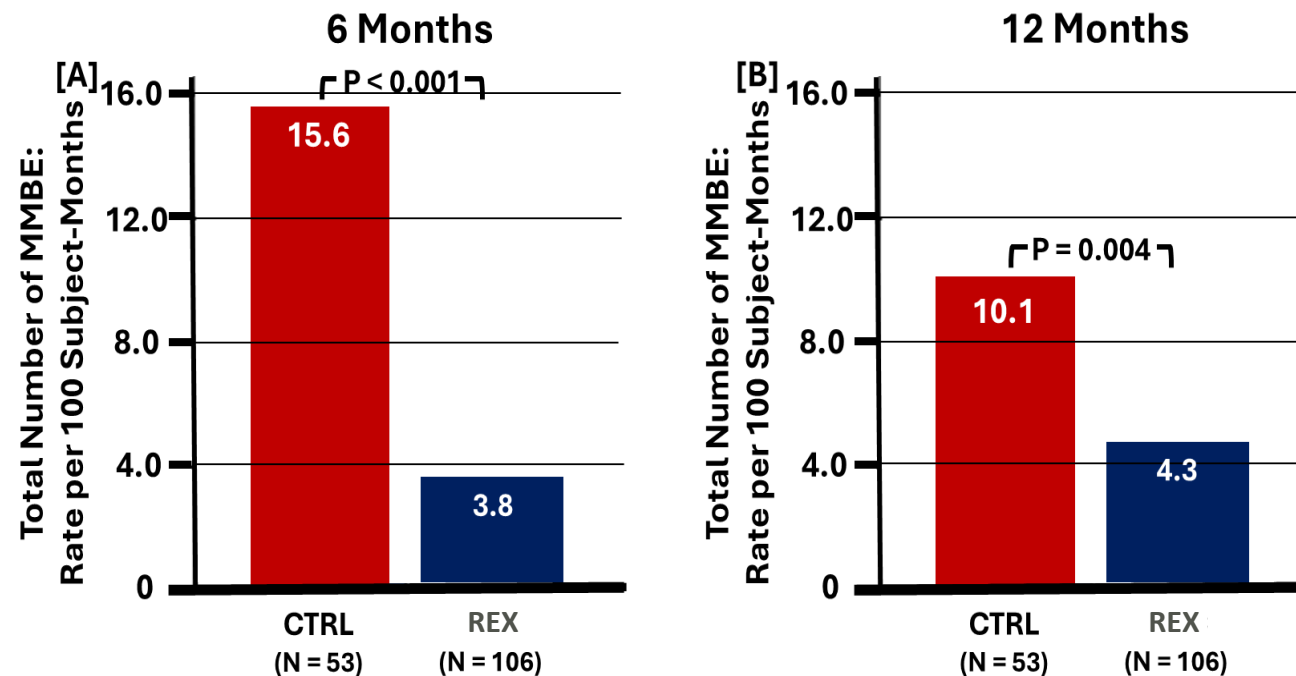
- Despite an LVAD in the left ventricle, progressive right heart failure (RHF) continues due to ongoing inflammation of the right ventricle
- Progressive RHF occurs in 15-30% of patients and is the primary cause of multi-organ failure and death
- A further complication of RHF is potentially life-threatening major mucosal bleeding events (MMBE), seen in ~30% of patients and the main cause of recurrent hospitalizations

# 12-Month 28% Mortality in Patients with Moderate Right Heart Failure (National INTERMACS LVAD Registry Data)



# LVAD Study: Rexlemestrocel-L in End-Stage HFrEF Patients with LVAD

- Improved right ventricular function
- Reduced right heart failure hospitalizations and mortality
- Reduced circulating inflammatory cytokines
- Reduced major GI bleeding events caused by hepatic venous congestion – FDA approvable endpoint



**Reduced Major Mucosal Bleeding Events in End-stage HFrEF Patients with LVAD Over 12 Months**

# CHF Franchise: Tactics & Strategy

- File with FDA for full approval for rex-L in patients with LVADs
- Filing is based on GI Bleeding being an FDA-acknowledged indication and having received Orphan Drug designation
- FDA's stated preference for randomized controlled trials has resulted in Mesoblast seeking a full FDA approval pathway, with benefit that an additional confirmatory trial is not required
- FDA approval of Rex-L in patients with LVADs will facilitate subsequent approval of Mesoblast's pre-LVAD (NYHA Class II/IIIA) chronic HFrEF patients via label extension

GI = gastrointestinal | CMC = chemistry, manufacturing & controls | HFrEF = heart failure reduced ejection fraction

# LVAD Approval Represents A Near Term Orphan Opportunity That Supports Label Extension Into The Larger Heart Failure Market

## Addressable LVAD Market in US

Pts. with Heart Failure

6,700,000

NYHA Class IV

500,000

Pts. Receiving an LVAD

2,500

LVAD Patients with Ischemia

2,000

- Sales price of \$200,000 would be supported based on phase 3 results and reduction in cardiac ICU hospitalizations
- Total addressable market potential is \$400M
- Approximately 190 LVAD certified centers in the US

# Inflammatory Heart Failure KOL Perspective

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## Emerson Perin, MD, PhD, FACC

**Baylor College of Medicine**

Medical Director of The Texas Heart Institute

Professor of Medicine, Baylor College of Medicine

## Eric Rose, MD

**Chief Medical Officer, Mesoblast**

Chief Medical Officer

World-renowned heart surgeon and scientist made history when he performed the first successful pediatric heart transplant



**Emerson C. Perin, MD, PhD**



**Eric Rose, MD**

# Leveraging FDA Approval for Ryoncil for New Pediatric Label Extension Indications

**Michael Schuster**

Head of Business Development



# Duchenne Muscular Dystrophy (DMD): An Inflammatory Disease with Unmet Need

- DMD is a genetic X-linked muscle disease with lack of dystrophin (a stabilizing protein essential for muscle strength) which ~15,000 patients in US
- Inflammation of skeletal muscle and fibrosis results in loss of ambulation by 12 years old
- Steroids are used in every patient for life and are the only agents proven to delay loss of ambulation and improve survival
- Dystrophin gene therapy replacement has only shown modest benefit

## DMD: Revenue Growth Opportunity Leveraging RYONCIL's Anti-Inflammatory Mechanism of Action

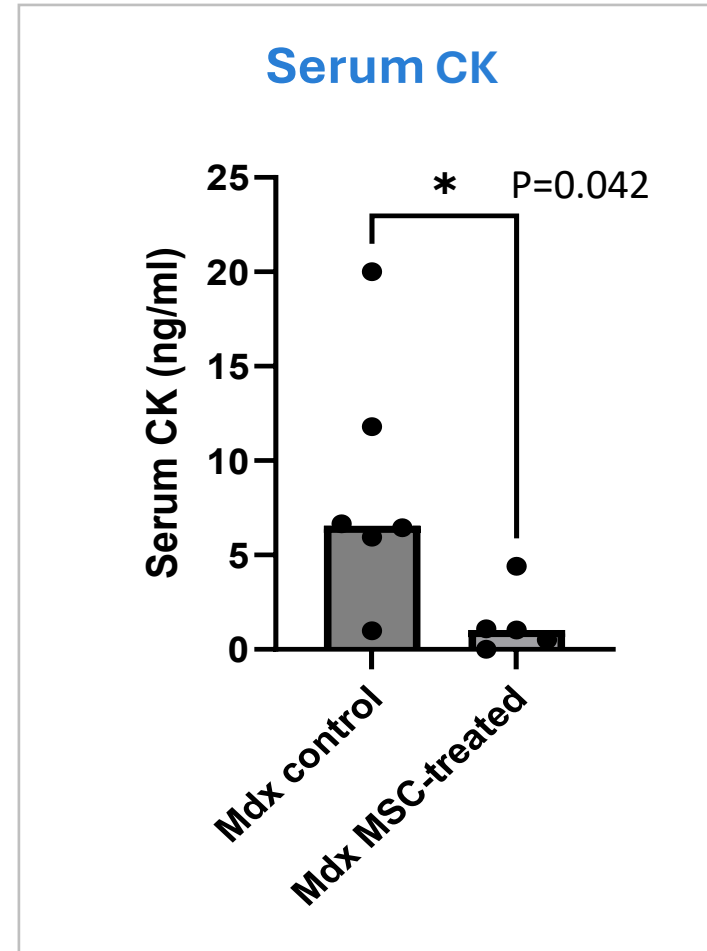
- RYONCIL has proven efficacy and safety in pediatric SR-aGvHD following steroid resistance, a disease of severe inflammation
- RYONCIL has demonstrated benefit alone and with gene therapy in animal models of DMD
- IND cleared by FDA for a trial that aims to extend RYONCIL label to ambulatory children with DMD
- Label extension in DMD maintains existing RYONCIL pricing structure

# Proprietary Mesoblast MSC Technology Improves Muscle Function in Duchenne Mice

## Ryoncil Reduces Serum Creatine Kinase (CK) Activity

### Administration of RYONCIL in mdx Mice Results in:

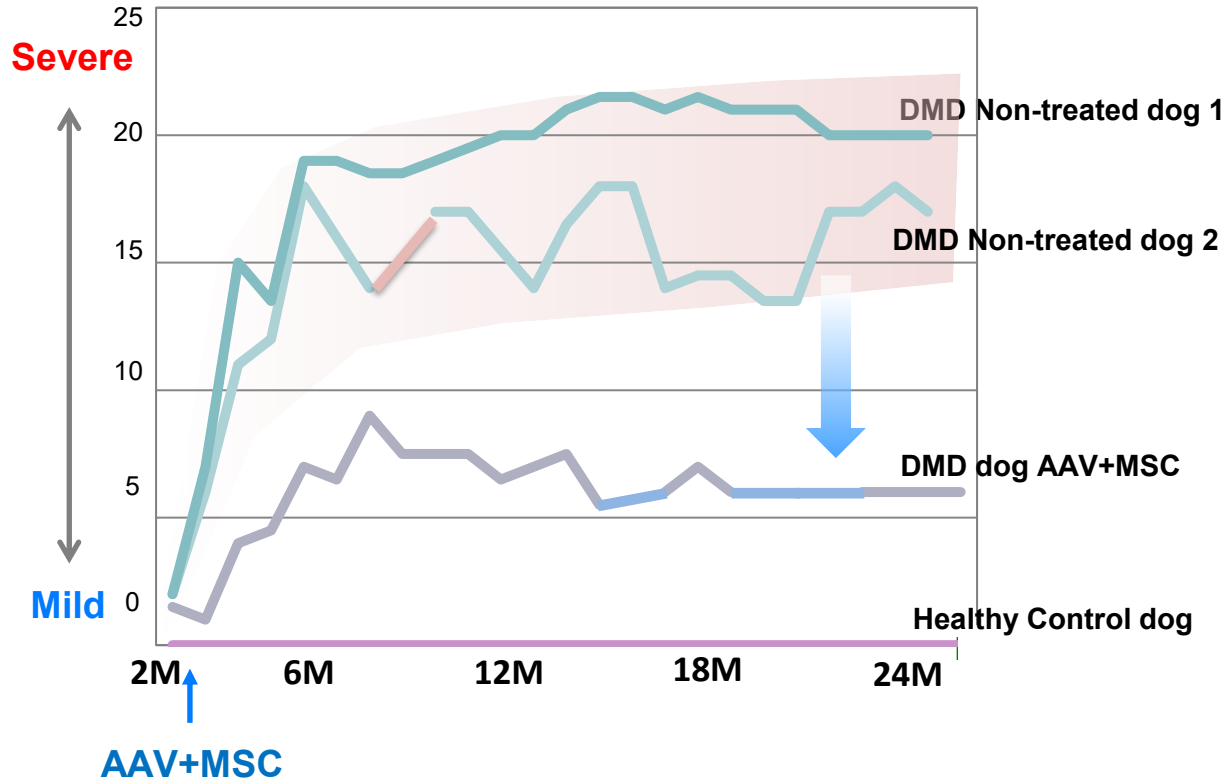
- Down regulation of T cell, macrophage and neutrophil immune activation pathways
- Increase in muscle regeneration pathways
- Improvement in exercise-induced muscle fatigue



1. McGreevy JW, et al. Dis Model Mech. 2015 Mar;8(3):195-213.  
2. Morrison J et al, Lab Invest 2000, 80:881-891.

# Mesoblast Proprietary MSC Combined with Micro Dose of Dystrophin Gene Therapy Shows Additive Benefit In Duchenne Dogs

Grading score



Composite score of gait, mobility, limb or temporal muscle atrophy, drooling, macroglossia, and dysphagia

DMD Beagle - Control



DMD Beagle 8 Months Post Treated

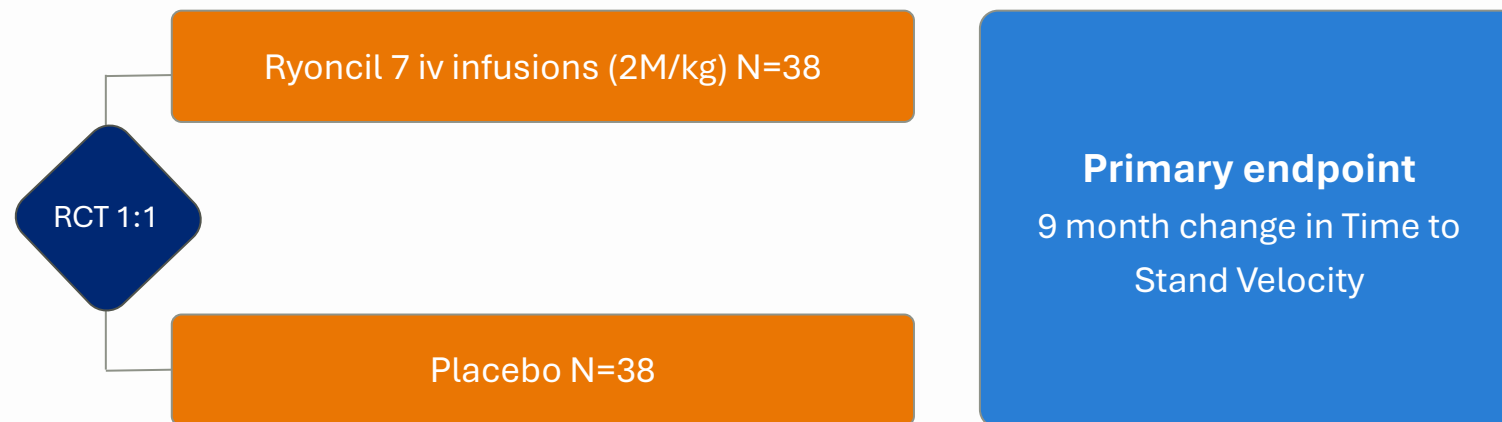


# IND Clearance Received from FDA for Phase 3 Registration Trial in Children Aged 5-9 Years with Duchenne Muscular Dystrophy

## Clinical Development Plan

### Inclusion & Exclusion Criteria

- Patients 5-9yo
- All patients ongoing treatment with steroids for >6months
- May have received gene therapy



- Collaboration with Parent Project Muscular Dystrophy (PPMD) for patient identification and trial awareness; PPMD is the leading advocacy group for afflicted patients and their families
- Expected to enroll over 12 months
- Prevalence of 5-9 year olds ~2,500 patients with ~500 new patients/year

# Next Generation MSC Therapies

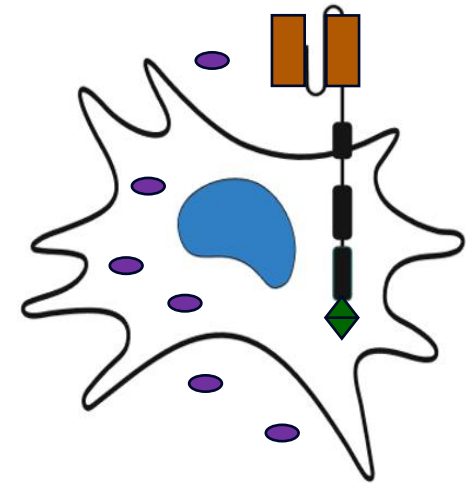
**Dan Devine**

Head of Special Projects



# Next Generation Gene Modified MSCs – Enhanced Products for New Indications

- Mesoblast is leveraging the only FDA-approved MSC platform to create genetically-modified next gen products
- Enhanced (a) potency via payload (●) or triggered pathway (◆), and (b) targeting via antigen binding moiety (■)
- Two proprietary next gen platforms (patents through 2043)
  - **Chimeric Antigen Receptor “CAR-MSCs” developed at Mayo Clinic (Saad Kenderian)\***
  - **Oncolytic Virus “OV-MSCs” developed at Baylor College of Medicine (Dr. Malcolm Brenner)\*\***
- IND-enabling development ongoing at each location; first IND in 1QCY2028



\*Nat Biomed Eng. 2024 April ; 8(4): 443–460. doi:10.1038/s41551-024-01195-6;\*\*<https://pubmed.ncbi.nlm.nih.gov/36989357>

# CAR-MSK Platform

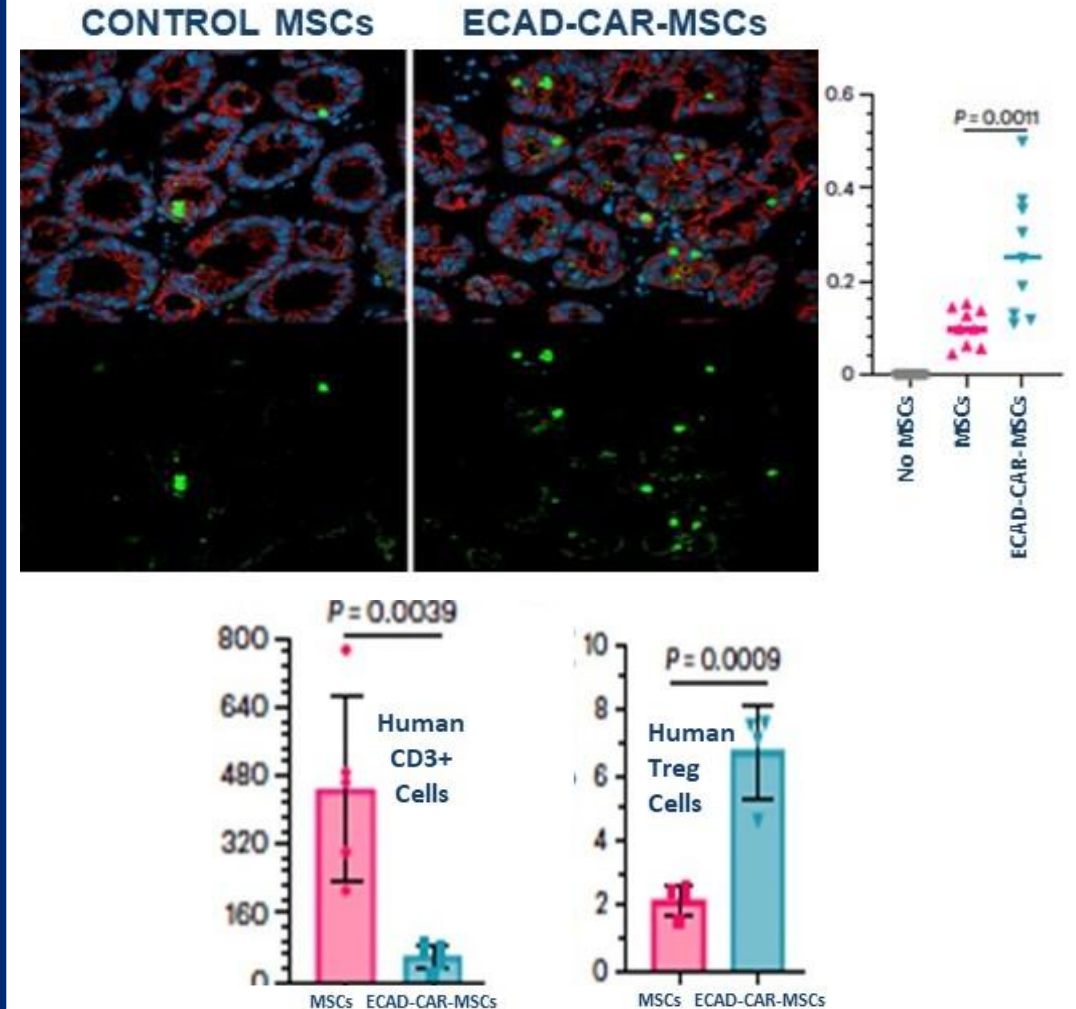


- Leverage tech behind CAR-T therapies *without* issues re: (i) safety and (ii) manufacturing
- Broad range of potential target antigens/intracellular pathway choices - plug and play system
- Enhanced targeting/increased potency can reduce dosing/COGS for all future indications
- Lead products target Lupus and UC/Crohn's, significant/unmet medical needs
- IND-enabling studies at Mayo Clinic; supervised by Dr. Kenderian

Antigen/Product	Target Tissue	Potential Indication(s)	Triggered Intracellular Pathway
CD19-CAR-MSK	CD19 B Cells	Lupus	CD28z, TLR3, TLR4, CD28, IFNy
ECAD-CAR-MSK	Inflamed tissue	UC/Crohn's	
MOG-CAR-MSK	Myelin Sheath	MS	
COL2A1-CAR-MSK	Collagen	RA	
AMPA-CAR-MSK	Neurons	Alzheimer's	
CAR-MSK-CCN1	Skin	Wounds	

# ECAD-CAR-MSC for Ulcerative Colitis/Crohn's

- Ulcerative Colitis and Crohn's are significant unmet medical needs; US sales projected to reach total of \$20 billion by 2030
- CAR modification will enhance the potency of and reduce dose requirements of Mesoblast's unmodified MSCs, which have already produced positive results in clinical trials
- ECAD-CAR-MSCs, which targets e-cadherin antigen, have shown promise in animal model of inflammation\*
  - Significantly increased homing to target inflamed colon vs. unmodified MSCs
  - Significantly greater inhibition of CD3+ T cell proliferation and induction of T regs vs unmodified MSCs



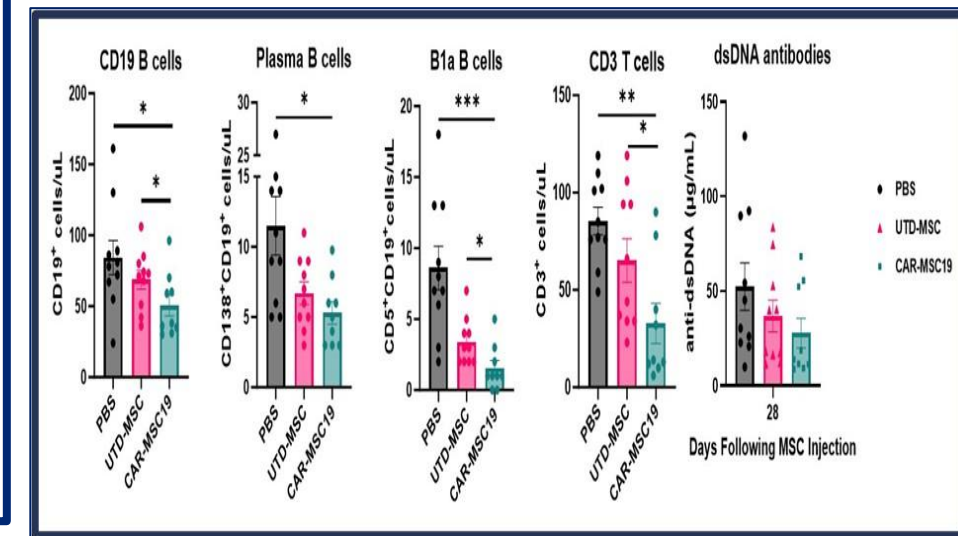
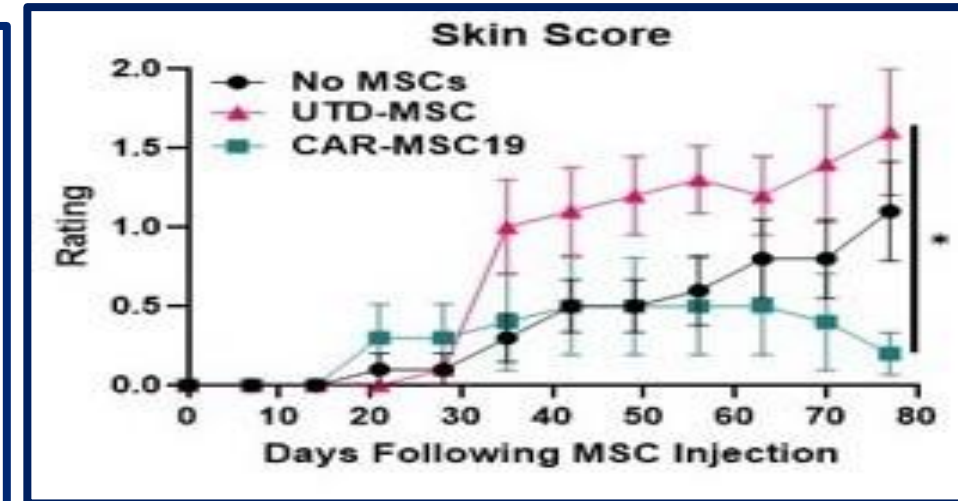
\*Nat Biomed Eng. 2024 April ; 8(4): 443-460. doi:10.1038/s41551-024-01195-6

# CD19-CAR-MSC for Lupus Nephritis

- Lupus nephritis (LN) represents a significant unmet medical need, as current treatments are only effective in 30% of patients
- CD19-CAR-MSCs have shown promise in animal models of Lupus by reducing key contributors to pathology and improving outcomes
- \*
- Relative to CD19-CAR T cells, which have shown efficacy in early trials, CD19-CAR-MSCs offer significant advantages:\*

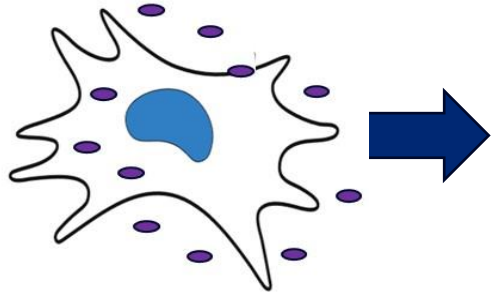
  - Avoidance of cytokine release syndrome
  - Avoidance of long-term B cell depletion/infection
  - Inhibition of CD3+ T cells
  - Recruit and induce T-Reg cells

- Lupus market projected to grow to US\$20 billion in 2034



\*Nat Biomed Eng. 2024 April ; 8(4): 443–460. doi:10.1038/s41551-024-01195-6;

# OV-MSD Platform



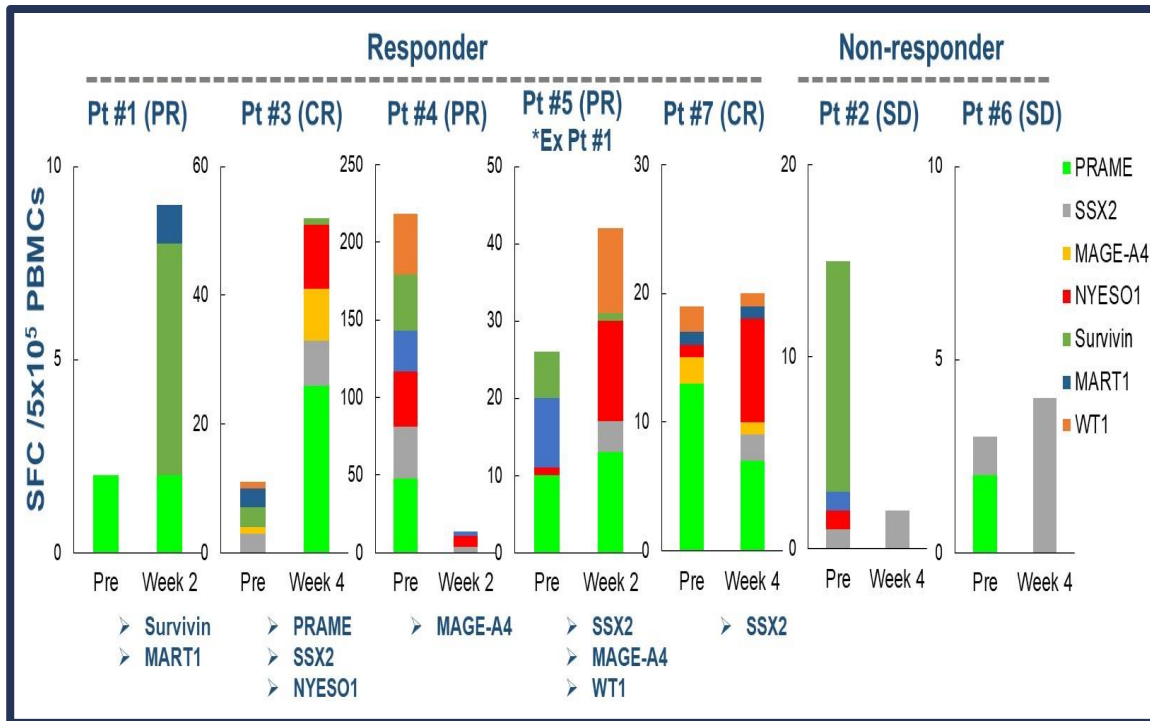
- MSCs loaded with an oncolytic virus (OV) genetically engineered to produce (i) binary T-cell engager (BiTE) that engage tumor cells and CD3+ T cells; and (ii) anti-cancer payloads
- MSCs protect payload as they navigate to targeted tissues
- OV and payloads released at tumor site as MSCs go through oncolysis

- Leverage technology behind CAR-T therapies without issues of safety and manufacturing
- IND-enabling studies ongoing at Baylor College of Medicine, under supervision of Dr. Malcolm Brenner, Director of the Center for Cell and Gene Therapy at Baylor

OV Payloads/Engagers Evaluated by BCM			
Chemokine	Cytokine	Checkpoint Inhibitor	Engager
MPI-1a RANTES	IL2 IL7 IL12 IL15 IL21	PD-L1 CTLA-4	CD19 CD44v6 MUC-1 FAP HER2

# OV/IL12/PDL1 (First Gen OV) and CD44v6-OV-MSV for Cancer

First Generation oncolytic virus (OV) encoded for IL12 and PDL1 inhibitor (OV/IL12/PDL1) responses in 5 of 7 patients (intratumoral admin) in Phase 1 clinical trial<sup>a</sup>



<sup>a</sup>Mesoblast has exclusive rights to this first gen oncolytic virus product

- Microdose of 1<sup>st</sup> Generation OV/IL12/PDL1 demonstrated safety and local efficacy intratumorally\*
- 2<sup>nd</sup> Generation OV has demonstrated greater potency in animal model, due to addition of bi-specific engager (BiTE) targeting CD3+ T cells and CD44v6 tumor associated antigen, along with IL12 and PDL1 inhibitor (CD44v6-OV-MSV)
- Diverse anti-cancer mechanisms: (i) oncolysis, (ii) T-cell engagement, (iii) IL12 and (iv) PDL1 inhibitor
- Baylor team has also demonstrated that MSC IV delivery significantly increases anti-tumor effect of engineered OV/IL12/PDL1\*\*
- CD44v6-OV-MSV in IND-enabling studies at Baylor, evaluating efficacy in lung, pancreatic and breast cancer

\*<https://pubmed.ncbi.nlm.nih.gov/36989357/>; \*\*<https://pubmed.ncbi.nlm.nih.gov/33571680/>

# Next-Gen MSC Technology

## Securing the Future While Aligned with Current Priorities

### **Next-Gen MSCs protect leadership position and enhance pipeline**

- Maintains leading competitive position well into the future (IP, technology, product performance)
- Opens promising/valuable new commercial opportunities
- Candidates for deployment of advanced manufacturing capabilities (e.g., bioreactors)

### **Development of Next-Gen MSCs strategically aligned with current corporate priorities**

- Leading institutions can advance products through Phase 1 trials onsite
- Building value w/o expansion of infrastructure
- Maintains internal focus on core commercial and late-stage clinical trial focus

# Next Generation MSC Platforms KOL Perspective

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## Saad Kenderian, MD, ChB

Mayo Clinic

Assistant Professor of Oncology, Medicine and  
Immunology at Mayo Clinic



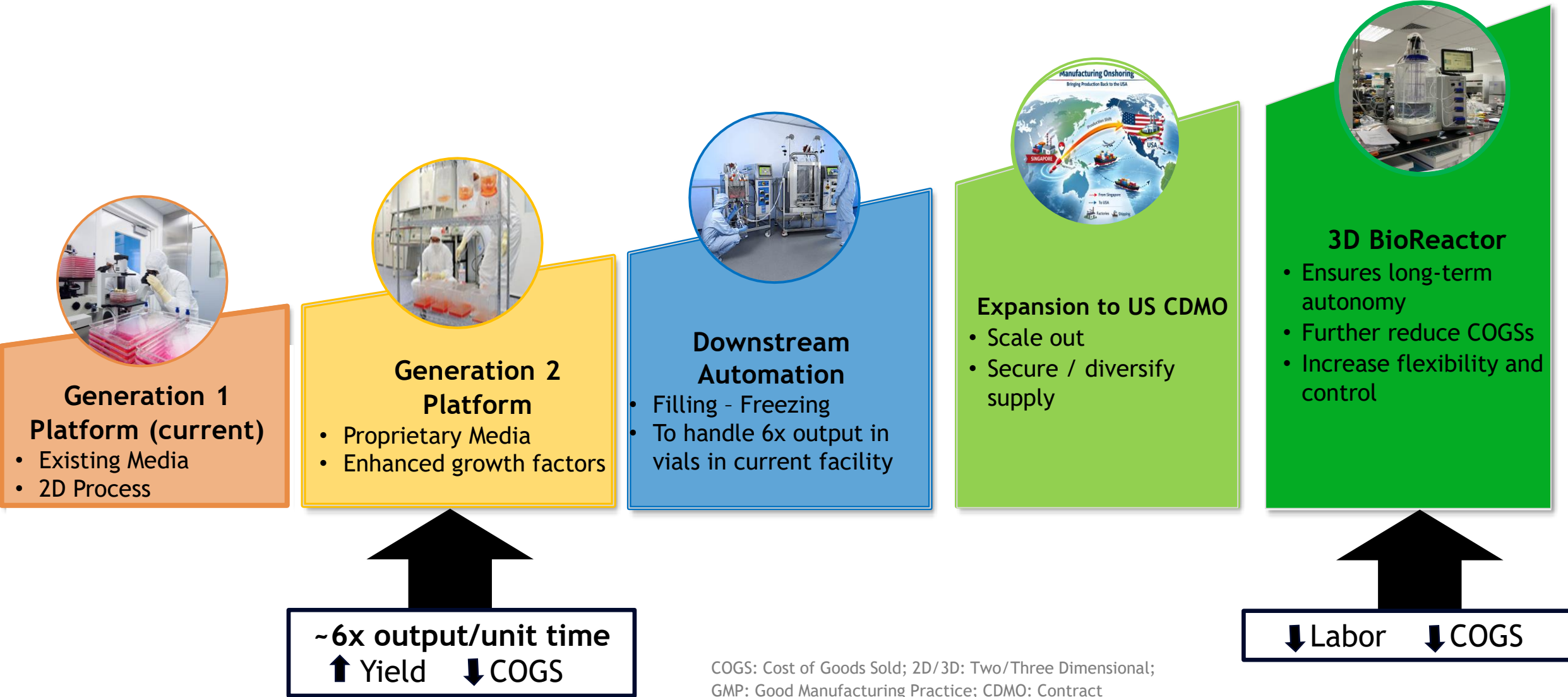
**Manufacturing**

**Justin Horst**

Head of Manufacturing



# Cutting Edge Innovations in Manufacturing: Drivers of Increased Yield, Capacity & Reduced COGS



COGS: Cost of Goods Sold; 2D/3D: Two/Three Dimensional;  
 GMP: Good Manufacturing Practice; CDMO: Contract  
 Development & Manufacturing Organization

# Manufacturing activities adequately funded internally to support projected demand and further drive down COGS

Manufacturing Activity & Strategic Initiatives	Timeframe
<ul style="list-style-type: none"> <li>Ensure RYONCIL commercial inventory supply meets projected growth in demand for pediatric and adult indications</li> </ul>	CDMO contracts in place for projected 3-year demand in commercial product
<ul style="list-style-type: none"> <li>Introduce <b>second generation manufacturing platform with proprietary media</b> post first approvals for initial remestemcel-L and rexlemestrocel-l products to meet requirements of large volume indications (Adult GVHD, CLBP, CHF)</li> </ul>	12-18 months
<ul style="list-style-type: none"> <li>Introduce automation to match increased production scale</li> </ul>	12-18 months
<ul style="list-style-type: none"> <li>Validate U.S. manufacturing site post approvals</li> </ul>	Planned for FY2028

**Financial**  
**James O'Brien**  
Chief Financial Officer

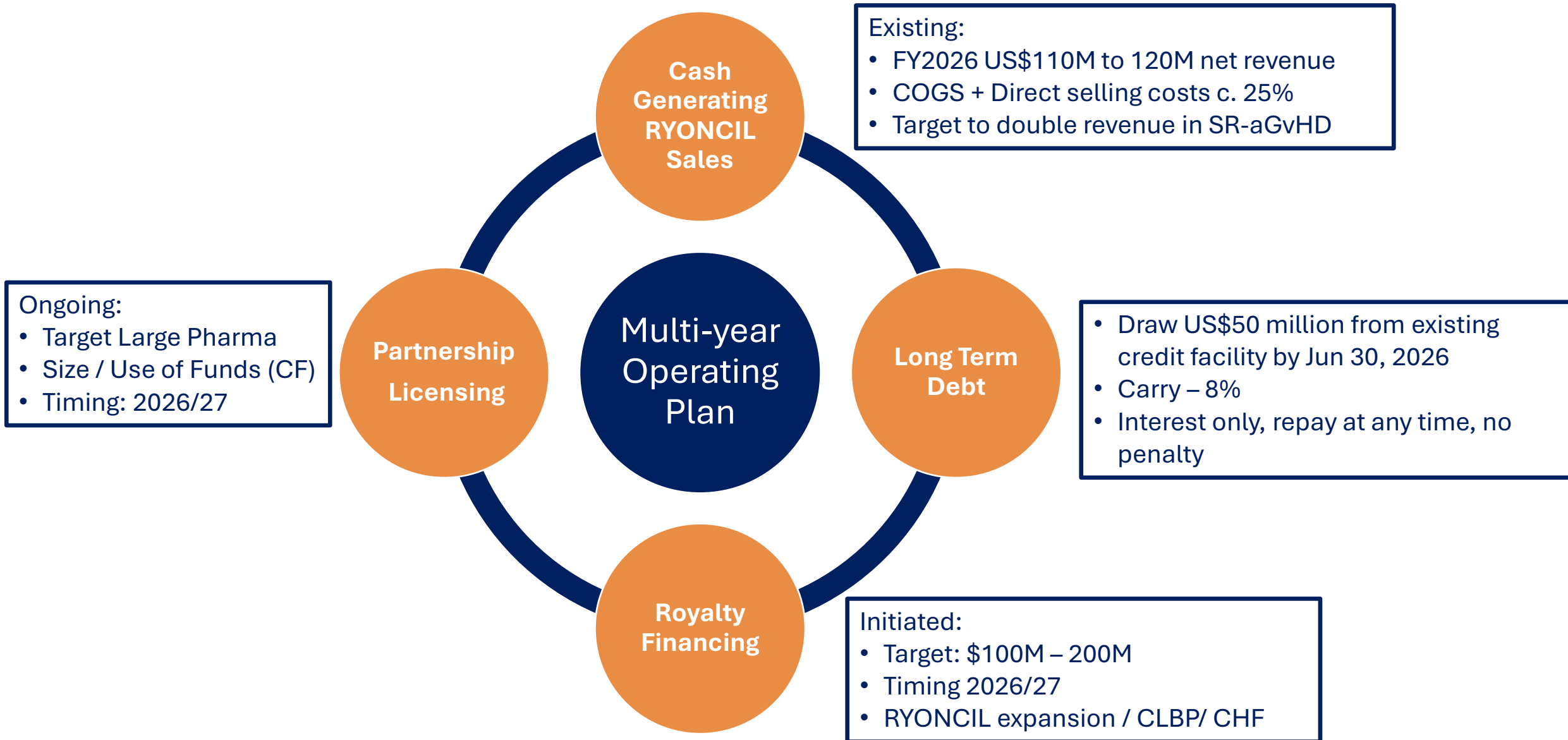


# Strong Financial Position

Cash balance  
**US\$130M**  
at Dec 31, 2025

- Gross revenue Q3 FY26 was US\$35.3M, with net revenue US\$30.3M
- RYONCIL gross profit for H1 FY26 was US\$44.2M, with US\$7.7M direct selling costs
- Net operating cash usage for H1 FY26 was US\$30.3M
- Mesoblast expects to see reduction in net cash spend over the remainder of the fiscal period based on projected receipts from quarterly revenues
- Cost discipline approach to managing spend in-line with revenue
- Operating plan includes spend on Phase 3 programs, manufacturing for BLA filing and commercial inventory
- New term loan totaling US\$125M replaces existing higher-cost debt

# Internal Revenue Supports Existing Operations, Various Non-Dilutive Sources of Capital For Growth



**Wrap-Up**  
**Silviu Itescu**  
Chief Executive



## MSC Magic – What Makes These Cells Special

- Multi-modal anti-inflammatory mechanism of action – means can act concurrently on multiple pathways of the immune system, not just one
- Inert and self-regulating in absence of inflammation equals excellent safety profile
- These features result in superior efficacy without concerns of off-target adverse events typical of small molecules or antibodies
- Platform technology can be leveraged across many indications with high unmet needs
- No requirement for matching or immunosuppression
- Highly expandable and scalable manufacturing means product made from one donor can be used in thousands of unrelated recipients
- These features underpin industrial scale supply chain with a sustainable high-margin business model

# Our 'MOAT' – What Sets Mesoblast Apart and Protects Our Market Leadership Position

- Globally IP portfolio >1,100 patents provide protection through >2044
- Dominant IP protects a cell type whose unique properties underpin a scalable commercial business model
- First mover advantage – the first and only MSC approved by FDA
- Completed large, US-based, randomized clinical trials which provide evidence of efficacy
- Benchmark in complex manufacturing with IP protection, significant know-how advantage, demonstrated FDA alignment, scale-up capacity, and ability to leverage across many products
- Next gen technology leadership to enhance tissue-homing characteristics and achieve even greater efficacy for existing products in areas such as inflammatory bowel disease, lupus nephritis and Alzheimer's disease, and completely open new areas such as cancer

# Anticipated Major Upcoming Milestones

## **RYONCIL – Commercial**

- Net revenue approaching US\$100M since launch
- Strategy in place to strongly grow revenue base
- Well-funded to execute on operational plans, RYONCIL sales to fund growth pipeline
- Focused on increasing penetration of pediatric SR-aGvHD market

## **RYONCIL - Label Extension**

- Label extension to adult SR-aGvHD; 3x larger market vs pediatric
- Adult SR-aGvHD trial in collaboration with BMT-CTN network, trial initiated, to complete in 12-18 months
- Pediatric Duchenne's in collaboration with PPMD patient advocates – FDA IND clearance received

## **Rexlemestrocel-L - CLBP Blockbuster**

- Complete enrollment of pivotal trial end of April
- Top-line primary endpoint mid-CY2027
- BLA filing for FDA approval Q3 CY2027
- Potential FDA approval and US launch Q2 CY2028

## **CHF: regulatory strategy to gain approval for blockbuster indication**

- File BLA with FDA for end-stage heart failure patients on LVADs this quarter
- Leverage approval to initiate confirmatory trial in NYHA II/III HFrEF

A young child with curly hair is lying in a hospital bed, looking thoughtful. A hand is resting on their forehead, and a white stuffed animal is visible in the foreground. The image is overlaid with a blue circular graphic on the left side.

**Thank You**