

(RESTEM



*Modulating immune  
response through advanced  
cell therapeutics*

December 2025

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# Company Overview

## Private



**Founded in 2018**, the company has established a strong foundation in the **field of cell-based therapeutics** and developed a **robust patent portfolio**

## Multi-asset



**3 proprietary platforms**, with the common focus of **modulating the immune system** and treating **inflammatory-associated diseases**

## Late-stage



Commencing in 2025 a **pivotal Phase 2/3 trial** in Idiopathic Inflammatory Myopathy (IIM). Successfully completed multiple INDs and eINDs across **11 different indications**, demonstrating initial **clinical benefits** and an excellent **safety profile**.

## Competitive Advantages



Breaking through the key limitations of cell therapeutics with **cost-effective manufacturing, enhanced scalability** and **minimized toxicity**.

# Platform Overview

## Restem-L *Autoimmunity*

**Umbilical-lining Modified Progenitor Cell (UMPC) product, developed using a patented **conditioning process**, designed to target **orphan** and **refractory autoimmune** diseases**

## Restem-X *Orthopedics*

**Secretome-based** product, **functionally optimized** to deliver ground-breaking therapeutic properties in **orthopedic** treatments

## aNK *Immuno-senescence*

**Activated natural killer** (aNK) cells, uniquely designed to restore immune function and target **aging-related diseases** by **reversing immuno-senescence**

# Experienced Management Team & Advisory Board

## Management Team



**Andres Isaias**

*Executive Chairman &  
Chief Executive Officer*



**Rafael Gonzalez, PhD**

*Chief Development &  
Scientific Officer*



**Keith March, MD, PhD**

*Chief Medical Officer*



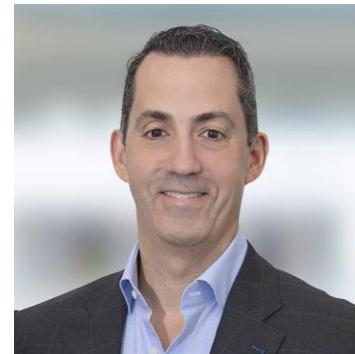
**Nelson Cabatuan**

*Chief Financial Officer*



**Barb Eppler-Mossler PhD**

*Sr. VP of Regulatory Affairs*



**Brian Pla**

*Chief Business  
Development Officer*

## Scientific Advisory Board

**Robert Sackstein, MD, PhD**

SVP for Global Health Affairs,  
Florida International University



**HARVARD  
MEDICAL SCHOOL**



**DANA-FARBER  
CANCER INSTITUTE**



**BRIGHAM AND  
WOMEN'S HOSPITAL**



**MASSACHUSETTS  
GENERAL HOSPITAL**

**Robert Negrin, MD, PhD**

Division Chief, Blood and Marrow  
Transplant Program, Medical  
Director, Clinical Bone Marrow  
Transplantation Laboratory



**Guenther Koehne, MD, PhD**

Deputy Director and Chief of  
Blood & Marrow Transplant and  
Hematologic Oncology



**Baptist Health  
South Florida**



**Memorial Sloan Kettering  
Cancer Center**

**Jonathan Krant, MD**

Chief of Rheumatology Division,  
Memorial Health System, and  
former Chairman of Medicine,  
Adirondack Health Systems



**MEMORIAL HEALTH SYSTEM**



**ADIRONDACK HEALTH**  
*Better Health, Better Lives*

# Advancing Pipeline of Restem Platforms

	Program	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Status
UMPC	<b>Restem-L:</b> <i>Autoimmune Diseases</i>	Idiopathic Inflammatory Myopathy (IIM)* / **					Phase 2/3 trial ongoing
		Rheumatoid Arthritis Refractory (ref-RA)					Phase 2 IND has been FDA Authorized
		Ulcerative Colitis Refractory (ref-UC)					Phase 2 submission in Q4 2025
Restem-L: <i>Other Diseases</i>	Left Ventricular Assisted Device (LVAD)						Partnering Opportunity
	Facioscapulohumeral Muscular Dystrophy (FSHD)**						Phase 1/2a trial ongoing
Restem-X: <i>Orthopedics</i>	Osteoarthritis (OA)						Phase 1 submission in Q4 2025
aNK	aNK: <i>Age-Associated Disorders</i>	Frailty / Sarcopenia					Phase 1 submission in Q2 2026

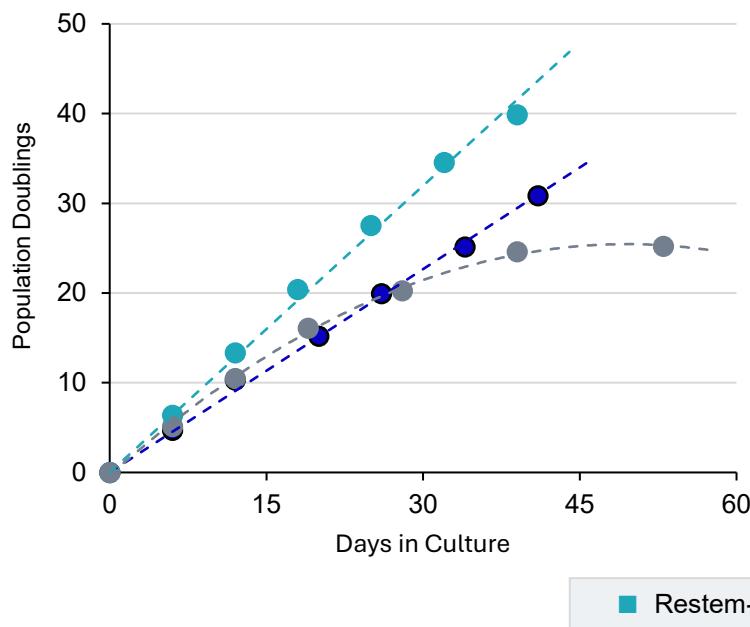
UMPC: Umbilical lining Modified Progenitor Cells; aNK: activated Natural Killer cells

\* FDA Fast Track and Orphan Drug designations granted

\*\* Fully Committed Funding

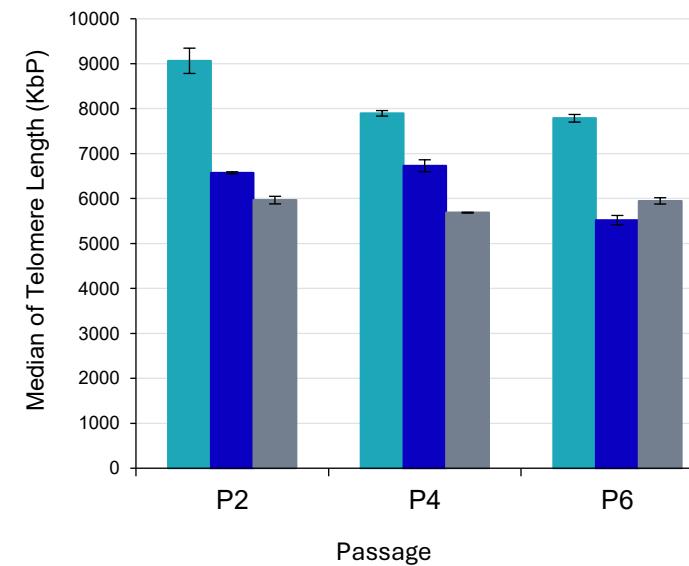
# Restem-L – Best-In-Class Cellular Therapeutic Product

## Higher Scalability



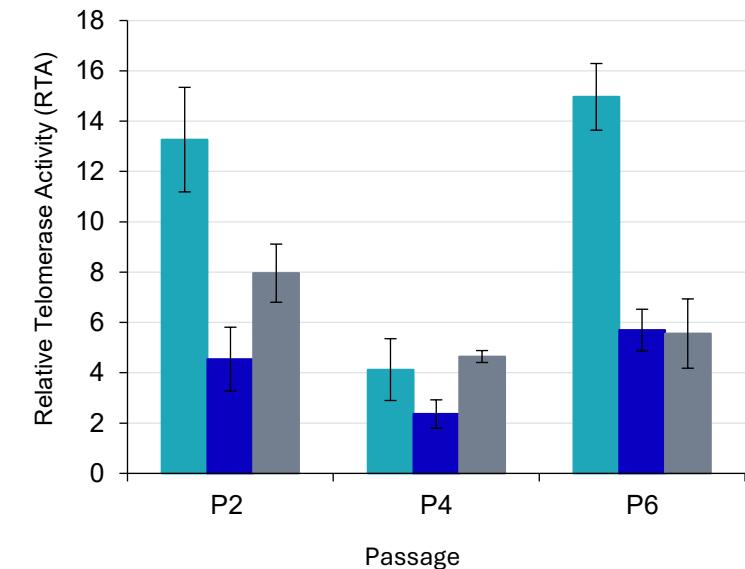
Exceptional proliferative ability yields greater growth and expansion of high-quality cells

## Younger & More Robust Cells



Maintains longer telomeres throughout multiple passages ensures younger and more robust cells

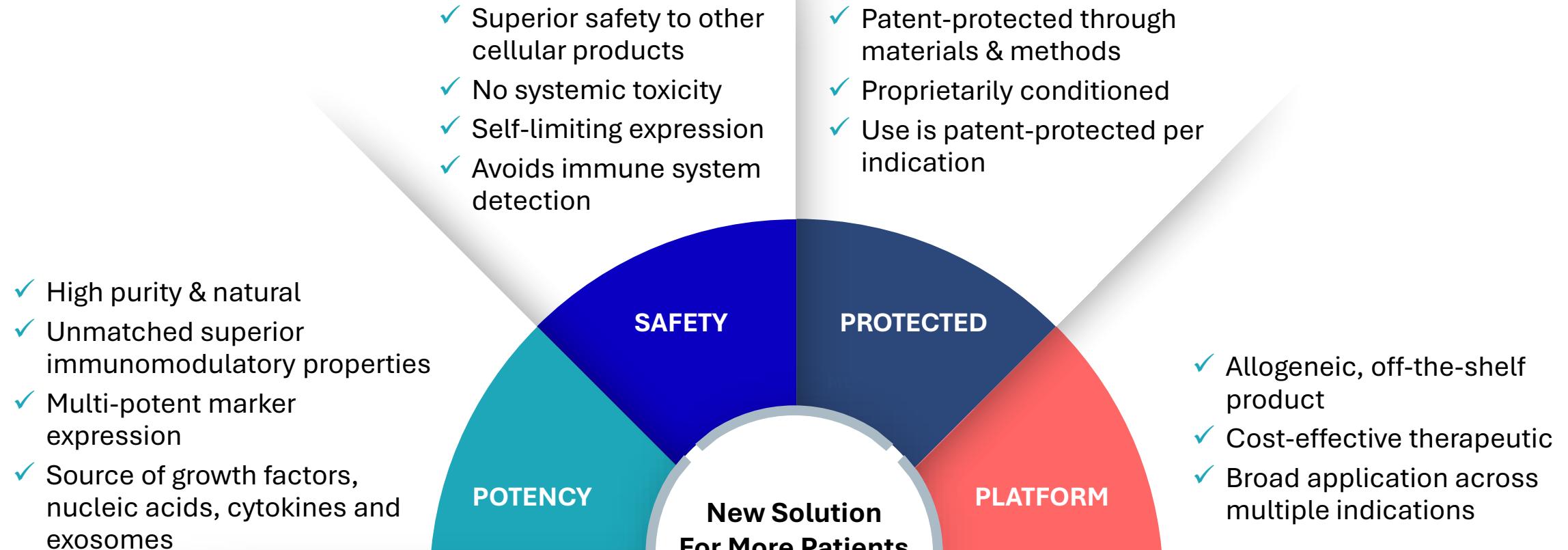
## Better Repair Mechanism



Higher telomerase activation in later passages supports a stronger DNA repair mechanism

Superior Properties than Other Cell-based Products

# Restem-L – Key Pillars



# Restem-L – Overcoming the Quintessential Cell Therapeutics Manufacturing Challenges

Scalability	Cost	Time	Consistency	Inventory
Extensive supply, with 3 master and working cell banks with a capability to produce  <b>&gt; 3 million doses</b>	Manufacturing costs are advantageous, with a production cost of just  <b>&lt; \$2,200 per dose</b>	Accelerated manufacturing timeline from master/working bank to final product  <b>Under 6 weeks</b>	Highly reproducible and complete characterization uniformity among donors and cell lines  <b>Superior lot-to-lot consistency</b>	GMP cells in inventory ready for use in clinic trials, with quick turn-around  <b>180 doses</b>

Uniquely positioned to support clinical trials and mass commercialization of cell-based products

# Addressing the Growing Need for Autoimmune Therapies

## Increasing Prevalence



**1 in 10**

individuals globally is affected with autoimmune diseases<sup>1</sup>

## Existing Market



**\$150 billion/yr**

Estimated autoimmune disease yearly market across multiple indications<sup>2</sup>

## Current Treatments



**↑AEs**

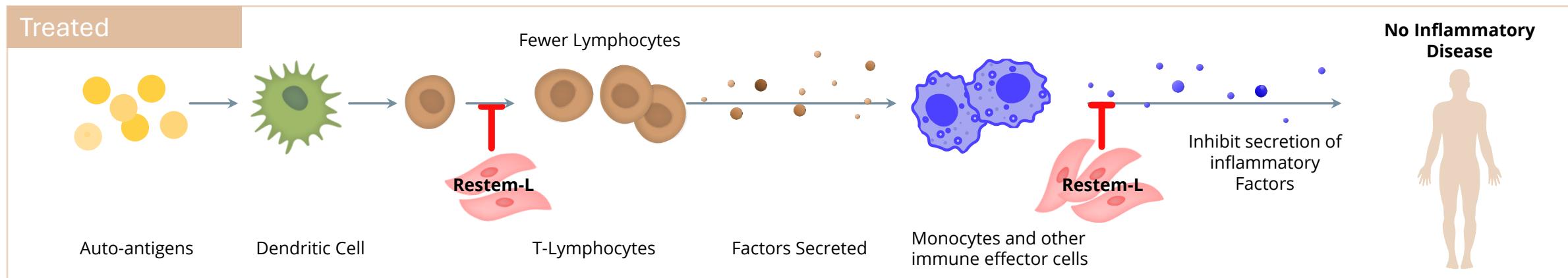
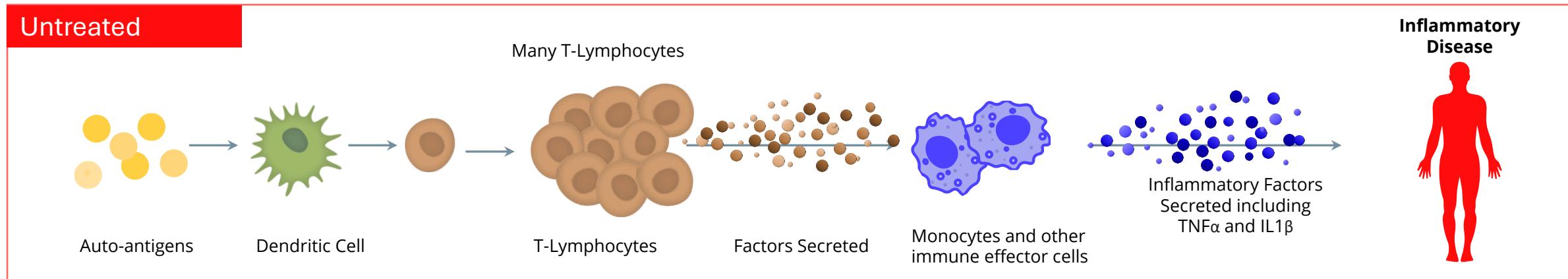
Currently approved treatments are associated with frequent and severe adverse events

1. Miller FW. The increasing prevalence of autoimmunity and autoimmune diseases: an urgent call to action for improved understanding, diagnosis, treatment, and prevention. *Curr Opin Immunol.* 2023 Feb;80:102266.

2. [www.einpresswire.com/article/495486226/autoimmune-disease-therapeutics-market-nears-150-billion-by-2025-market-is-witnessing-a-strong-presence-of-late-stage-pipeline-drugs](http://www.einpresswire.com/article/495486226/autoimmune-disease-therapeutics-market-nears-150-billion-by-2025-market-is-witnessing-a-strong-presence-of-late-stage-pipeline-drugs)

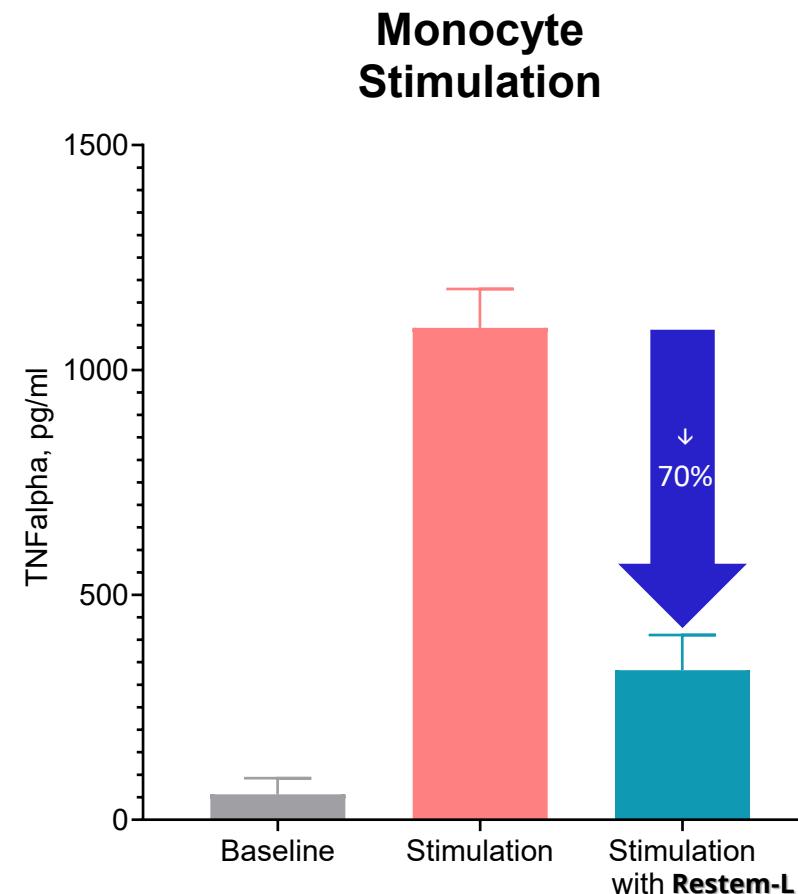
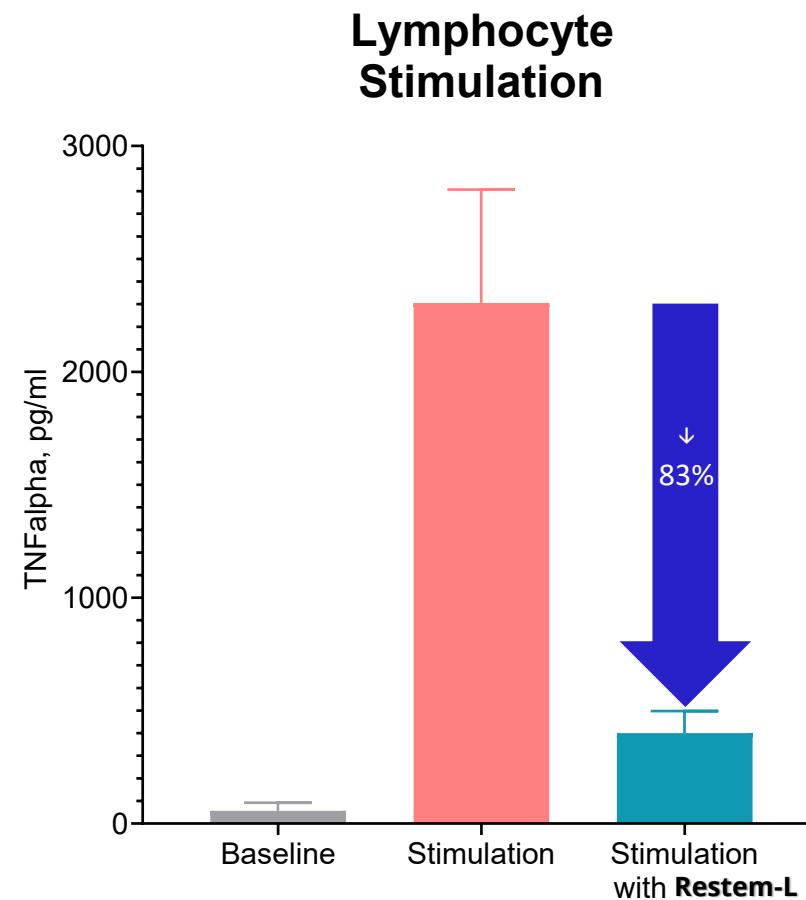
# Restem-L Strongly Modulates the Inflammatory Response

Inflammation is the driving force of autoimmune tissue injury



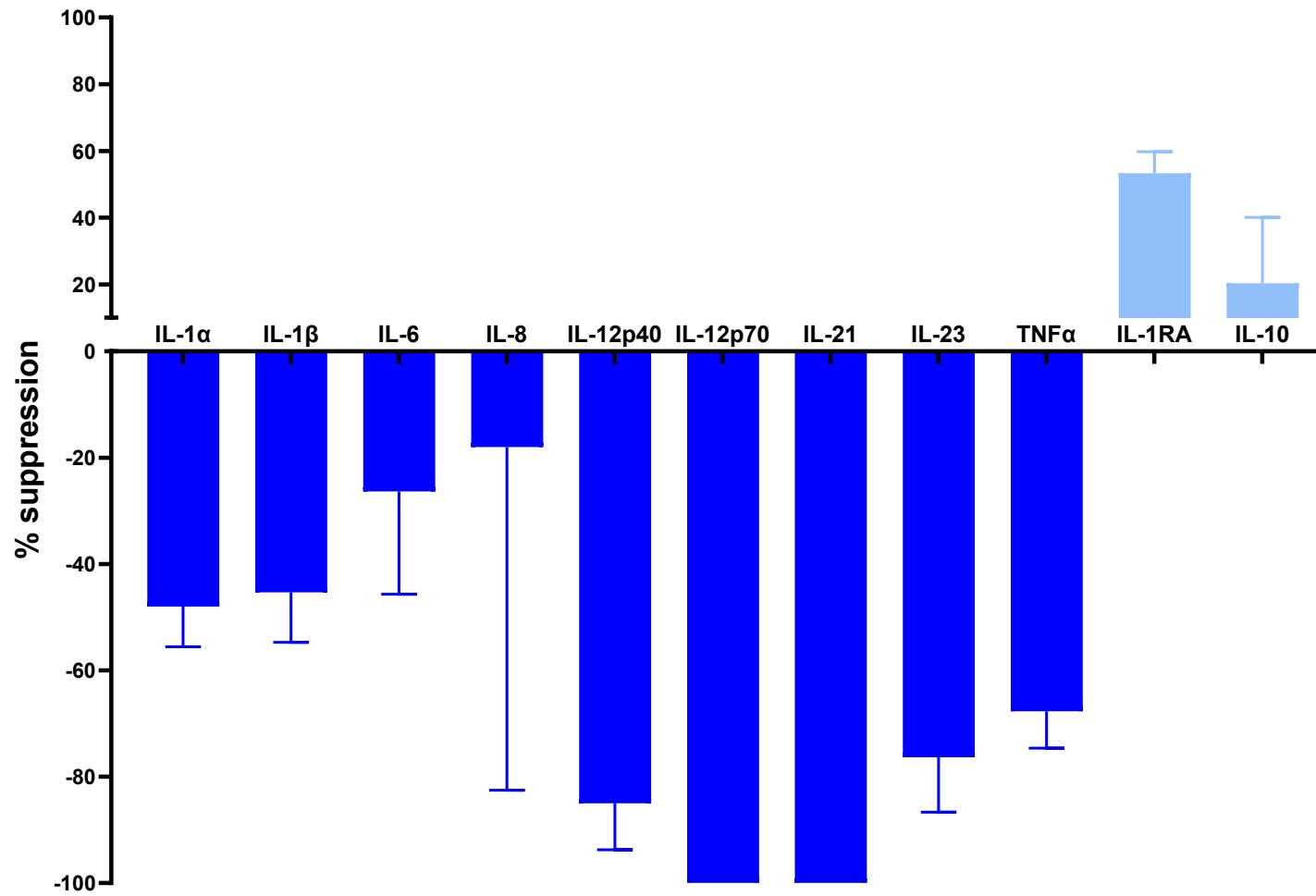
Restem-L Modulates Lymphocyte and Monocyte Factor Secretion to Treat Disease

# Restem-L - Strongly Reduced Inflammatory Responses of White Cells in Clinical Trials



Restem-L markedly suppresses TNF $\alpha$ , a strong mediator of inflammation

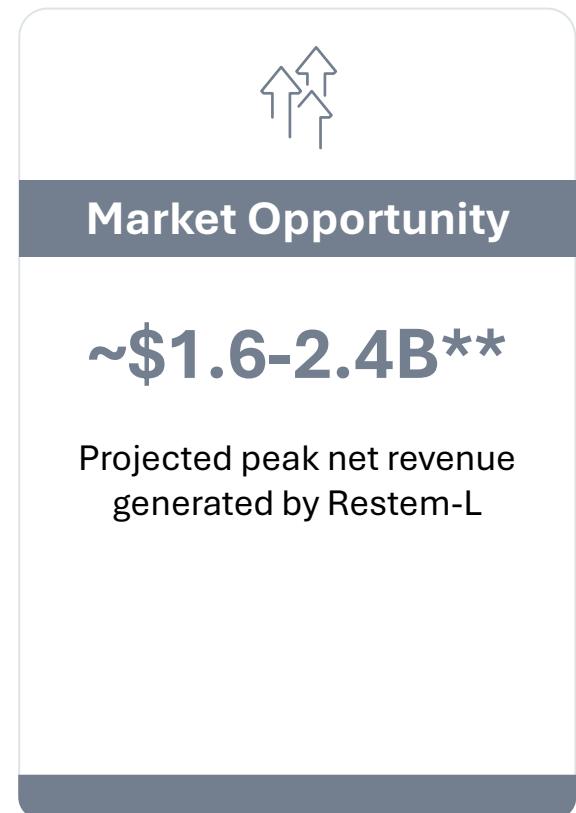
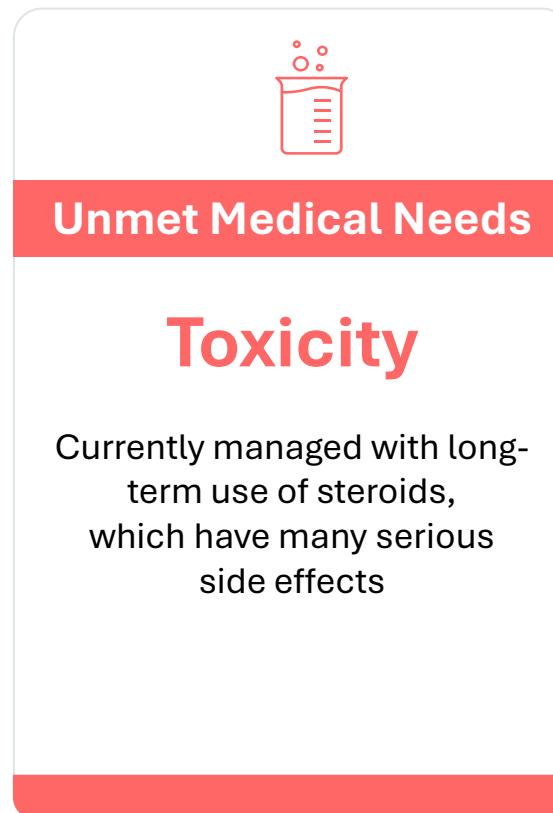
# Restem-L Reduced Inflammatory Responses of White Cells in Clinical Trial Patients



Restem-L markedly suppresses multiple inflammatory biomarkers

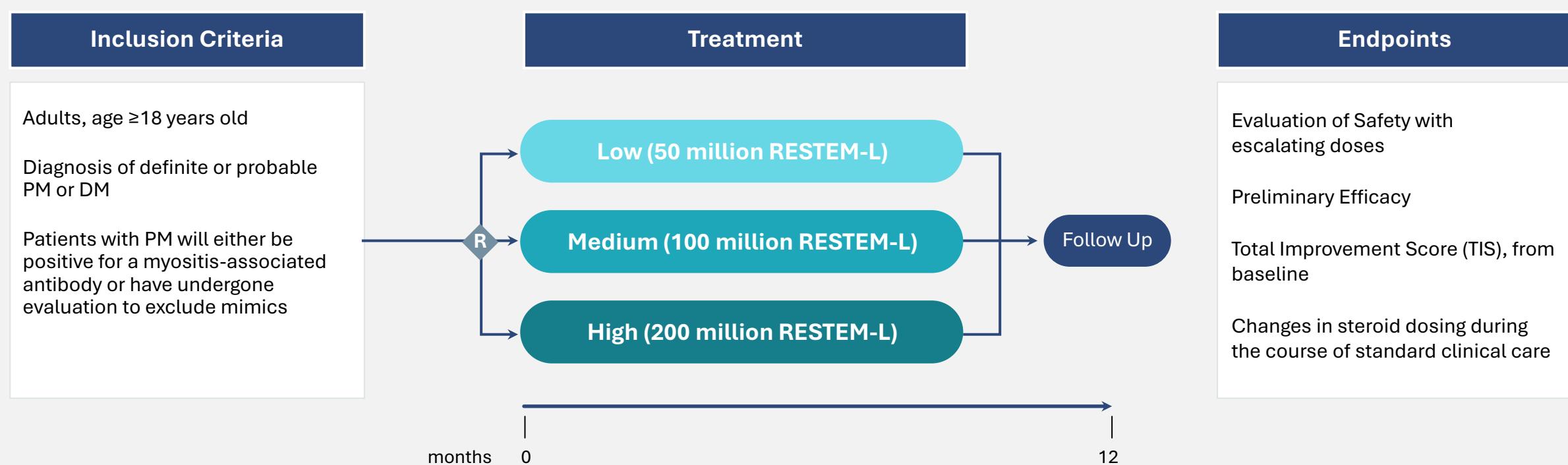
# Restem-L in Adult Idiopathic Inflammatory Myopathy (IIM)

An autoimmune disease, with Polymyositis/Dermatomyositis (PM/DM) as its primary subtypes



# IIM Phase 1 Study Design

Open-label, dose escalation trial to investigate Restem-L therapy in IIM (both in PM and DM)



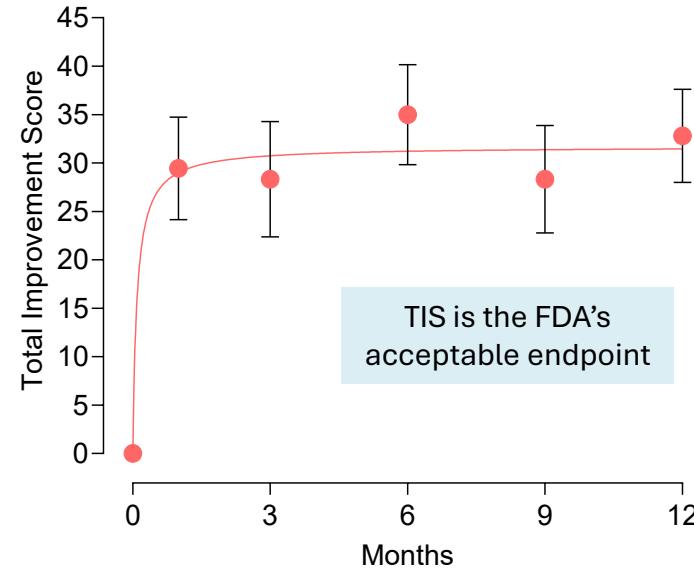
## Investigator:

Michael Bubb, MD (Principal Investigator)  
Associate Professor of Medicine  
University of Florida Medical Center

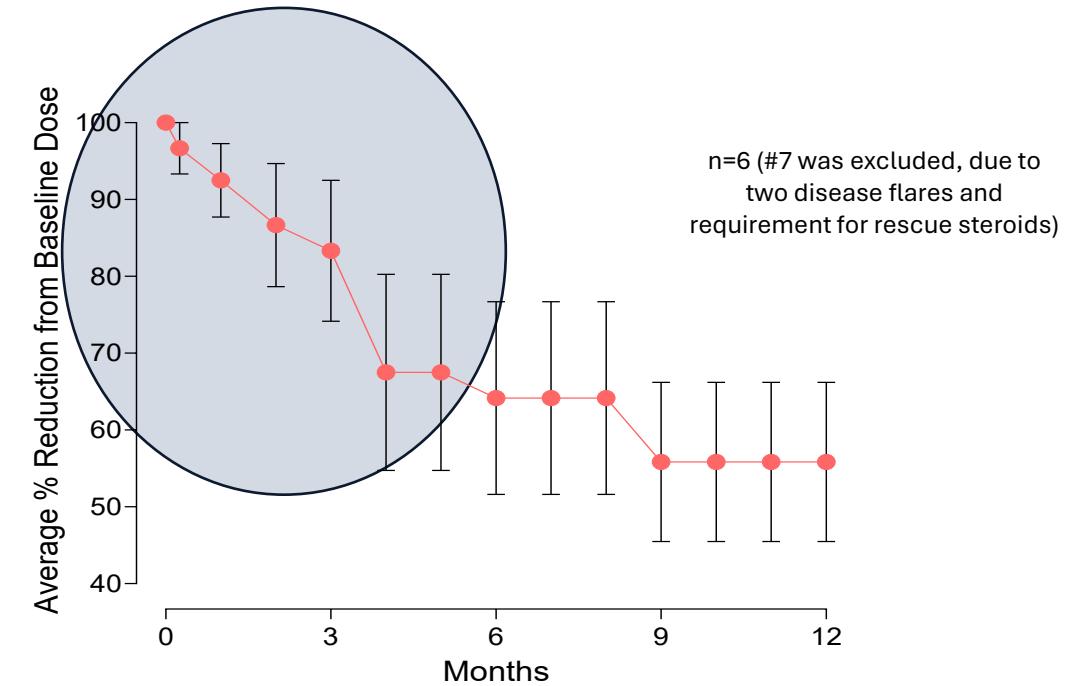
# Restem-L Improved Symptoms while Reducing Steroids Use in IIM

Data featured in an oral presentation at the American College of Rheumatology's (ACR) 2024

## Durable Improvement



## Reduction of Required Prednisone Dose



- The Total Improvement Score (TIS) averaged for all participants is within 30-35% range; 20% is considered a meaningful improvement by the FDA and Key Opinion Leaders
- The overall improvement in various scales was seen concurrently with a reduction in 6 of the 7 participants of the Prednisone daily dose

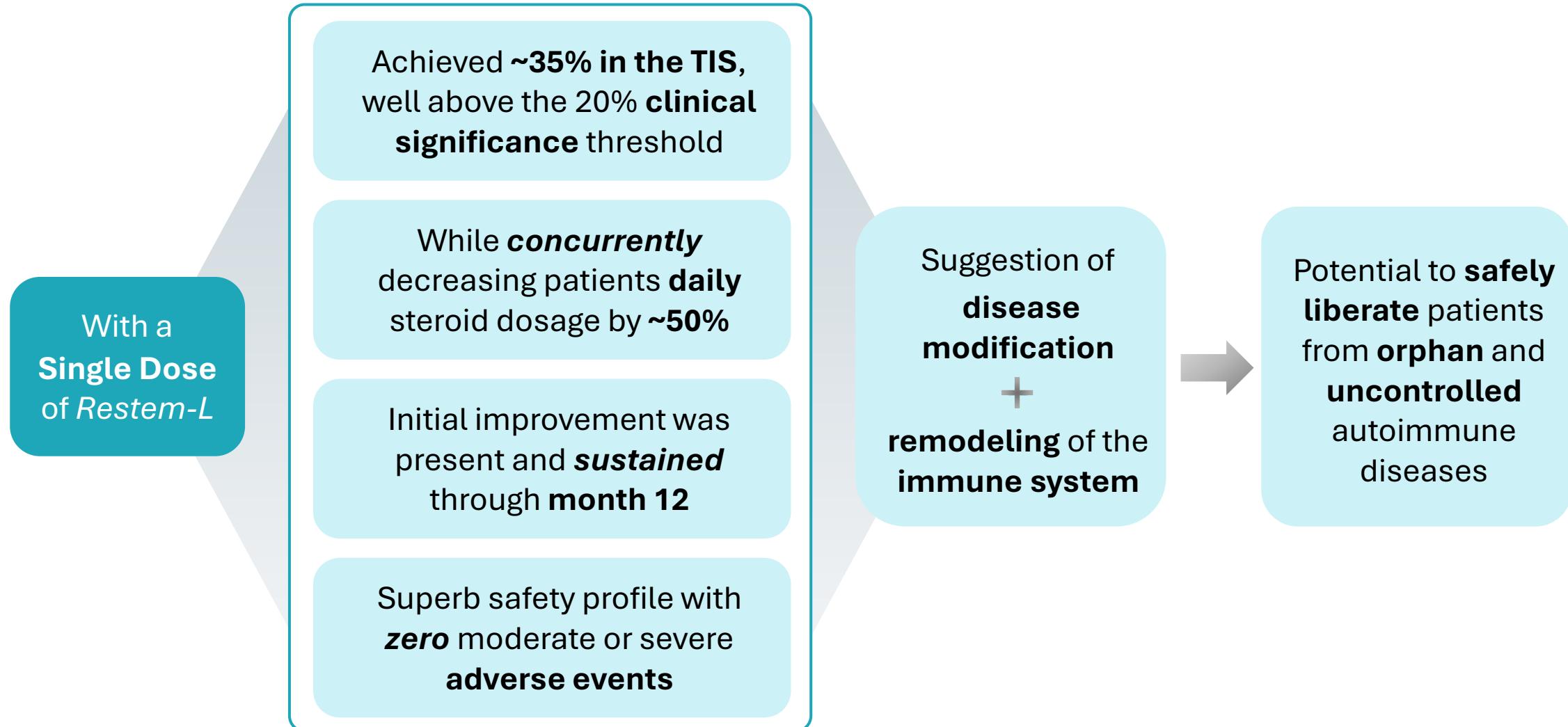
- The average daily dose of Prednisone was tapered by more than 5.5 mg by managing clinician (*chronic use of as little as 2.5 mg daily leads to increased adverse side effects*)
- 7 out of the 9 participants used Prednisone daily
- 6 out of the 7 daily users of Prednisone had an average of ~50% decrease in their steroid use

# Aggressive Regulatory Strategy Supported by Strong Clinical Success

Positive results achieved in challenging autoimmune disease

- Granted Orphan Drug Designation (ODD)
- Granted Fast-Track Designation (FTD)
- Authorized straight to Phase 2/3 IND
- Possibility for RMAT Designation
- Potential Registrational Trial

# Restem-L: IIM Trial Results - Disease Paradigm Shift



## **IIMPACT - FDA-Authorized Phase 2/3 in IIM, a Potentially Registrational Trial**

## Pivotal, Adaptive double-blinded, randomized, dose-repeating, crossover study

**Inclusion Criteria**

≥18 years old with diagnosis of PM/DM based on EULAR/ACR score and Active Disease;  
Participants must be receiving stable treatment, with one or more oral immunosuppressant medications, HCQ, and/or corticosteroids

**Treatment Arms**

80 patients

Readout

Readout

Follow Up

Months 0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 24

IV Infusion ◇

Steroid Taper Initiation ♦

**Endpoints**

Total Improvement Score (TIS), from baseline and by comparison with placebo;  
Pre-specified steroid step-down to solidify the finding of the concurrent efficacy and steroid reduction



**Institution / Investigator:**

Veterans Affairs Medical Center / Michael Bubb, MD (Principal Investigator)

# Restem-L in Rheumatoid Arthritis (RA)



RA is a chronic, autoimmune disease of unknown etiology that primarily affects synovial joints

<b>Prevalence</b>  <b>~ 1,650,000</b>  Diagnosed adult RA patients in 2024 in the US alone*	<b>Cost per Patient</b>  <b>\$80,000-\$120,000</b>  Yearly cost of biologics which accounts for approximately 60% of RA patients	<b>Unmet Medical Needs</b>  <b>~21%</b>  Uncontrolled or refractory patient population**	<b>Market Opportunity</b>  <b>~\$1.1-2.1B***</b>  Projected peak net revenue generated by Restem-L in 2034

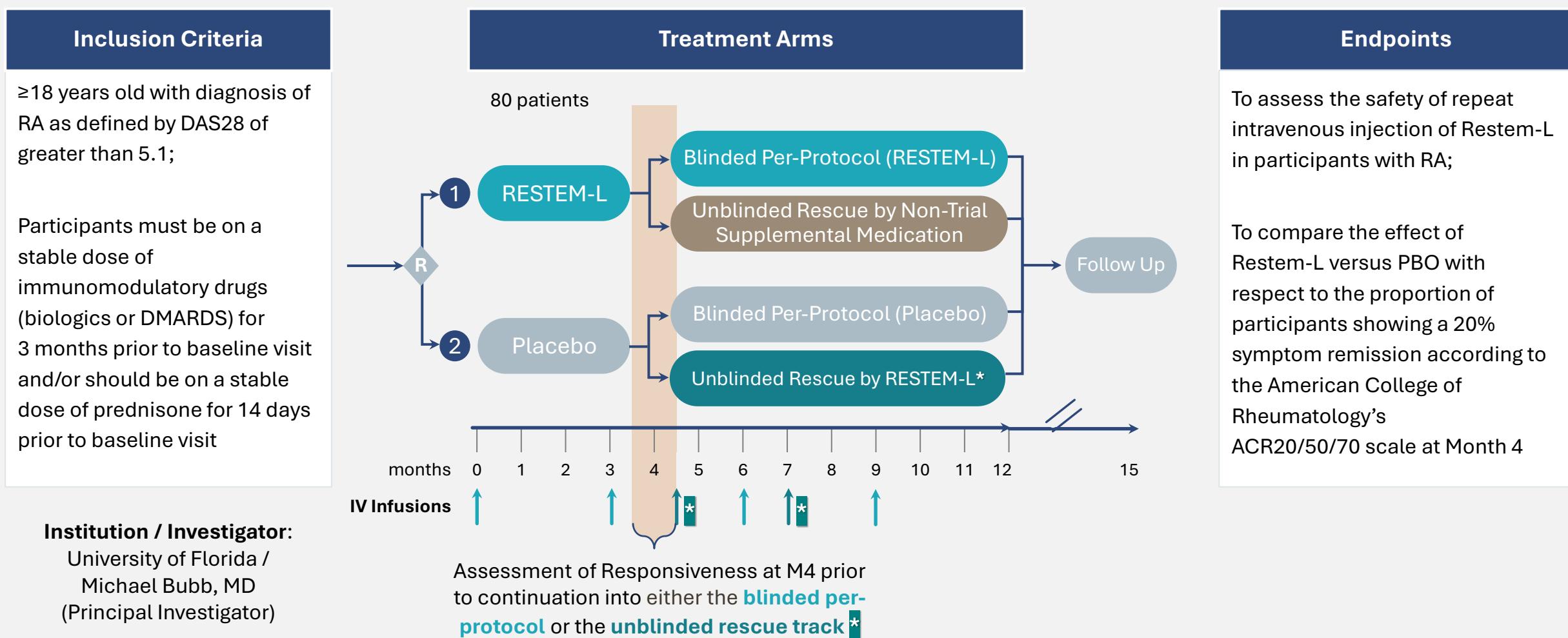
\*Note: Average volume of diagnosed RA cases was calculated for sources reporting a range of diagnosed prevalence rates : [Hunter, et al](#), [Myasoedova, et al](#), [Almutairi, et al](#)

\*\* [www.arthritis.org/news/stories-of-yes/dr-daniel-solomon-researching-refractory-ra](http://www.arthritis.org/news/stories-of-yes/dr-daniel-solomon-researching-refractory-ra).

\*\*\* Source: LifeSci Consulting market analysis, 2024

# FDA-Authorized Phase 2 Trial in RA

Adaptive double-blinded, randomized, dose-repeating, parallel-group study



## Institution / Investigator:

University of Florida /  
Michael Bubb, MD  
(Principal Investigator)

# Restem-L in Ulcerative Colitis (UC)



UC is a chronic, inflammatory autoimmune condition characterized by relapsing and remitting mucosal inflammation

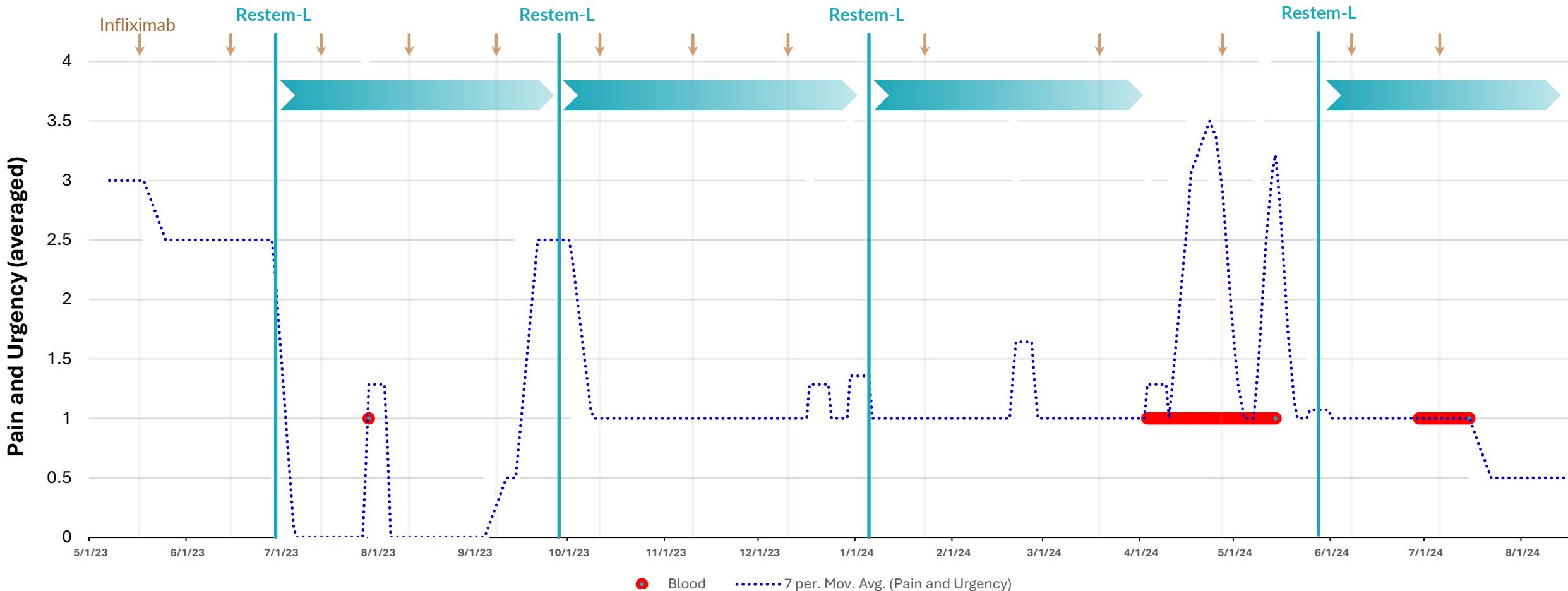
Prevalence	Cost per Patient	Unmet Medical Needs	Market Opportunity
<b>~ 1,000,000</b>  Diagnosed adult UC patients in 2024 in the US alone*	<b>\$51,000-\$180,000</b>  Yearly cost of biologics which are used as a 1L or 2L option to treat patients with moderate to severe active UC	<b>~20%</b>  Uncontrolled or refractory patient population**	<b>~\$830M-1.6B***</b>  Projected peak net revenue generated by Restem-L in 2034

\* Average volume of diagnosed UC cases was calculated for sources reporting a range of diagnosed prevalence rates : [Lewis, et al](#), [Weisman, et al](#), [Shivashankar, et al](#), [Kappelman, et al](#)  
SoC- standard of care

\*\* [https://journals.lww.com/ajg/fulltext/2019/03000/acg\\_clinical\\_guideline\\_ulcerative\\_colitis\\_in.10.aspx#xd\\_co\\_f=M2QwOGIwMDItM2NhNC00MWQ2LThiNWYtYzMzNzIwOWVmM2U4~](https://journals.lww.com/ajg/fulltext/2019/03000/acg_clinical_guideline_ulcerative_colitis_in.10.aspx#xd_co_f=M2QwOGIwMDItM2NhNC00MWQ2LThiNWYtYzMzNzIwOWVmM2U4~)

\*\*\* Source: LifeSci Consulting market analysis, 2024

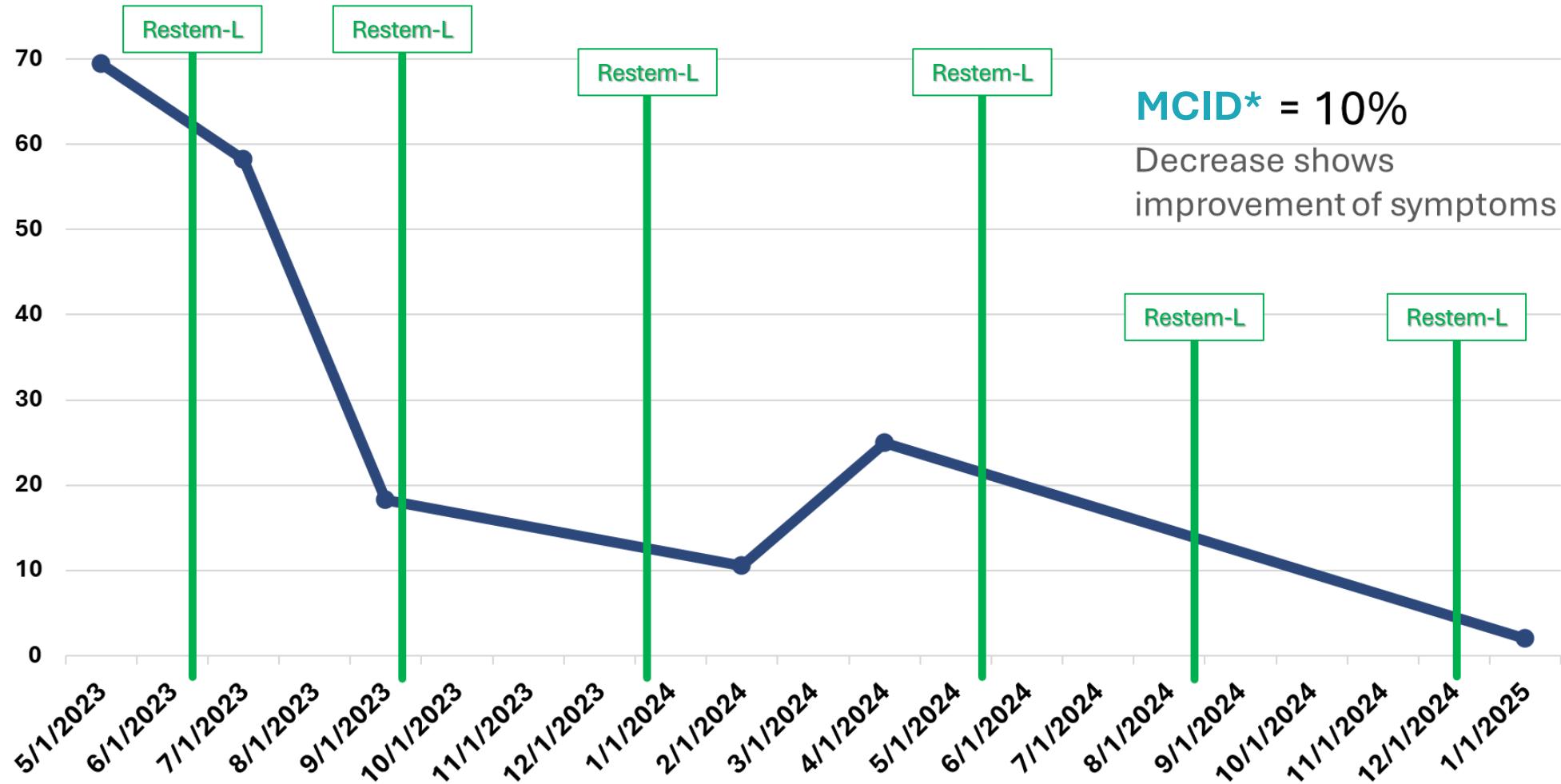
# eIND UC Patient Data



*Treatment with Restem-L led to prolonged remission and significant symptomatic improvement, whereas infliximab showed no association with symptom relief.*

# eIND UC Patient Data (Compounding Effect)

Irritable Bowel Syndrome Quality of Life Instrument (IBS-QOL) Questionnaire Scores: 2023 – Present



MCID\* = 10%

Decrease shows  
improvement of symptoms

A condition-specific measure for assessing health-related QoL among persons with irritable bowel syndrome

## Diverse Clinical Indications - Restem-L

Indication	Participants	Doses
1. IIM / DM-PM (Phase 1)	9	9
2. LVAD (Phase 1)	9	9
3. COVID (Phase 1)	17	23
COVID (eINDs)	9	9
4. HLH, SL (eIND)	1	1
5. Graft v. Host, SG (eIND)	1	2
6. Pulmonary Fibrosis, GK (eIND)	1	4
7. Interstitial Lung Disease, BM (eIND)	1	1
8. Autoimmune Hep, TC (eIND)	1	6
9. Neuromyelitis Optica, KL (eIND)	1	1
10. Ulcerative Colitis, AC (eIND)	1	6
11. Crohn's Disease, JW (eIND)	1	3
<b>TOTAL</b>	<b>53</b>	<b>74</b>

# Superb Clinical Safety Profile - Restem-L

Positive safety profile across different types of disease indications supports the potential for early additive or combination treatment opportunities

Adverse Reaction	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
<b>Infusion Reactions:</b>					
Anaphylaxis	0	0	0	0	0
Chills	0	0	0	0	0
Skin Reaction	0	0	0	0	0
Hyper/Hypotension	0	0	0	0	0
Flushing	1	0	0	0	0
<b>CNS Reactions:</b>					
Fatigue	0	0	0	0	0
Confusion	0	0	0	0	0
Headache	0	0	0	0	0
<b>Nausea</b>	0	0	0	0	0
<b>Cardiopulmonary Reactions</b>	0	0	0	0	0
<b>Gastrointestinal Reactions</b>	0	0	0	0	0
<b>Infection</b>	0	0	0	0	0
<b>Thromboembolic Events</b>	0	0	0	0	0
<b>TOTAL</b>	1/74	0/74	0/74	0/74	0/74

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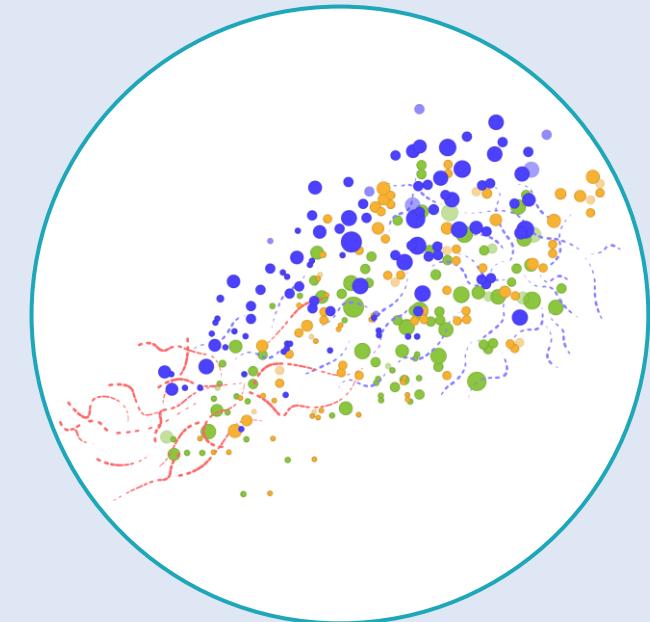


# Restem-X: A Regenerative Secretome

# Restem-X — Clinical Applications

## Natural Product with a Strong Orthopedic Therapeutic Potential

- Restem-X is a cell-based secretome derived from our proprietary Restem-L (UMPC) product
- UMPCs are stimulated to secrete a functionally optimized profile of bioactive molecules which create an ideal formulation to collectively support joint health
- These bioactive molecules enhance cellular communication and promote tissue repair and regeneration



# Key Components of RESTEM-X

<b>Collagen I</b>	Provides structure to skin, regenerating properties to bone health such as flexibility and strength
<b>Collagen III</b>	Helps form new bone and plays a critical role in tissue repair
<b>Hyaluronic Acid (HA)</b>	Lubricates and support the entire joint, its the main fluid in all joint capsules
<b>Fibroblast Growth Factor-2 (FGF-2)</b>	It's a strong regenerative and mitogen, while helping heal tendons, ligaments and cartilage
<b>Fibroblast Growth Factor-7 (FGF-7)</b>	Critical role in wound healing and bone restructuring

# Restem-X — Future Price Competitiveness (per Treatment)

Visco-supplementation market valuation of \$5.12 B in 2024\*

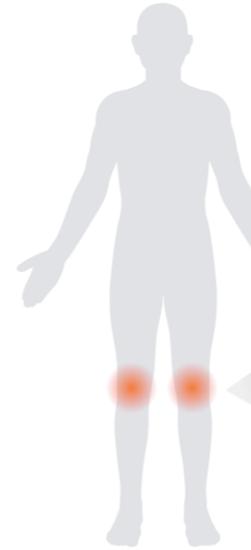
Restem-X Production Cost	Standard of Care #1 Retail Price	Standard of Care #2 Retail Price	Market Opportunity
~ \$35	\$359.98	\$1,477.00	~\$118-265M**
Restem-X 5 ml vial	SynviscOne 1 Injection of 6ml	Orthovisc 3 injections of 2ml	Projected peak net revenue generated by Restem-X in osteoarthritis

\*<https://www.globenewswire.com/news-release/2025/01/06/3004788/0/en/Global-Viscosupplementation-Market-to-Hit-Valuation-US-11-31-Billion-By-2033-Astute-Analytica.html>

\*\* Source LifeSci Consulting market analysis, 2025

# Restem-X — Potential Disease Resolution vs Symptomatic Suppression

## Osteoarthritis



STANDARD  
OF CARE

Steroids & Visco-supplementation



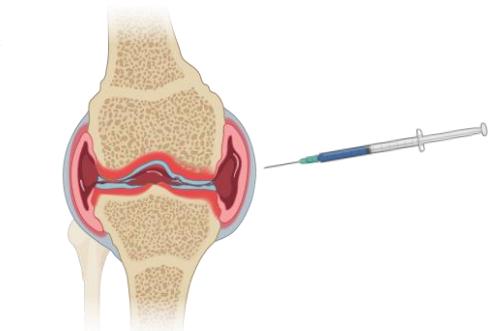
Temporary pain  
relief with  
cartilage loss



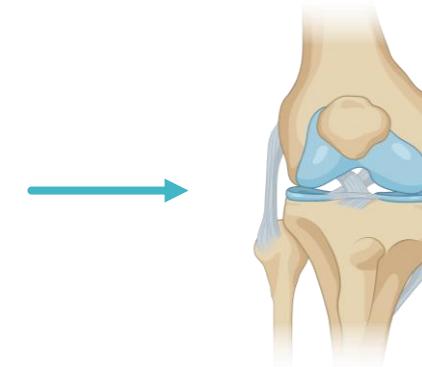
Total Knee  
Replacement



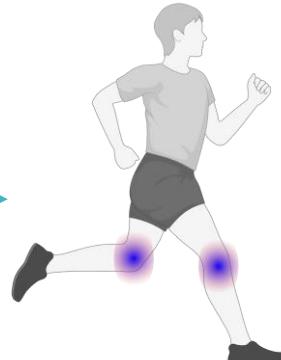
Decreases inflammation &  
provides structural support  
via extra cellular matrix



Long-term pain relief  
without cartilage loss



Improved  
Quality of Life



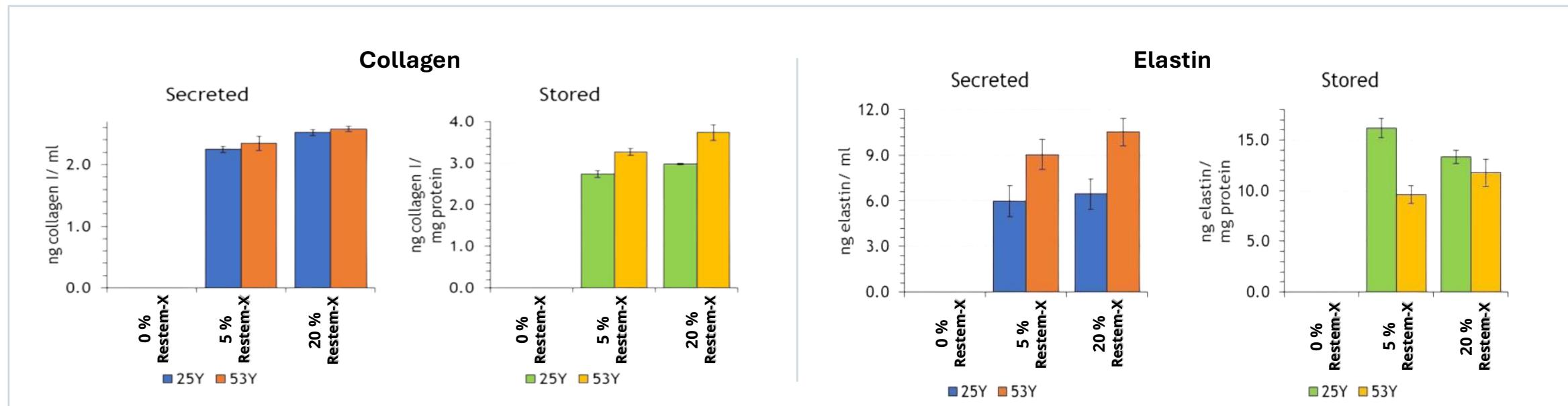
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# Restem-X Revolutionizing Joint Regeneration and Repair

## Supports Joint Health and Tissue Repair

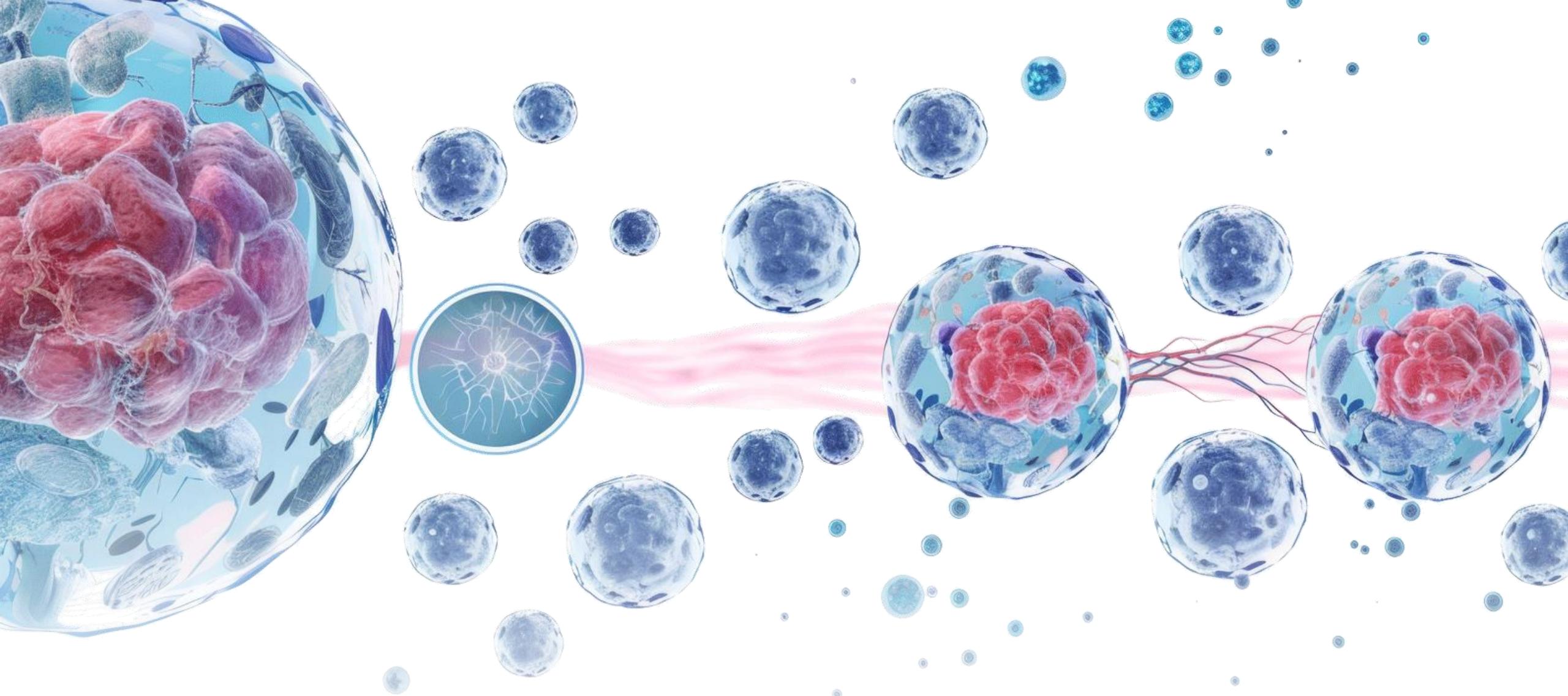
- Contains key components for orthopedics, including high molecular weight (MW) hyaluronic acid (HA), collagen, and elastin offering enhanced elasticity and overall regeneration and repair
- Targets the root causes of osteoarthritis by addressing both inflammation and cartilage damage, leading to improved mobility and reduced pain

### Enhanced Fibroblast Collagen and Elastin Production with Restem-X



Safe and effective rejuvenation in joint health

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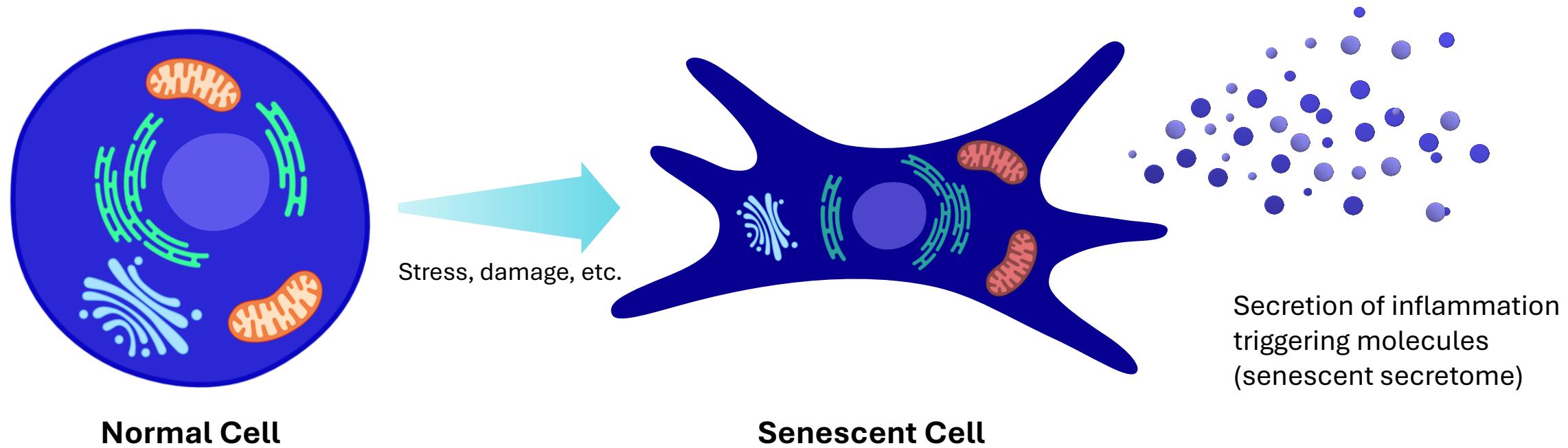


## Activated Natural Killer Cells: Reducing the Burden of Senescent Cells

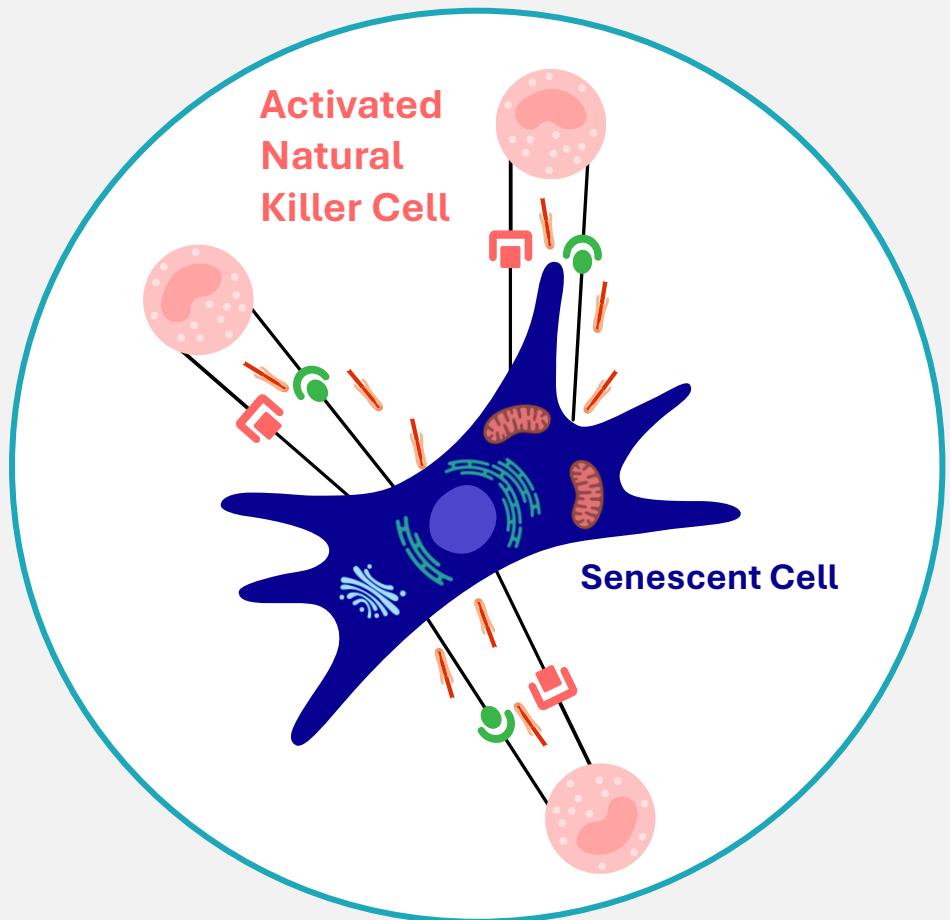
# Senescent Cells and Cellular Apoptosis

Aging is marked by damage caused by senescent cells, which cease to divide and occupy space becoming resistant to programmed cell apoptosis (natural cell death)

The accumulation of senescent cells impairs tissue removal and disrupts local homeostasis



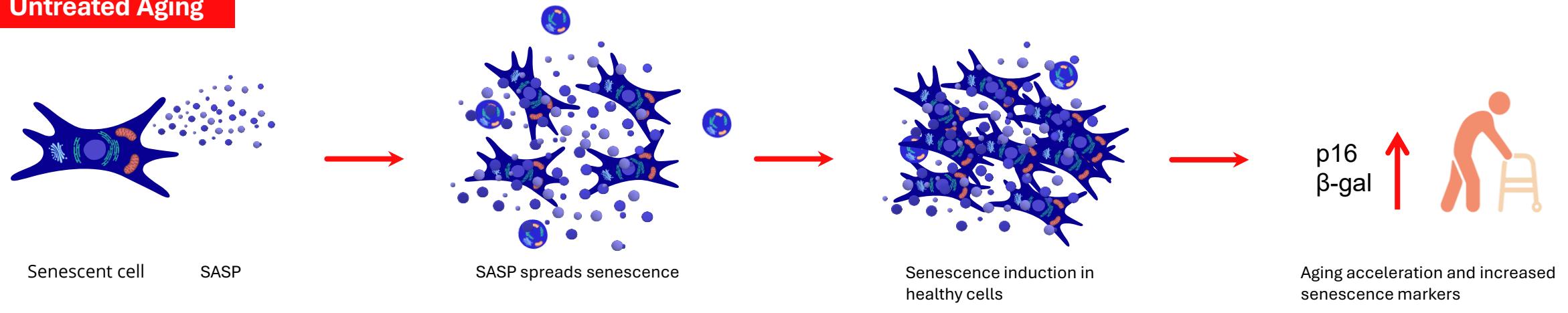
# Activated Natural Killer (aNK) Cells – Target Senescent Cells



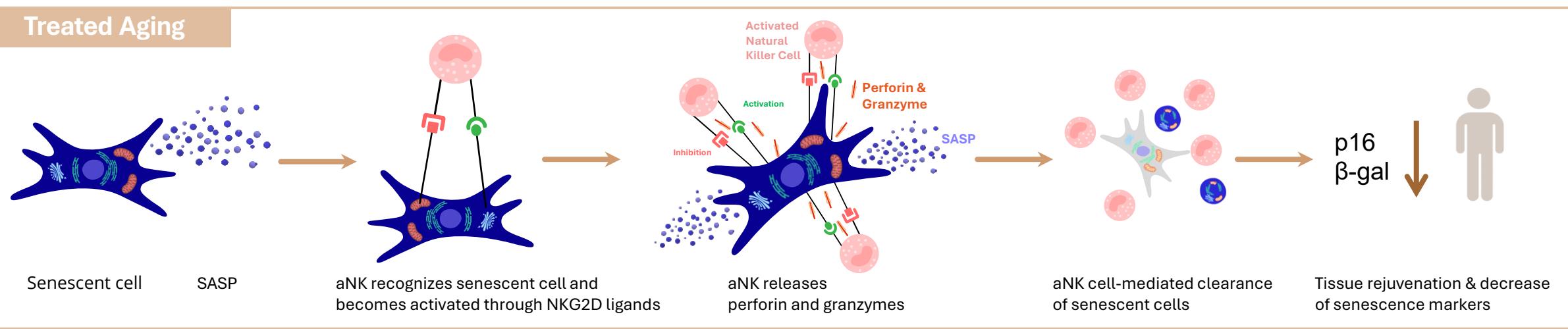
- Our activated Natural Killer (aNK) cells are proprietary immune cells specifically enhanced to recognize and eliminate senescent cells which may reverse age-associated diseases
- Patented methods to isolate, purify, expand and activate NK cells
- Restem is only company harnessing the power of NK cells to target and reverse cellular senescence

# Activated Natural Killer (aNK) Cells - Reduces Immunosenescence

## Untreated Aging

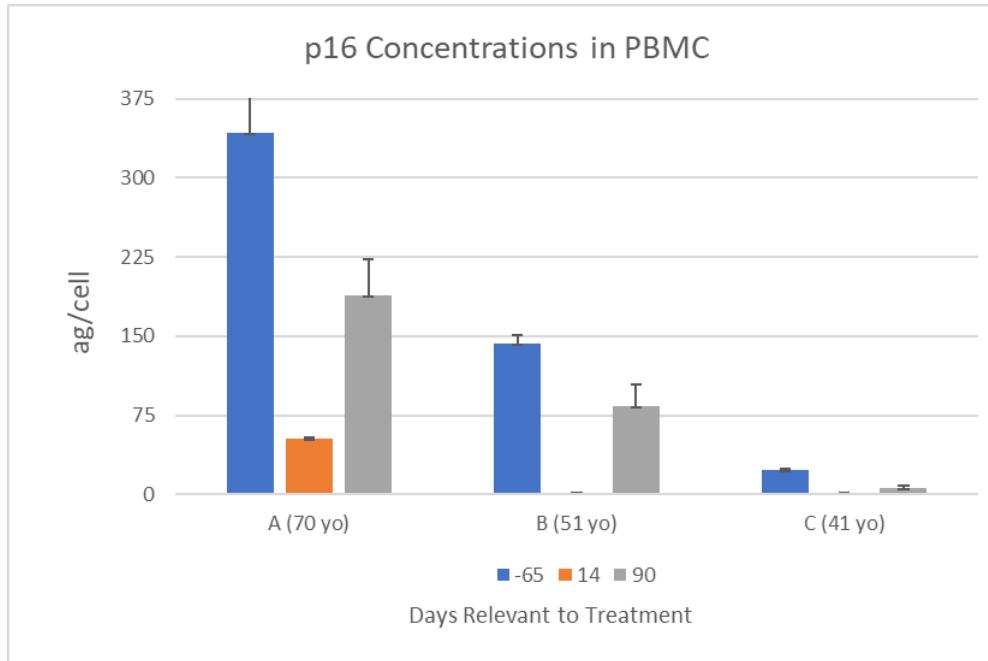


## Treated Aging

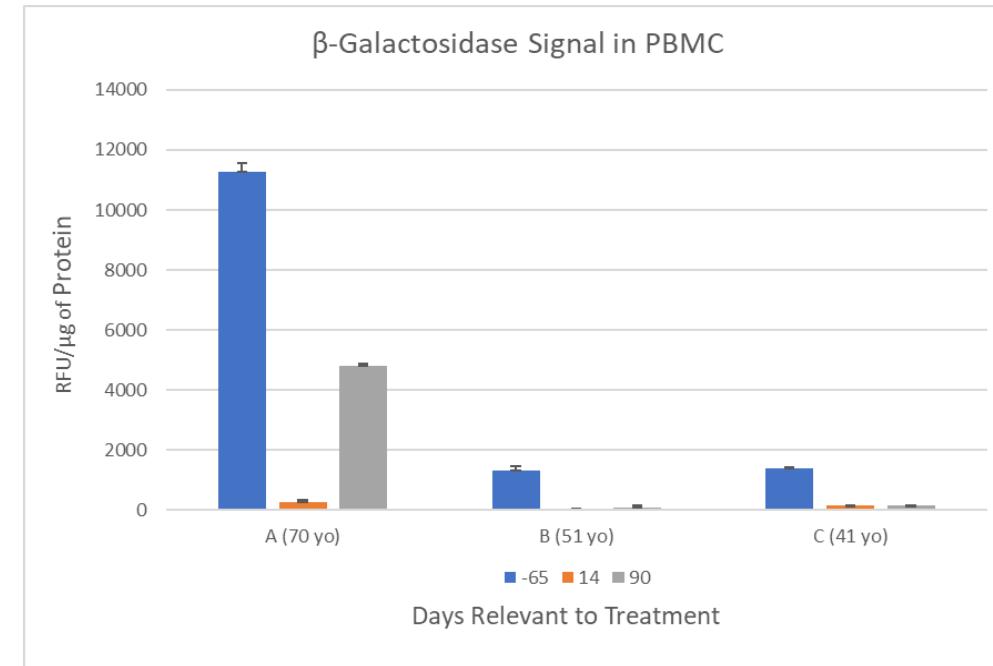


# Effects of aNK on Senescence Biomarkers in Patients

aNK treatment significantly reduced key senescence markers (p16 and  $\beta$ -gal) in PBMCs isolated from donors



Significant reduction in p16 levels, post aNK treatment



Decrease in  $\beta$ -gal activity in all donors, post aNK treatment

These findings support the therapeutic potential of aNK in restoring immune function and targeting senescent cells in aging-associated diseases

# Program Milestones & Cash Runway

	H2 2025	H1 2026	H2 2026
<b>Restem-L</b>	Start of Phase 2/3 in IIM & Start of Phase 1 in FSHD	Start of Phase 2 trial in RA	Start of Phase 2 in UC & Interim Phase 2/3 data in IIM
<b>Restem-X</b>	IND submission of Phase 1 in Osteoarthritis (OA)	Start of Phase 1 in OA	Interim Phase 1 data in OA
<b>aNK</b>		IND submission of Phase 1 in Frailty	Start of Phase 1 in Frailty
<b>Cash Runway</b>	 <b>Closed Friends&amp;Family \$18M*</b>		
	 <b>Series A / Crossover Round \$50M-\$60M**</b>		
	 <b>Secured non-dilutive funding for IIM Trial \$5.7M</b>		

\* \$108M post-money valuation

\*\* Expected IPO in 2027Q2 & Series A/Crossover Round cash runway through 2028Q3.

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*Thank You*