

INVESTOR OVERVIEW

# Maximizing GLP-1 Benefits with Oral **MS 001**

To control weight regain, preserve muscle, and improve long-term health.

Investment

**\$10M**

divided into \$3M + \$7M milestone events

Cash payback

**20X–100X**

target range after attractive Phase 2 readout

Exit year

**2029**

planned proof-of-concept inflection point

A BIG PROBLEM

# Obesity: A Global Health Crisis

**1B+** people living with obesity

**880M** adults

**159M** children

Worldwide adult obesity has more than doubled and adolescent obesity has quadrupled since 1990.

# GLP-1 Drugs: Discovery of the Decade

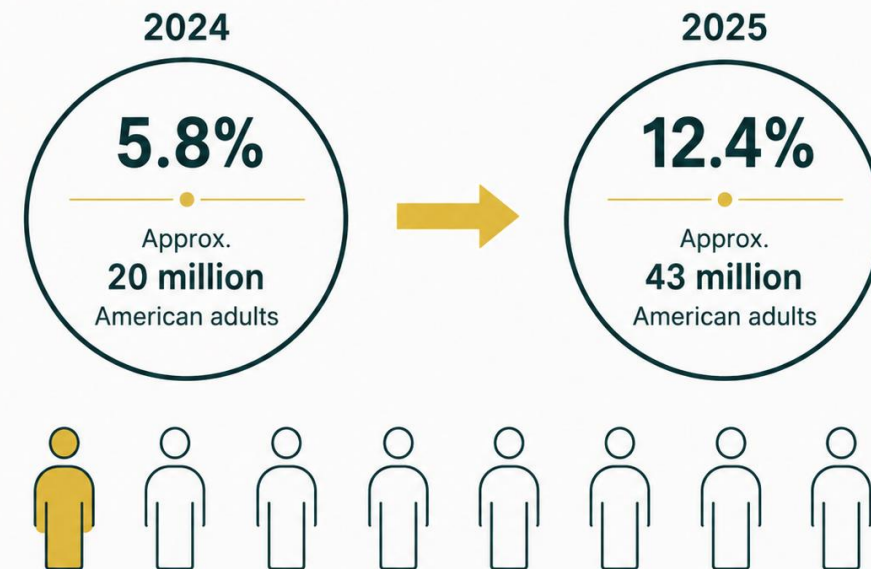
1 Mimic the glucagon-like peptide-1 (GLP-1) hormone

2 Suppress appetite and slow gastric emptying leading to **significant weight loss**

3 Improve blood sugar control in Type 2 Diabetes

## GLP-1 use is rising rapidly

Now used by roughly 1 in 8 American adults



Source: Wilding Noguchi, Y. (2025, October 28). NPR.

THE OPPORTUNITY

# GLP-1s Need a Next-Generation Enhancer

## Rising demand

for GLP-1 therapies is creating a multi-billion-dollar market.

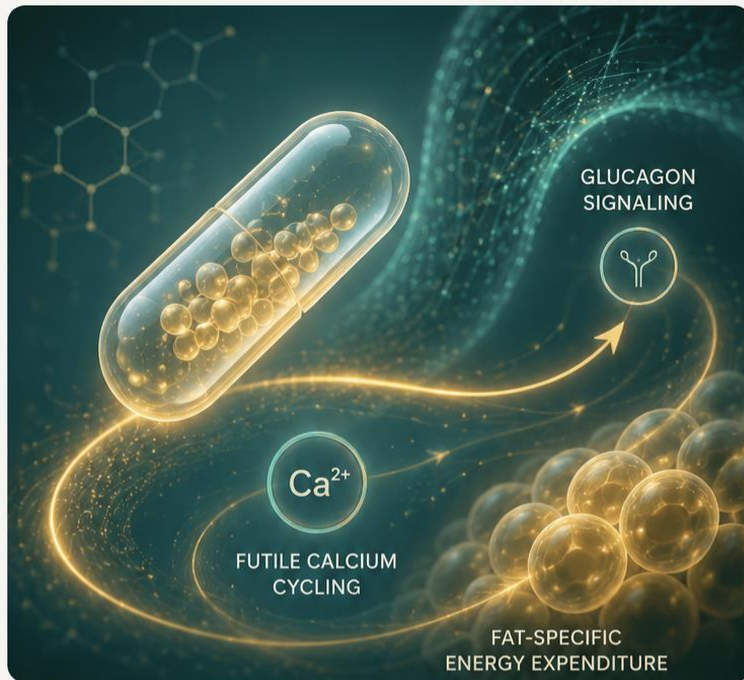
## Limitations persist

including plateauing weight loss, muscle loss, and variable responses in high adiposity patients.

## Unmet need

for a complementary mechanism that increases fat-specific energy expenditure.

**Strategic takeaway:** A differentiated metabolic amplifier can expand outcomes, extend market reach, and strengthen competitive positioning.



MS 001

**Oral, small molecule with novel mechanism of action**

Activates futile calcium-cycling and glucagon-linked pathway to increase fat-specific energy expenditure.

**Positioning**

- Co-therapy with GLP-1, followed by MS 001 monotherapy

MS 001

# Amplifying the Value of GLP-1 Therapies

**Drives deeper weight loss** Without further reducing caloric intake.

**Preserves muscle** Addressing a key limitation of current GLP-1s.

**Reduces weight rebound** Following GLP-1 discontinuation (preclinical).

**Enhances outcomes** Higher adiposity correlates with greater fat loss when paired with GLP-1s (preclinical).

**Expands the Market** MS 001 is positioned as a force multiplier that broadens GLP-1 utility + strengthens therapeutic differentiation.

STRATEGIC VALUE



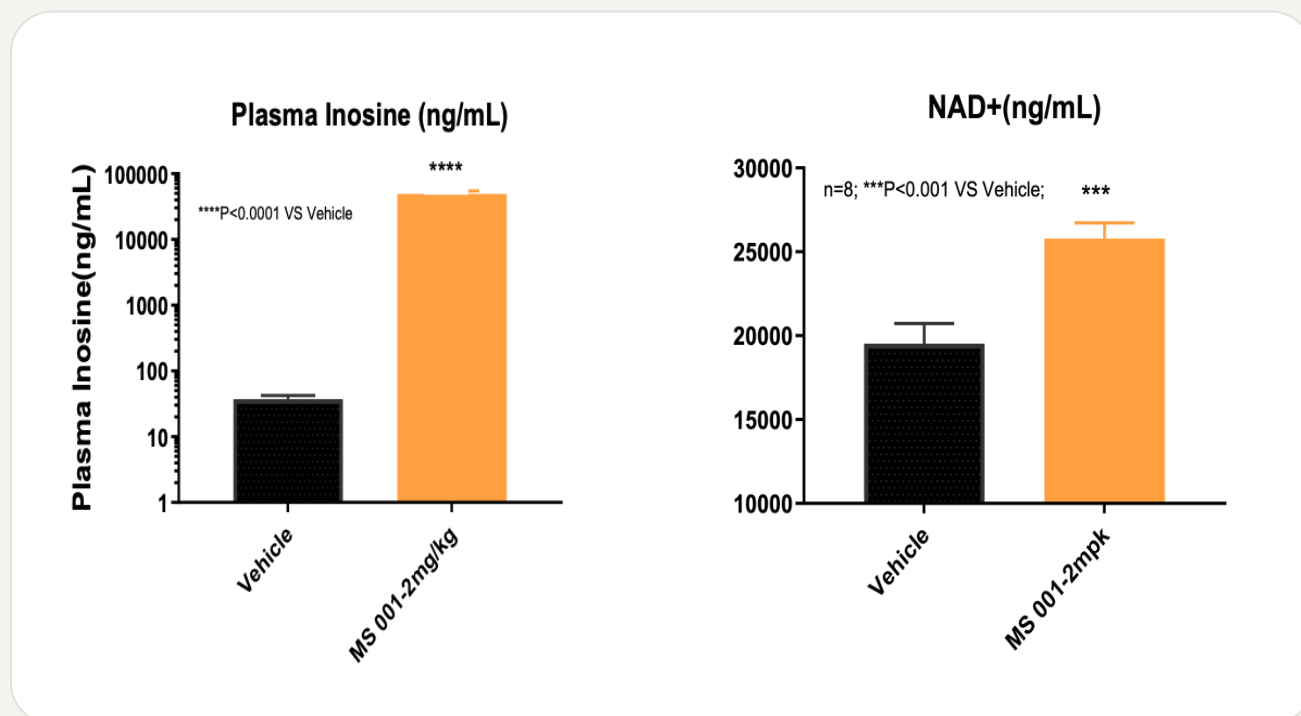
**High-impact pipeline in rapidly growing metabolic health market**



**Elevates NAD+ → potential applications in longevity & metabolic health**

# How Does MS 001 Work?

## MS 001 Increases Inosine and NAD+



## Role of Inosine and NAD+ in improving metabolic health and obesity

GLP-1RAs attenuated obesity and reversed leptin resistance partly *via* activating the microbiome-derived **inosine**/A2A pathway

Chunyan Dong, Bailing Zhou, Binyan Zhao, Ke Lin, Yaomei Tian, Rui Zhang, Daoyuan Xie, Siwen Wu, Li Yang\*

Apoptotic brown adipocytes enhance energy expenditure via extracellular **inosine**

<https://doi.org/10.1038/s41586-022-05041-0> Birte Niemann<sup>1,2,3</sup>, Saskia Haufs-Brusberg<sup>1,2</sup>, Laura Puetz<sup>1</sup>, Martin Feickert<sup>1</sup>, Michelle Y. Jaeckstein<sup>1</sup>, Anne Hoffmann<sup>1</sup>, Jelena Zurkovic<sup>1</sup>, Markus Heine<sup>1</sup>, Eva-Maria Trautmann<sup>1</sup>, Christa E. Müller<sup>1,4</sup>, Anke Tönjes<sup>1</sup>, Christian Schlein<sup>1</sup>, Azin Jafari<sup>1</sup>, Holger K. Eitzschig<sup>1,5</sup>, Thorsten Gnad<sup>1</sup>, Matthias Blüher<sup>1,6</sup>, Natalie Kraher<sup>1,1</sup>, Peter Kovacs<sup>1</sup>, Joerg Heeren<sup>1</sup> & Alexander Pfeiffer<sup>1,6,7</sup>

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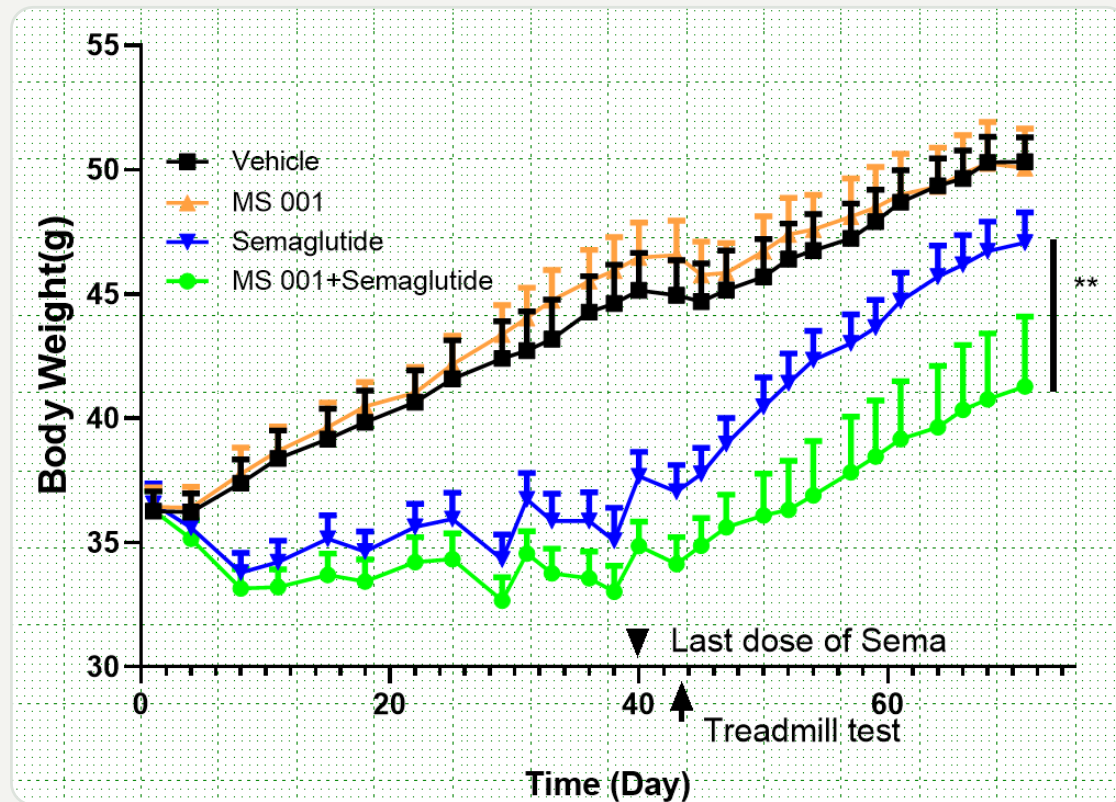
Adipose tissue **NAD<sup>+</sup>** biosynthesis is required for regulating adaptive thermogenesis and whole-body energy homeostasis in mice

Shintaro Yamaguchi<sup>a,1</sup>, Michael P. Franczyk<sup>a,1</sup>, Maria Chondronikola<sup>a</sup>, Nathan Qi<sup>b</sup>, Subhadra C. Gunawardana<sup>c</sup>, Kelly L. Stromsdorfer<sup>a</sup>, Lane C. Porter<sup>a</sup>, David F. Wozniak<sup>d,e</sup>, Yo Sasaki<sup>f</sup>, Nicholas Rensing<sup>g</sup>, Michael Wong<sup>g</sup>, David W. Piston<sup>c</sup>, Samuel Klein<sup>a,c</sup>, and Jun Yoshino<sup>a,h,2</sup>

The Role of **NAD<sup>+</sup>** in Metabolic Regulation of Adipose Tissue: Implications for Obesity-Induced Insulin Resistance

Tatjana Ruskovska<sup>1</sup> and David A. Bernlohr<sup>2,\*</sup>

# Synergy: Weight Loss, Strong Results



## 50% less weight gain vs GLP-1 alone

Greater weight loss control on high fat diet

Group	Day 71	
	BW (g)	BW (%) change
Vehicle	50.3	~38%
MS 001	50	~37%
Sema (d/c day 40)	47.1	~29%
Sema + MS 001; then stop Sema, continue only MS 001	41.3	~14%

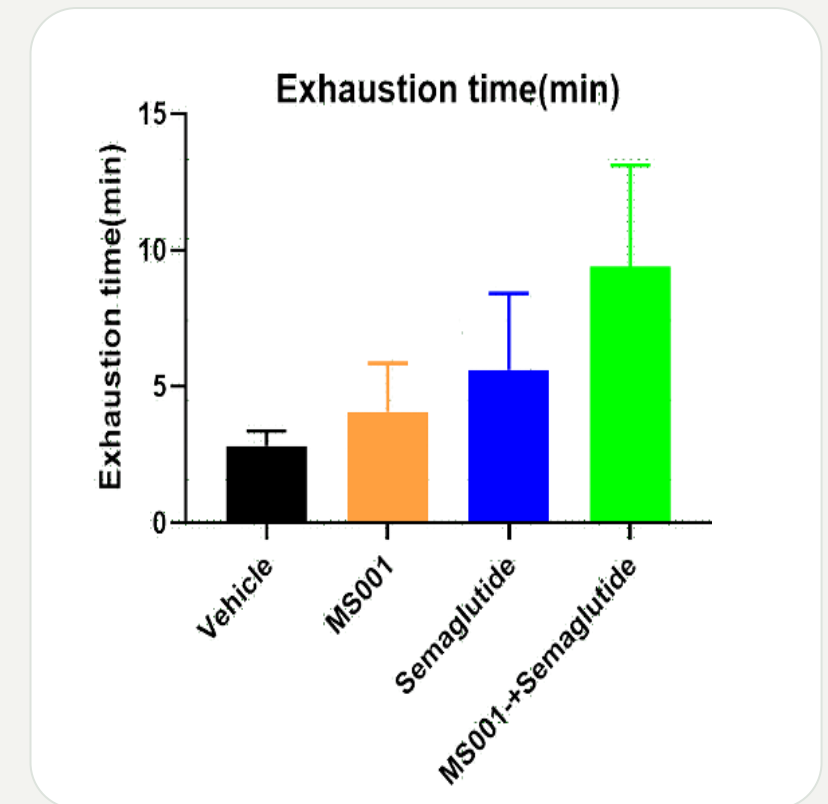
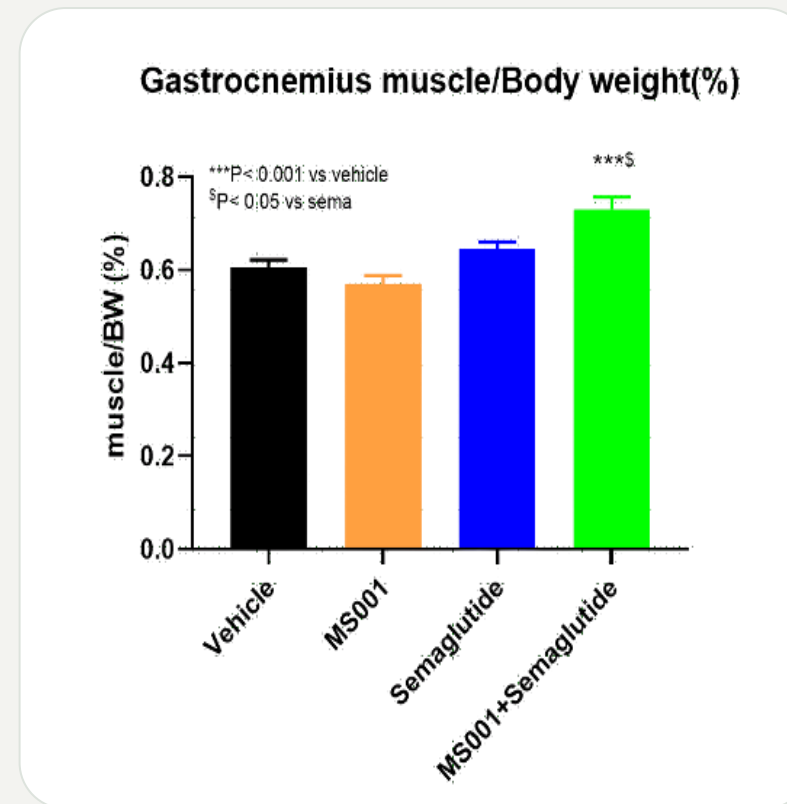
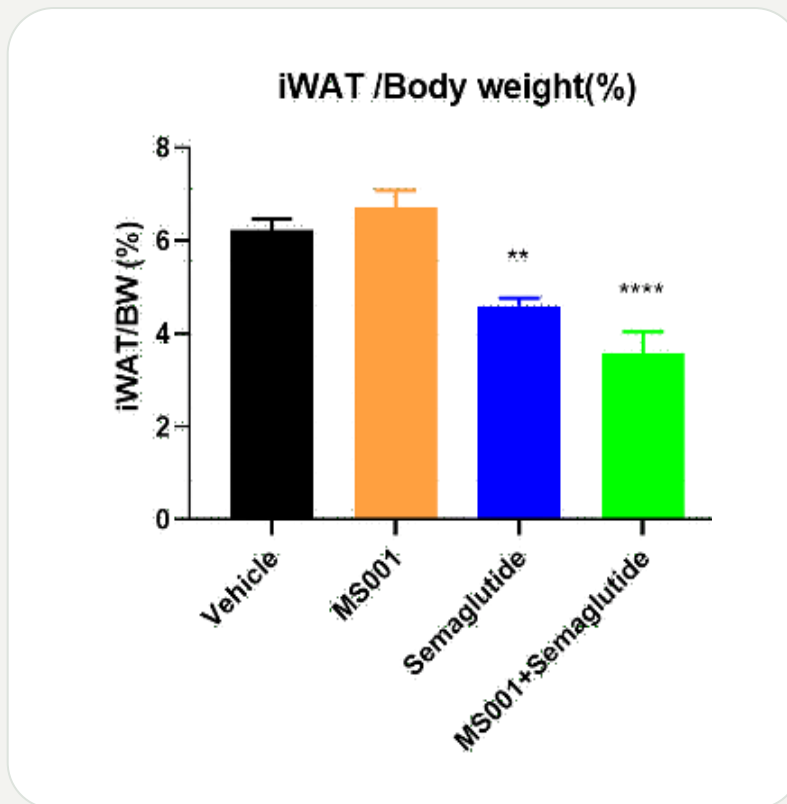
Starting body weight ~ 36.5 g | Semaglutide therapy stopped on day 40

C57BL/6J mice are fed an obesogenic diet from the age of 6 weeks. Approximately 18-week-old mice are either treated with vehicle, or MS 001, or semaglutide, or combination of MS 001+Semaglutide.



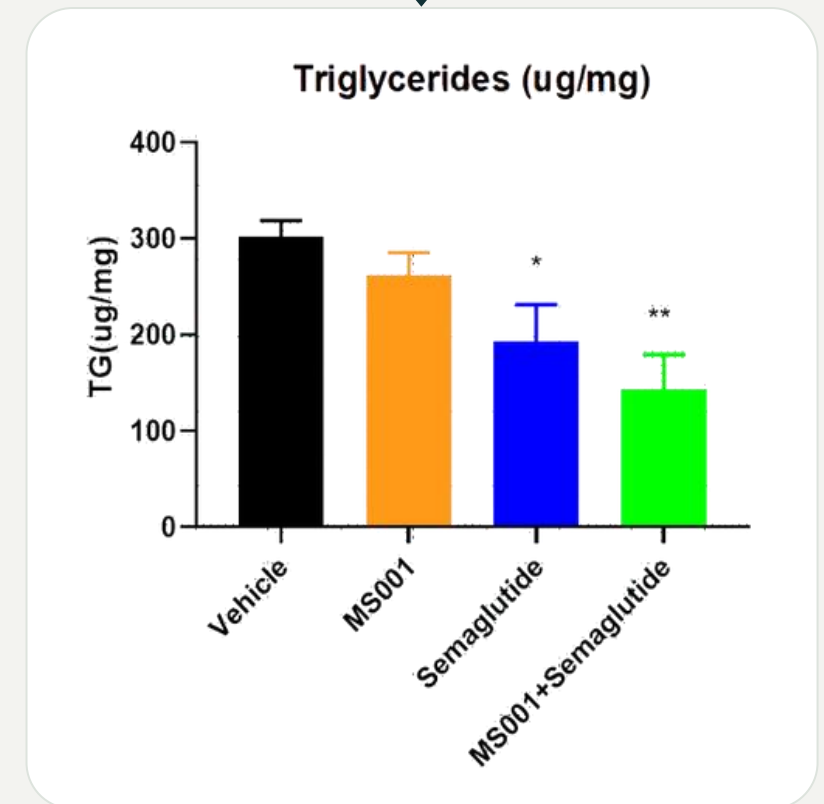
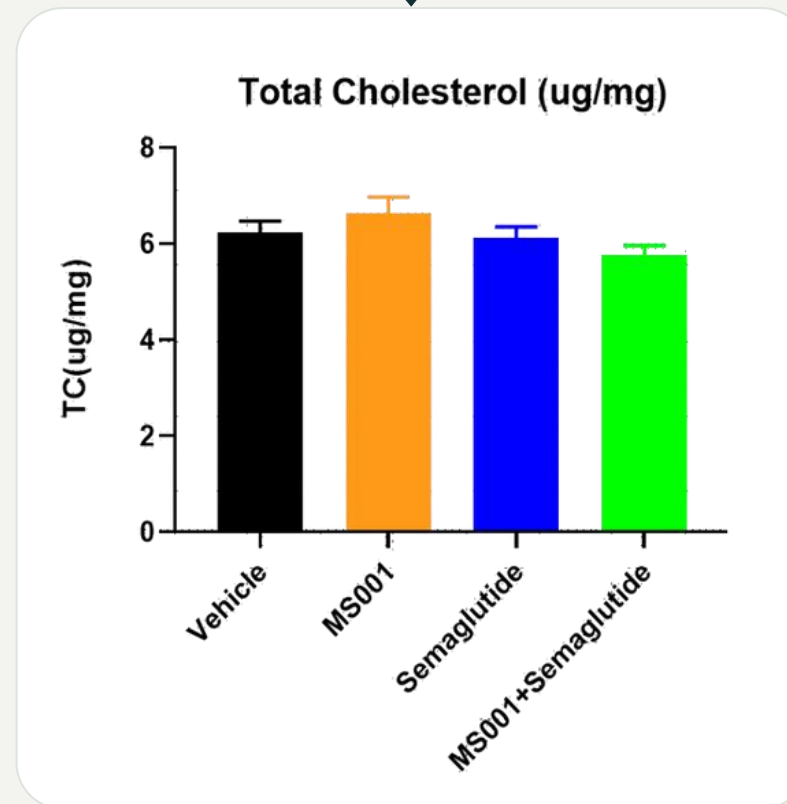
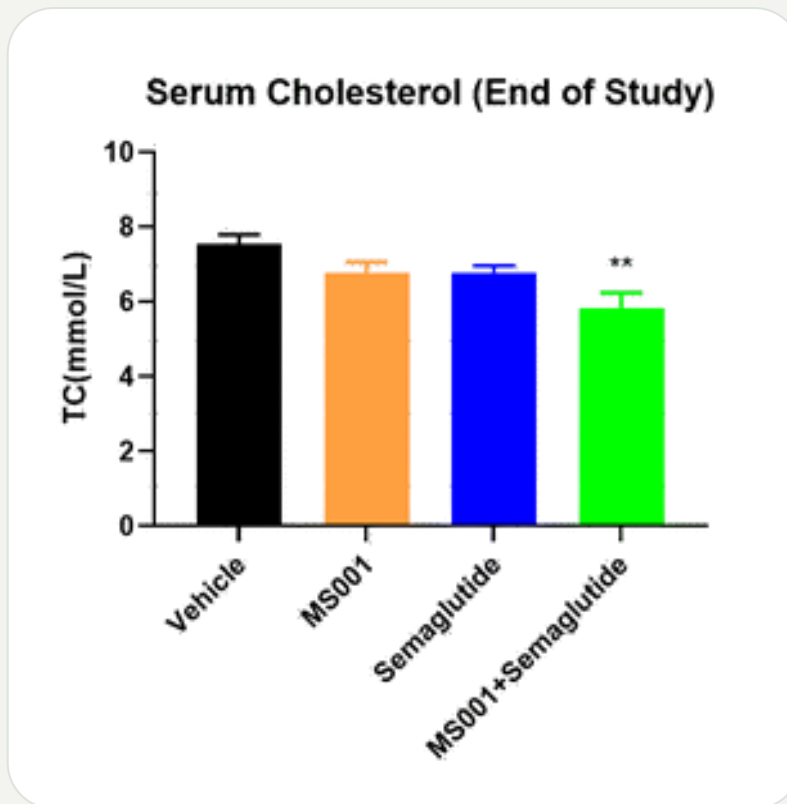
# Synergy: Fat Decrease, Muscle Increase, and Improved Endurance

## Treadmill Test



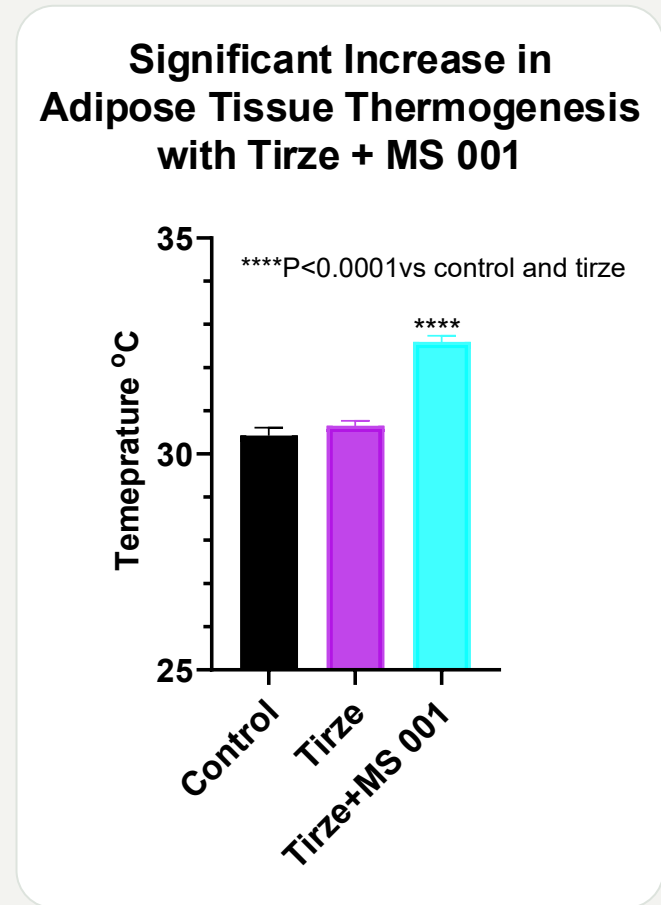
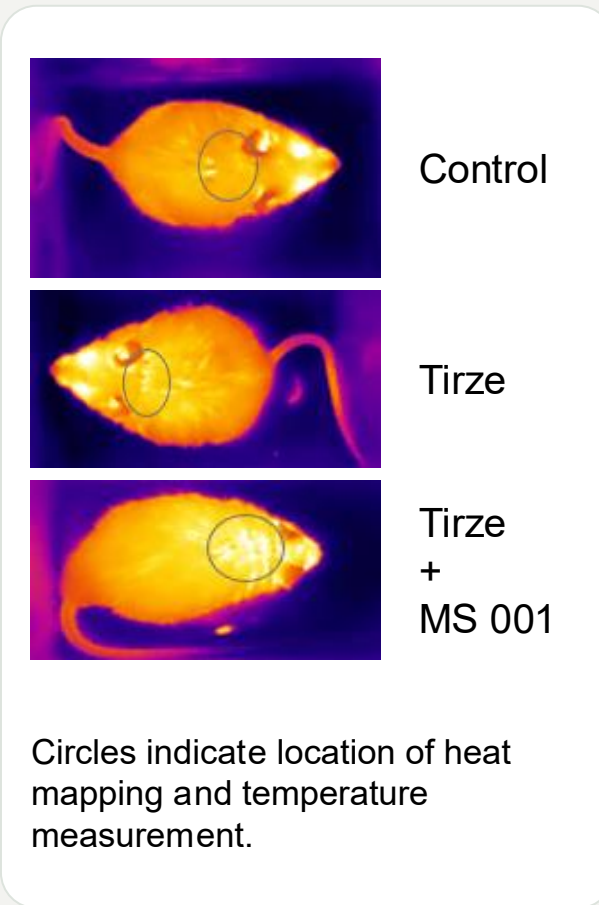
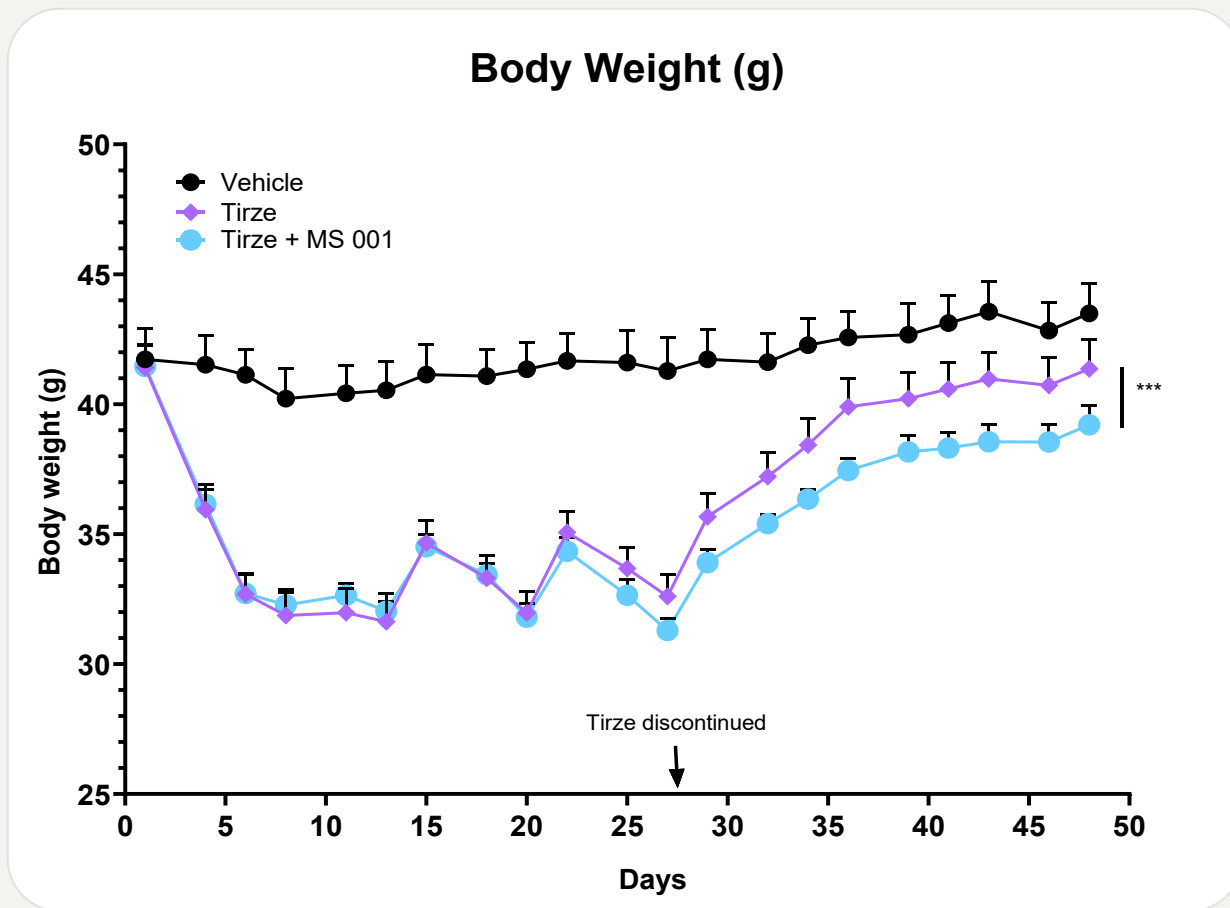
# Synergy: Improved Lipid and Liver Profile

Liver Profile



Source slide visual

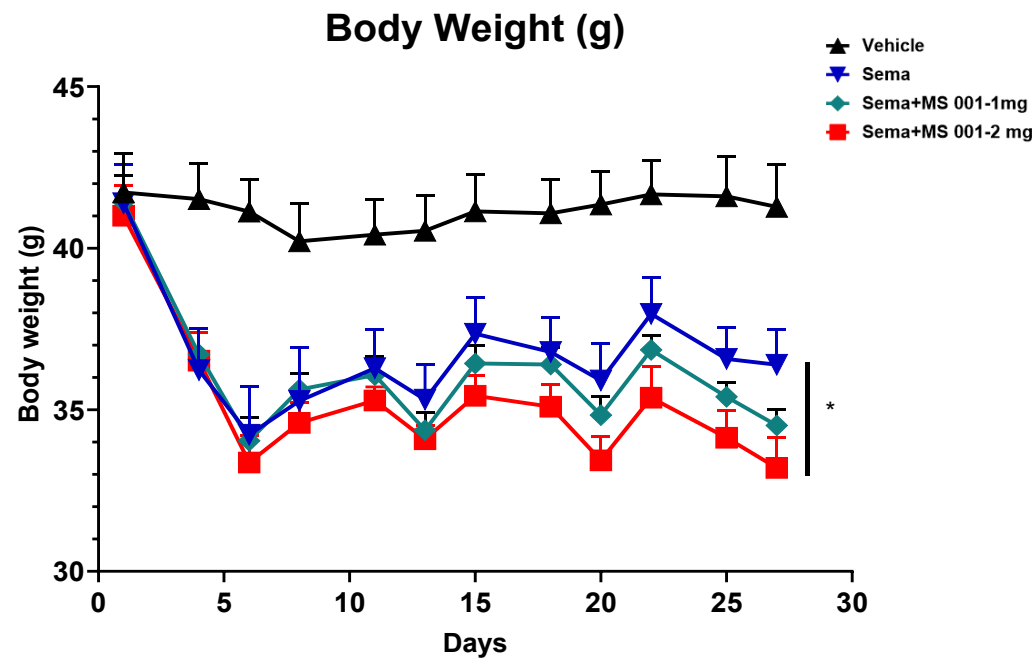
# MS 001 Boosts Tirzepatide Efficacy via Enhanced Fat Burning



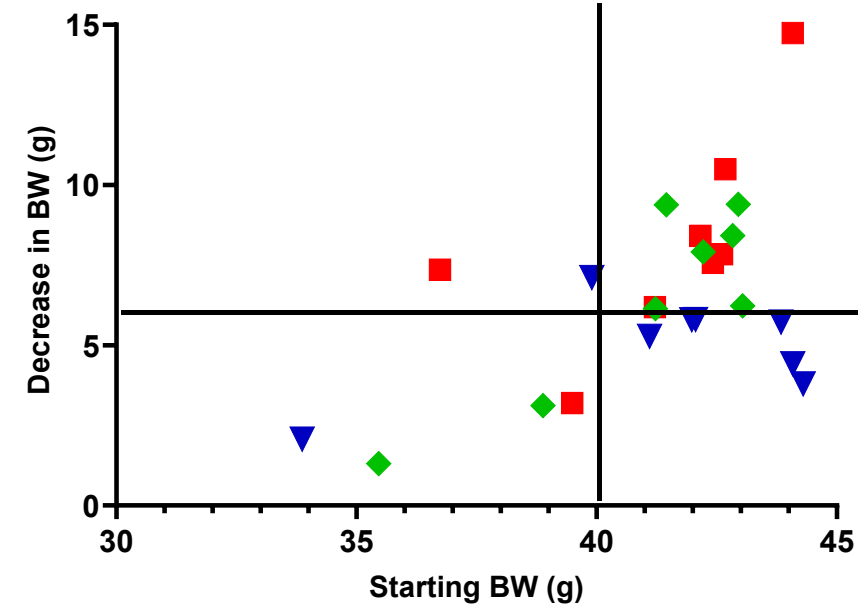
Study design: C57BL/6N; 30-week-old; 8 mice/gp. Tirze was given twice a week 0.05 mg/kg except for the first 2 doses (0.3 mg/kg; first week) and MS 001 was given orally 3 days/week at 1mg/kg dose. Thermal imaging performed Day 45.

# Higher Body Fat Drives Increased Weight Loss with MS 001 + Semaglutide

MS 001 DOSE DEPENDENT INCREASE IN WEIGHT LOSS



Decrease in BW day 27 vs Starting BW



Study design: C57BL/6N; 30-week-old; 8 mice/gp. Sema was given twice a week 0.05 mg/kg except for the first 2 doses (0.3 mg/kg; first week) and MS 001 was given orally 3 days/week at 1mg/kg or 2mg/kg dose.

# MS 001: Backed by Human Clinical Safety Data

Clean safety profile with daily administration demonstrated in Phase I & II studies in 500+ subjects.

		Allopurinol 300mg +			
Infectious Adverse Events (AEs)	Placebo (n=56)	5mg (n=56)	10mg (n=56)	20mg (n=56)	40mg (n=54)
<b>Any infections AEs N(%)</b>	<b>11 (20%)</b>	10 (18%)	10 (18%)	9 (16%)	<b>11 (20%)</b>
Typical cold symptoms	6 (11%)	7 (13%)	2 (4%)	4 (8%)	4 (7%)
Lower respiratory tract	2 (4%)	0	1 (2%)	0	1 (2%)
Bacterial/Potentially bacterial	5 (9%)	2 (4%)	9 (16%)	5 (9%)	7 (13%)
Viral/Potentially viral	10 (18%)	9 (16%)	3 (5%)	4 (8%)	6 (11%)
Fungal/Potentially fungal	1 (2%)	1 (2%)	1 (2%)	1 (2%)	1 (2%)

Phase 2 BCX-4208 (ulodesine) study in patients with gout has demonstrated long-term safety and tolerability, at high doses of **40 mg daily for 6 months**

**5mg/Day** or less of MS 001 as a GLP-1 co-therapy for obesity.

Long-Term Safety: A Phase 2 BCX4208 24-Week Blinded Safety Extension and Vaccine Challenge Study. Presented at EULAR, Berlin, June 6 – 9 2012.

SUMMARY

# MS 001 Significantly Enhances the Metabolic Effects of GLP-1 Receptor Agonists

Drives deeper, increased fat loss in mice with higher baseline body mass

Activates thermogenesis, primarily in adipose (fat) tissue

Preserves muscle mass and muscle health

Improves lipid and liver profiles

Reduces weight rebound following GLP-1 discontinuation

Favorable safety profile of predecessor compound in humans

# Long Patent Runway

## Method-of-Use Application

**Exp. 2042**

Covering **all PNP inhibitors** for the treatment of obesity, cardiometabolic disorders & neurological diseases.

## Composition-of-Matter Application

**Exp. 2041**

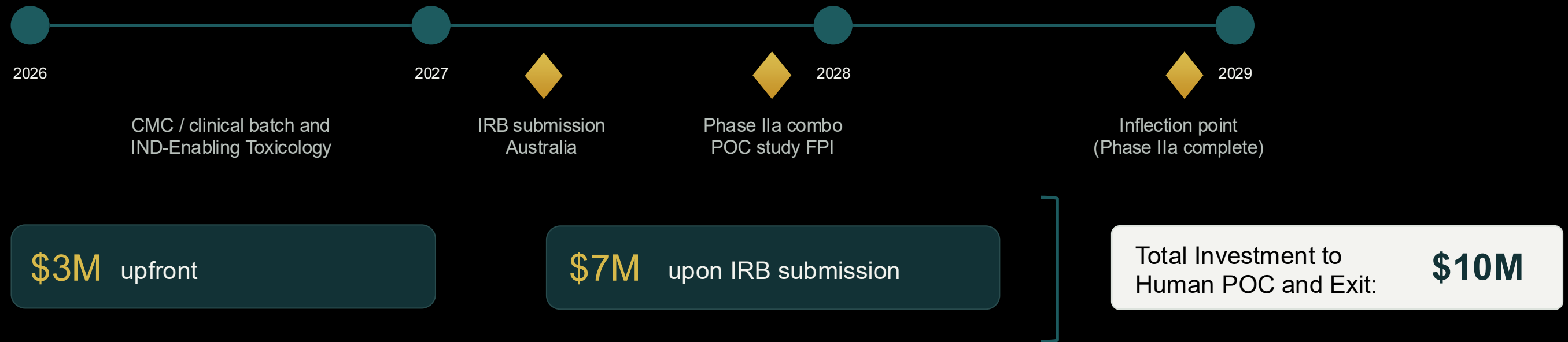
Covering novel, stable salt form of ulodesine under an exclusive license for non-oncological indications.

Applications under examination for exclusivity and long patent runway. Historical clinical data suggests MS 001 is an excellent candidate for combination with GLP-1 drugs.

DEVELOPMENT PLAN (Values in USD)

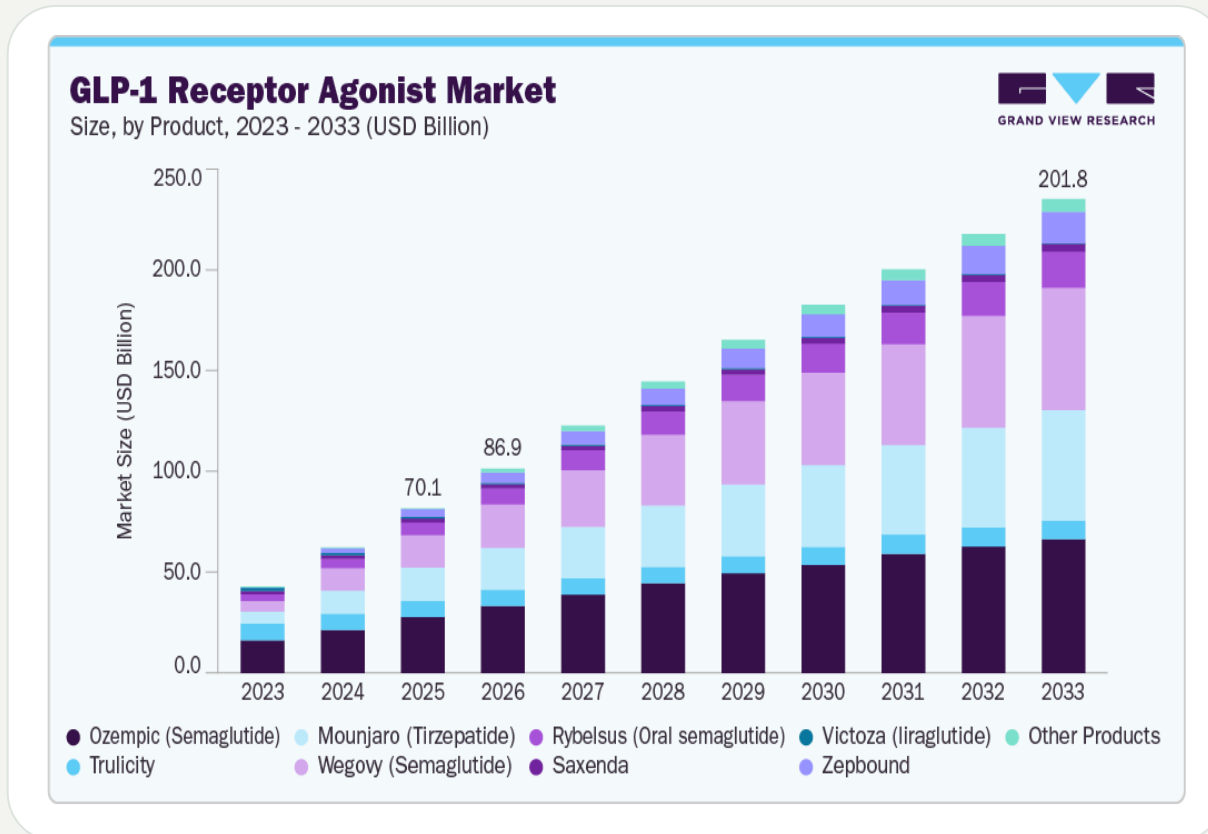
# Investment to High Value Inflection and Exit

MetaShape is working with iNGENU, an Australian CRO, to conduct a Phase IIa proof-of-concept study in Australia under standards aligned with FDA regulatory expectations. This approach is designed to generate human proof-of-concept data more efficiently and cost-effectively, supporting a potential licensing or M&A transaction with large pharma.



FPI: First-Patient In

# Total Addressable Market for MS 001



More than 2% of Americans are taking GLP-1 drugs for overweight or obesity, up nearly 600% over six years, according to [FAIR Health](#).

## Assumptions and Peak Annual Sales

- 260 million American Adults
- 30% or 78 million Americans consider taking GLP-1s
- 10% or 7.8 million Americans take GLP-1s
- MS 001 TAM of 7.8 million Americans
- Only 7% (546K) Americans take MS001/year in combo with GLP-1s
- Cost of therapy for 1 year = \$100/month (\$1,200/year)
- \$1,200/pt./year \* 546K patients per year, equals (=)

**\$655,200,000 in first 12 consecutive months on market**

**\$2 Billion+ in peak annual sales 5 years out.**

INVESTMENT RETURN SCENARIO

# Potential Return at POC / Phase IIa

Comparable recent transactions with Phase I or II candidates in the cardiometabolic space command high dollar values.

Companies ▼	Deal Year ▼	M&A ▼	License ▼	Upfront ▼	Milestone ▼	Candidate Drug ▼
Novo / United Laboratories	2025		X	\$200M	\$1.8 B	triple agonist GLP/GIP and glucagon - in Phase Ib
Pfizer / Metsera	2025	X		\$10 B		GLP-1 and Amylin - Ph. 2
Abbvie / Gubra	2025		X	\$350M	\$1.875 B	Amylin hormone - Ph. 1
Roche / Zealand Pharma	2025		X	\$1.4 B	\$3.6 B	Amylin hormone - Ph. 2
AstraZeneca / SixPeaks Bio	2025	X		\$200M	\$100M	Activins/TGF-beta - Preclinical

MS 001 POTENTIAL

- \$200M+** potential upfront at attractive Phase II readout
- \$1Bn** potential over time
- 20-100x** cash payback on \$10M investment<sup>1</sup>
- 2029** Timing to exit

<sup>1</sup>Does not account for new discovery by Case Western University of MS 001's potential upside in treating and reversing Alzheimer's Disease (Global Alzheimer's market projected at \$106 Bn by 2032).

Note: investment return scenarios are illustrative and dependent on attractive Phase II outcomes.

OUR TEAM

# Thoughtfully Assembled Based on Our Past Experience Working Together



**Randall Riggs, MBA**

Chief Executive Officer



**Thomas Mehring, MD, PhD**

Chief Medical Officer, Founder



**Shanta Bantia, PhD**

Chief Scientific Officer, Founder



**Pooran Chand, PhD**

Chief Development Officer



**Jessica Kourniaktis, DPhil**

Chief Operating Officer



**Shingo Kajimura, MD, PhD**

Scientific Advisor



**Caius Radu, MD, PhD**

Professor in the Departments of Molecular and Medical Pharmacology, UCLA Health



**Steve Mittleman, MD, PhD**

Professor Solomon A. and Marie M. Kaplan Chair of Pediatric Endocrinology; physiology of obesity research, UCLA Health



**Vincenzo Sorrentino, PhD**

Associate Professor, Department of Biochemistry, National University of Singapore

KEY STRATEGIC COLLABORATORS

THANK YOU

# Maximizing GLP-1 Benefits with Oral **MS 001**

To control weight regain, preserve muscle, and improve long-term health.

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