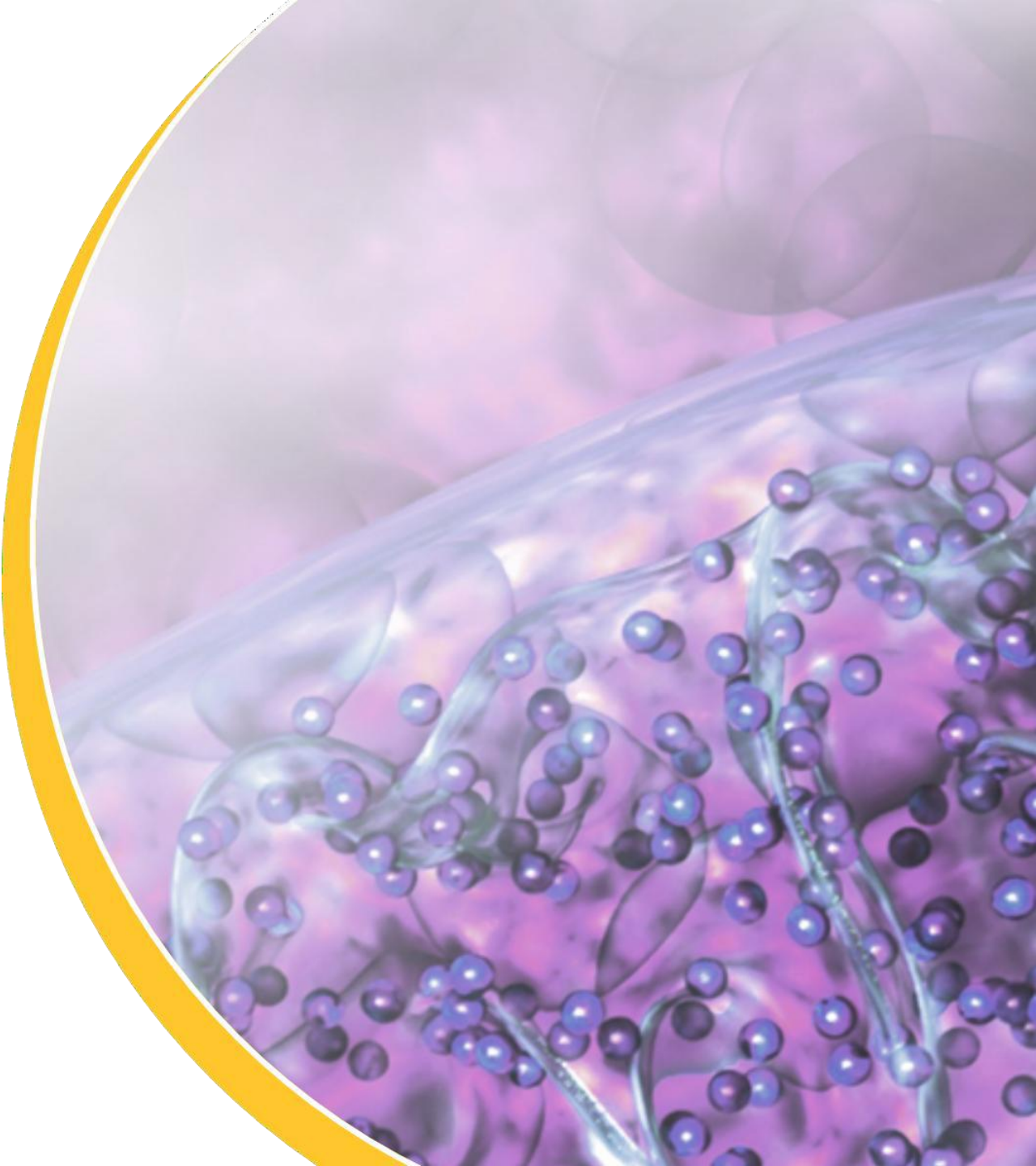




Oral 15-PGDH Inhibitor Platform:

Leveraging PGE₂ Signaling To Treat Sarcopenia, Neuromuscular & Inflammatory Diseases (IBD):

- **MF-300, lead oral small molecule: Phase 2b Sarcopenia**



Experienced Team with a Demonstrated Track Record of Success



Epirium Leadership Team



Alex Casdin, CEO

30+ year track record success in biotech & healthcare:

Port. Mgr: Pequot Capital; CEO & PM: Cooper Hil Partners, Reneo Capital

VP Finance, Amylin; CFO, Sophiris

Investor, Board Member & Audit Chair – Ignyta (acq. Roche), Erasca; Board: Dusa (acq. Sun Pharma), 454 Life Sciences (acq. Roche)



Eric Miller, CFO

Head Finance, Synthorx (acquired by Sanofi)

Corp. Controller & Head FP&A, Acadia Pharm.

Cadence Pharm. (acquired by Mallinckrodt)



Micah Webster, Ph.D. Sr. Director, TS

Ph.D. in Cellular and Molecular Biology, JHU

Scholar Rock, Associate Director, Translational Science

Discovery programs & Biomarker Strategy for apitegromab

Key Consultant Advisors



Leigh MacConell, Ph.D. Head, Clinical Development

25 years drug development, primarily in metabolic and liver disease

Led multiple drug approvals including first in class for T₂DM (GLP-1) and primary biliary cholangitis (PBC)

Collaborated with FDA to define approval pathways for disease areas without regulatory precedence, including PBC & MASH



Elaine Chiquette, Pharm.D. Scientific Affairs

C-Suite executive with 20+ years experience in pharma, biotech, and medical device

Led regulatory approvals for NDA, BLA, PMA across USA, EU and China

Formerly served as CSO and head of regulatory & medical affairs at Gelesis

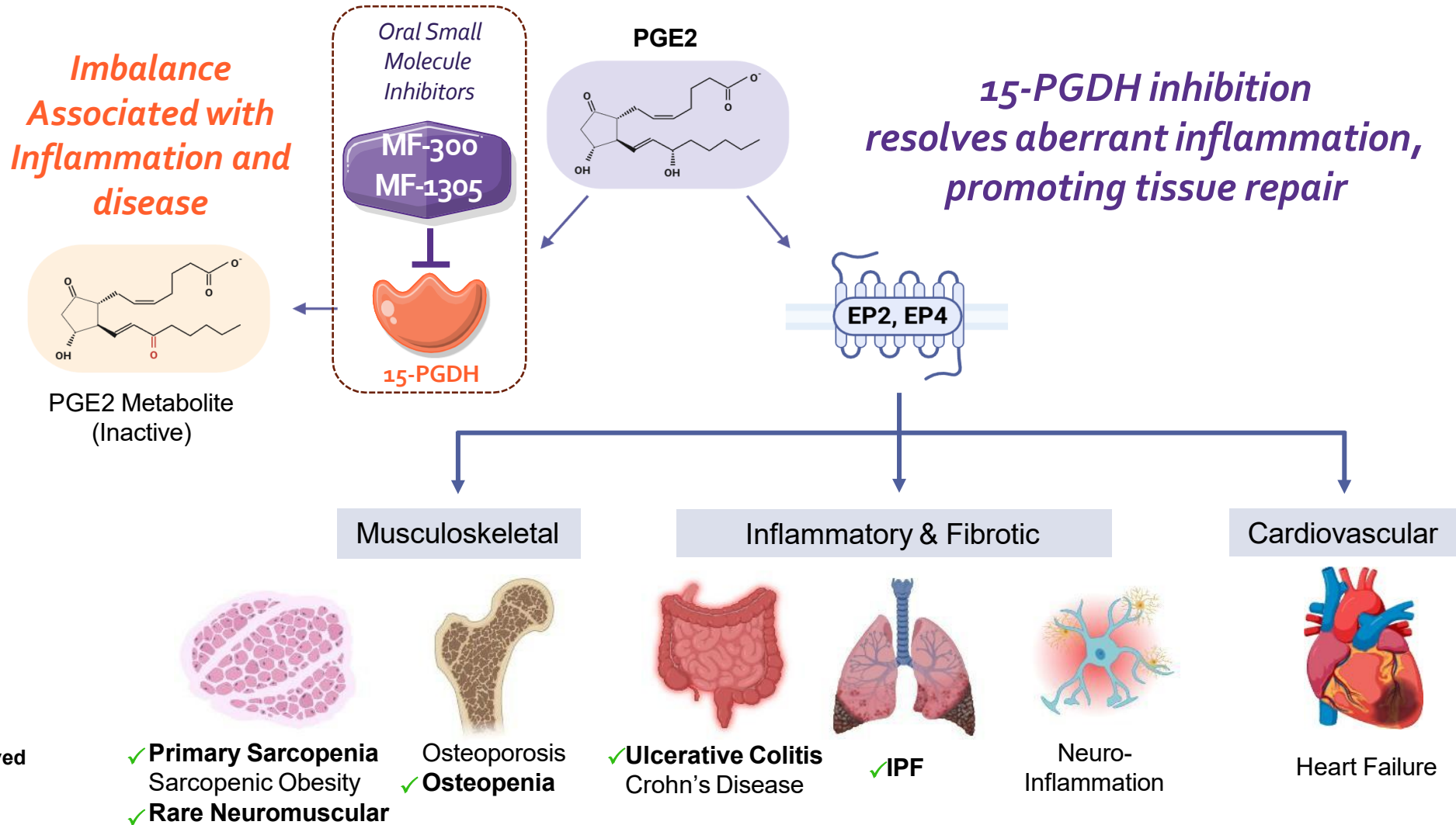


Lois Lee, Pharm.D. Clinical Development

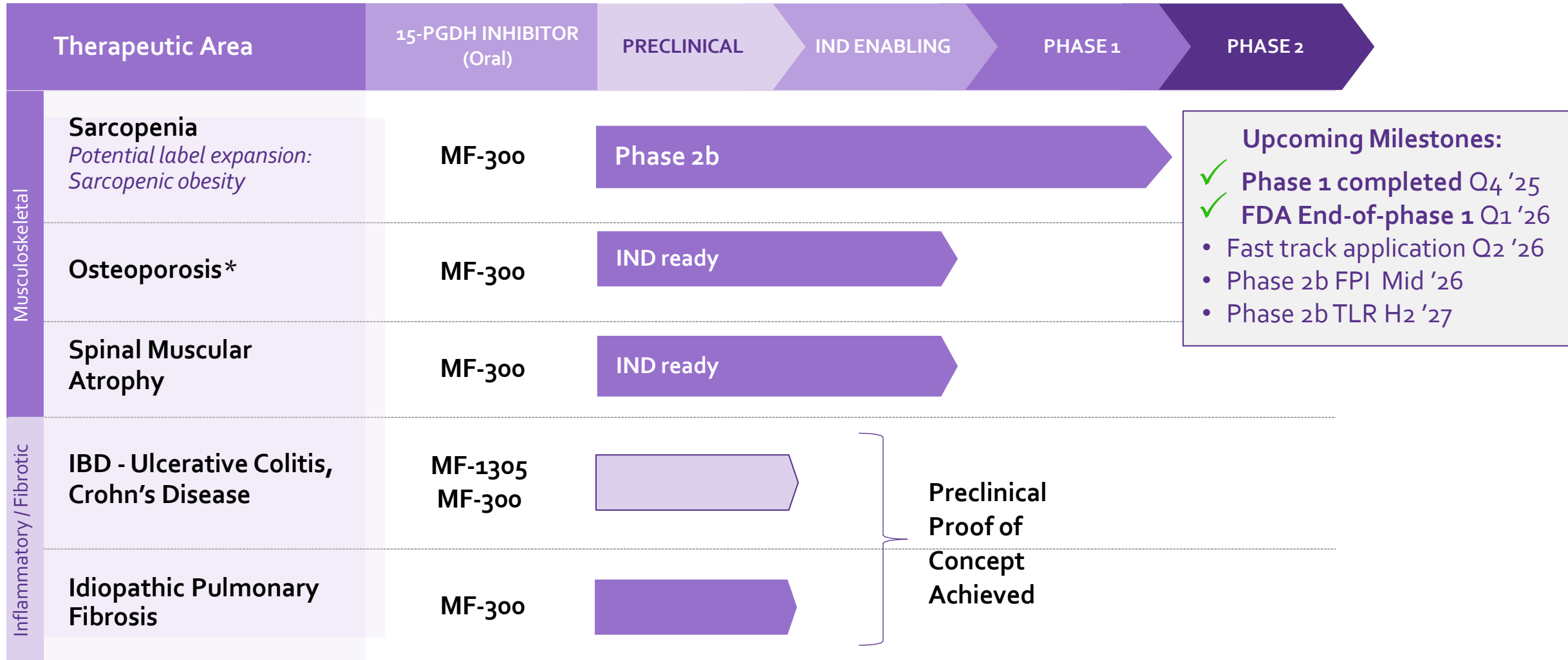
20+ years of industry experience leading early- and late-phase drug development across multiple TAs including liver, metabolic, and neurodegenerative diseases.

Extensive experience in collaborating with FDA and EMA on indications lacking regulatory precedent including MASH, MASH cirrhosis, and Alexander disease

Inhibiting 15-PGDH to leverage the potential of PGE₂ signaling in restoring tissue homeostasis: rebalancing inflammation, stimulating regeneration, reducing fibrosis



Epirium 15-PGDH Inhibitor Platform: "Pipeline in Mechanism"



*Human proof of concept (bone biomarkers & bone mineral density) to be generated in Sarcopenia Phase 2b study

Epirium MF-300 Lead Program in Sarcopenia:

- Unmet Need
- Scientific Rationale
- Preclinical Muscle Force & Biomarker Results



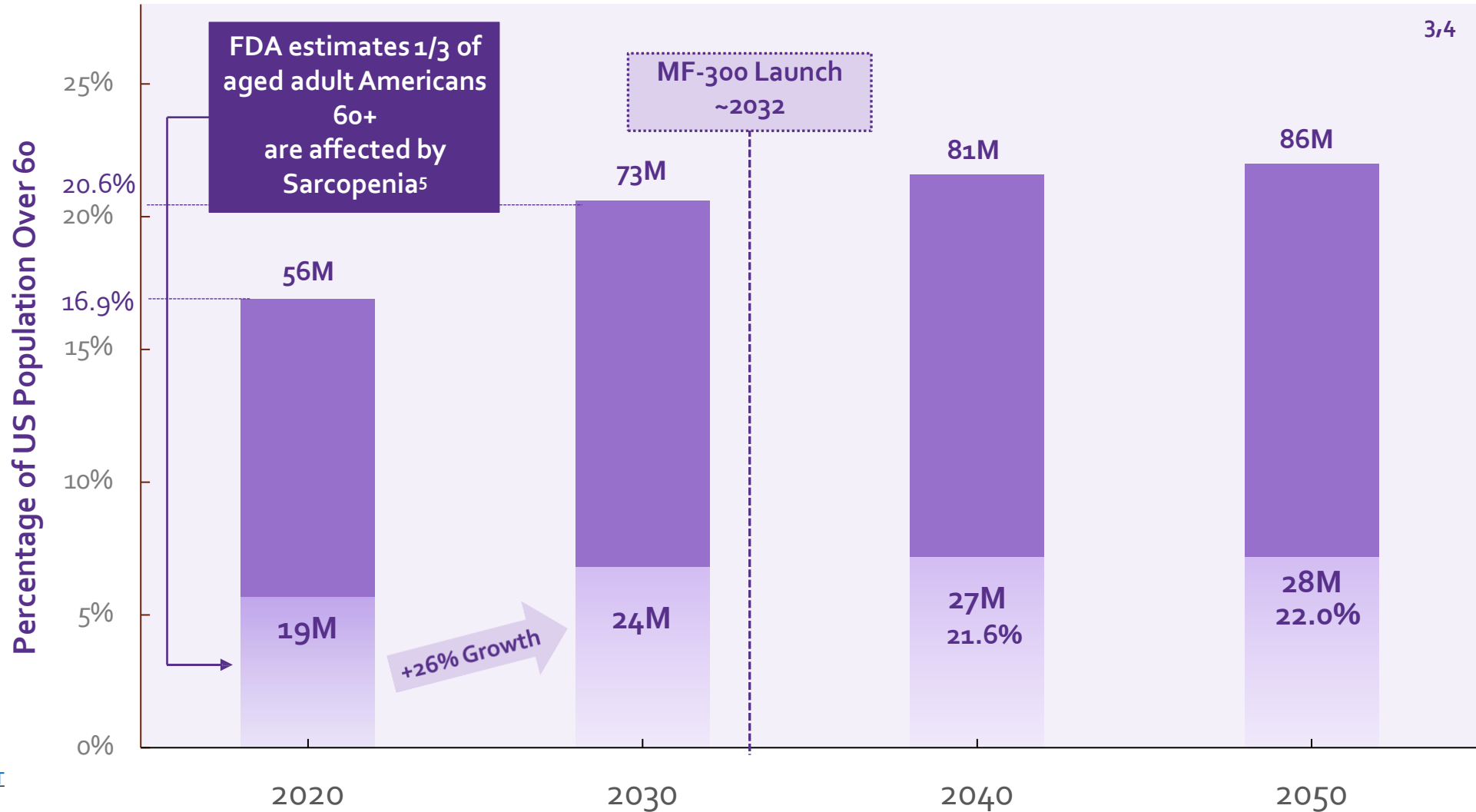
Sarcopenia: Large and Growing Unmet Medical Need w/ No FDA Approved Therapy

Current U.S. Healthcare Sarcopenia Spending Estimated >\$40 Billion Annually¹

Dependence
Increased risk losing independence

Falls
Increased Morbidity & Mortality²

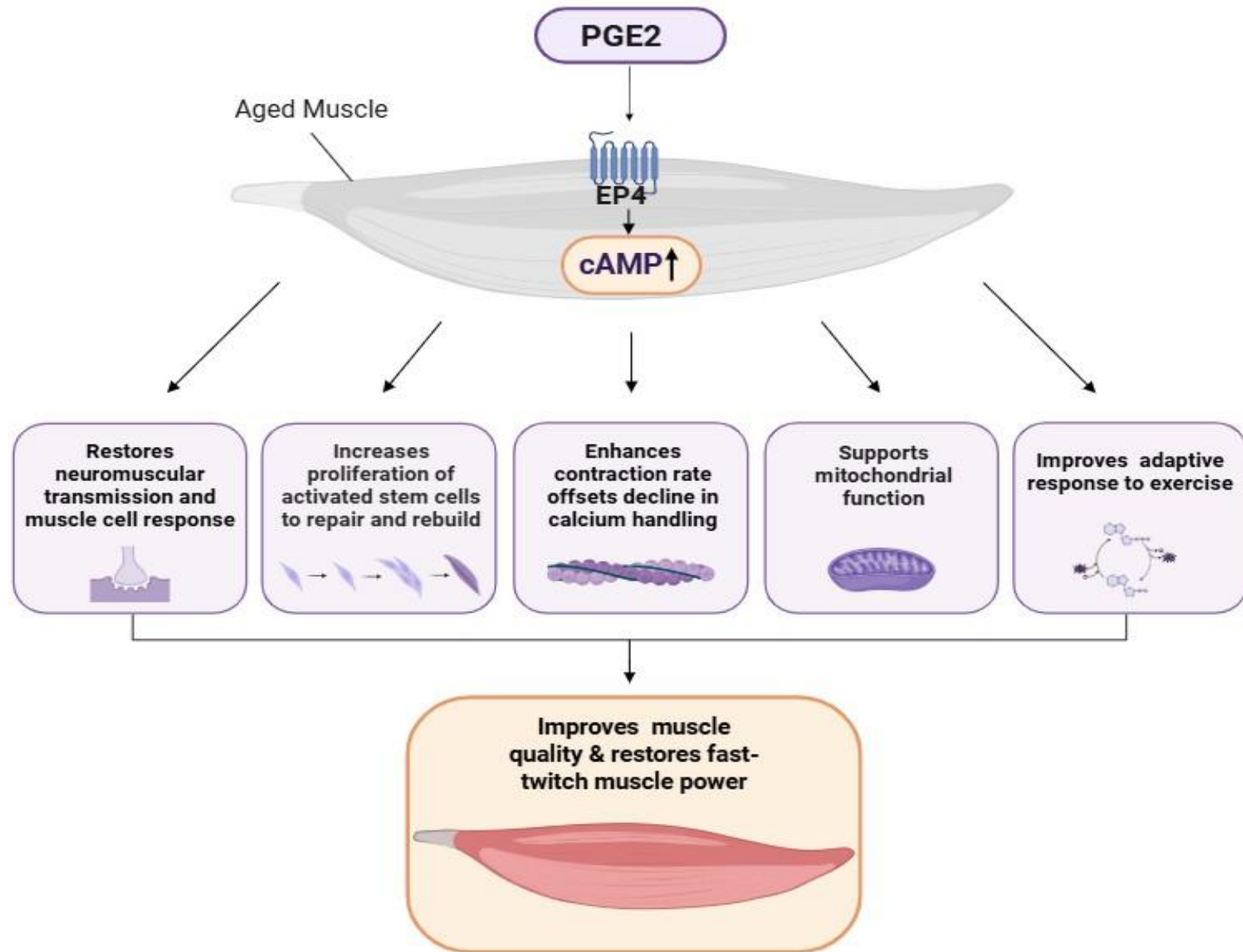
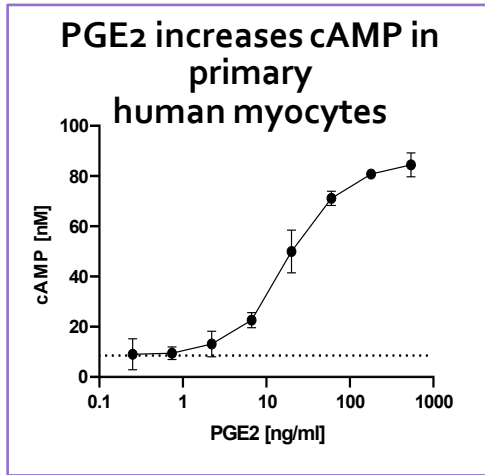
Mortality
Increased risk of death²



U.S. Population est. 331M

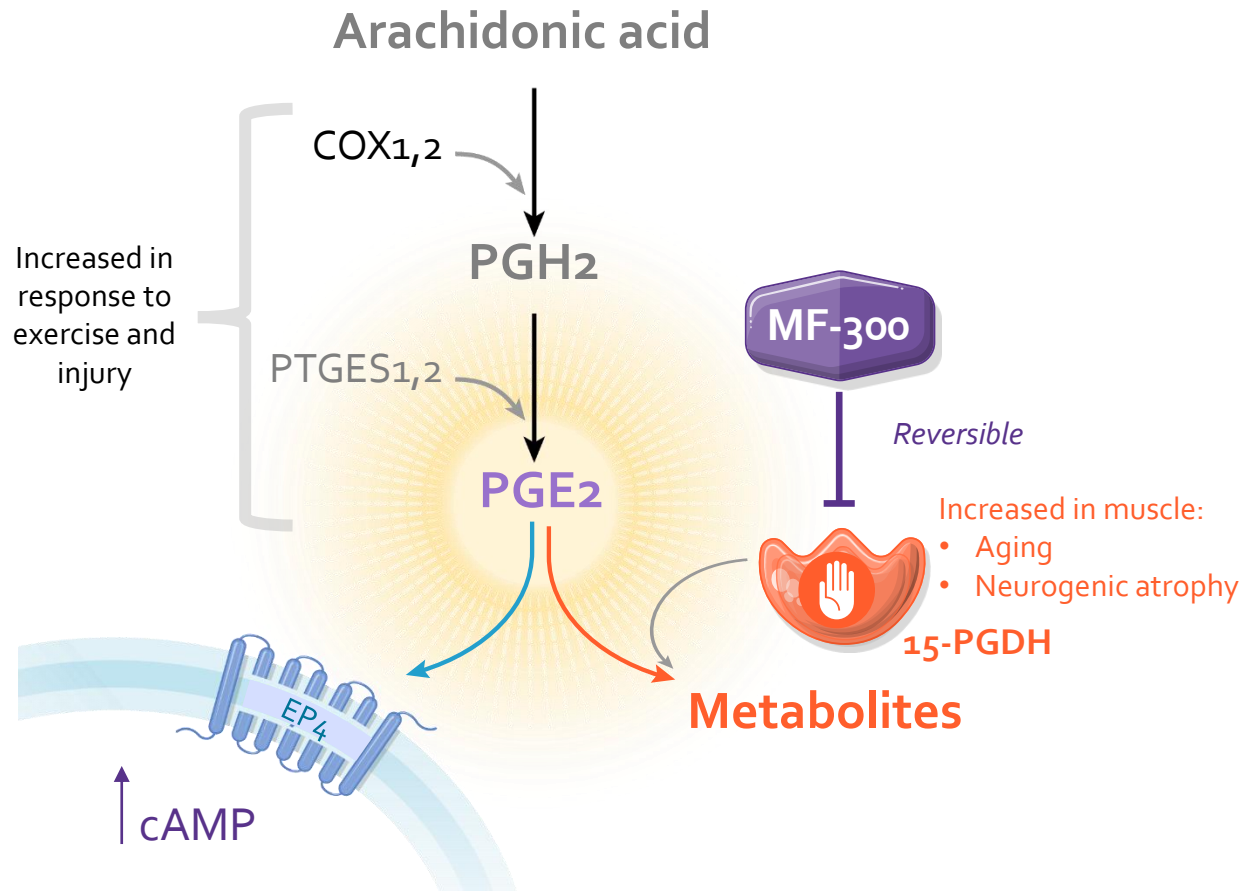
1. Goates S, et al. J Frailty Aging. 2019.
2. www.agingresearch.org. Sarcopenia Facts and Figures
3. Burns ER, J Safety Res. 2016.
4. Papadopoulou SK. Nutrients. 2020.
5. <https://www.fda.gov/files/about%20of%20fda/published/T%20he-Voice-of-the-Patient--Sarcopenia.pdf>

PGE₂-EP₄ Signaling Elevates cAMP to Promote Muscle Function

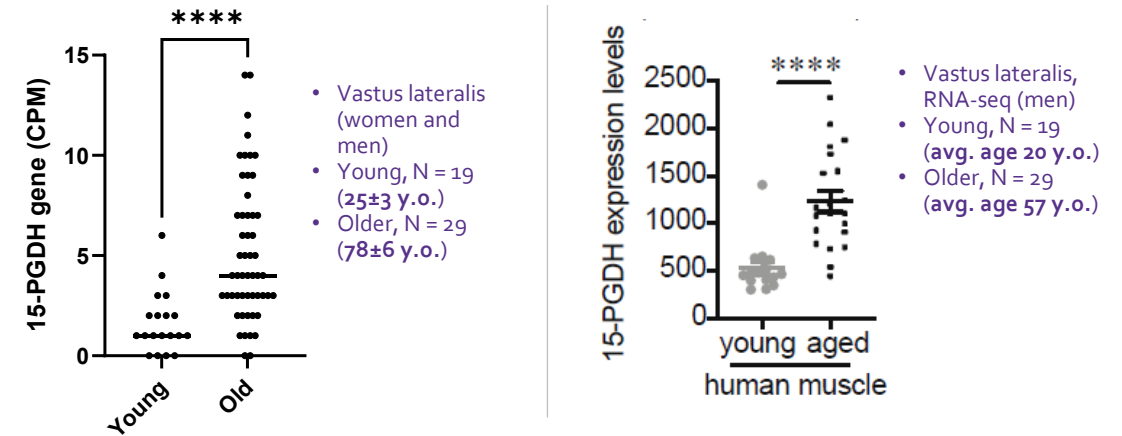


15-PGDH, a Gerotherapeutic Target that Reduces PGE₂ Levels, is Upregulated in Aged Muscle

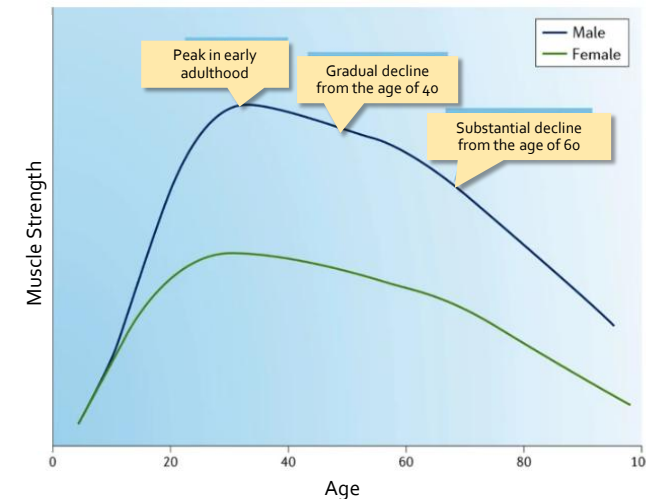
15-HydroxyProstaglandin Dehydrogenase (15-PGDH) Reduces levels of PGE₂



15-PGDH gene expression Elevated in aged human muscle^{1,2}



Grip strength, a predictor of sarcopenia risk, declines with age³

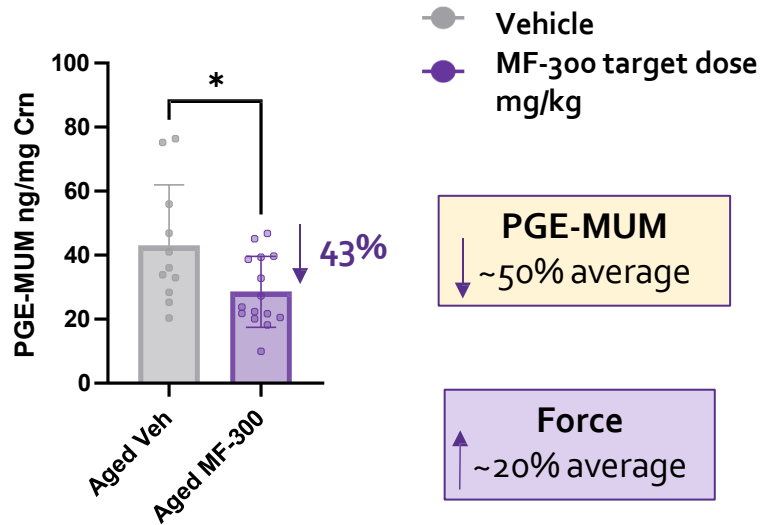


¹ GEO167186, ² Raue et al., *J Appl Physiol* 2012 (published in Palla et al., *Science* 2021), ³ Dennison et al., *Nat Rev Rheum* 2017

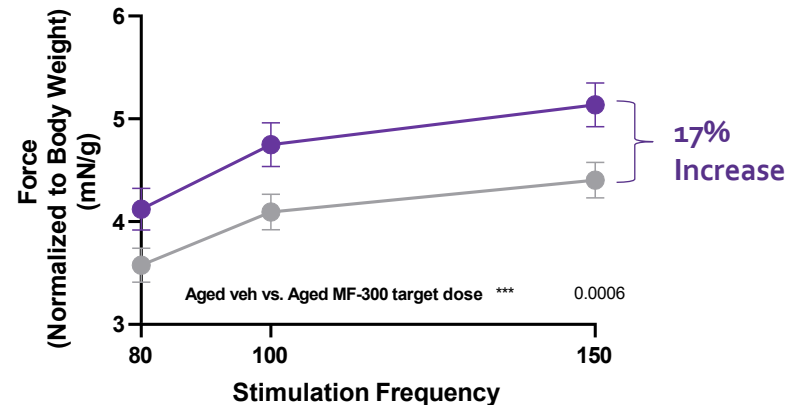
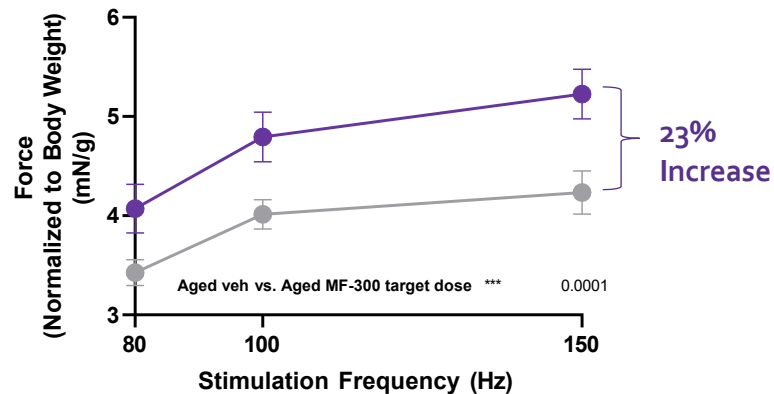
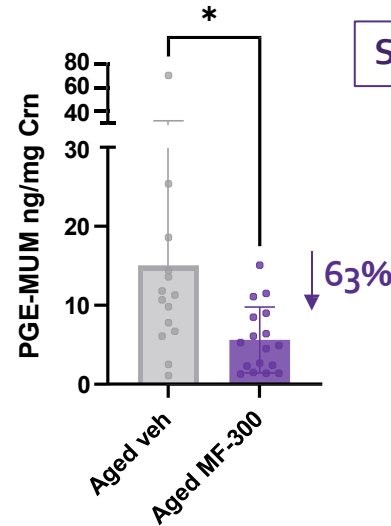
Preclinical Sarcopenia Studies

MF-300 target dose
Increased muscle force and reduced PGE₂ Metabolite in aged mice

Study 1



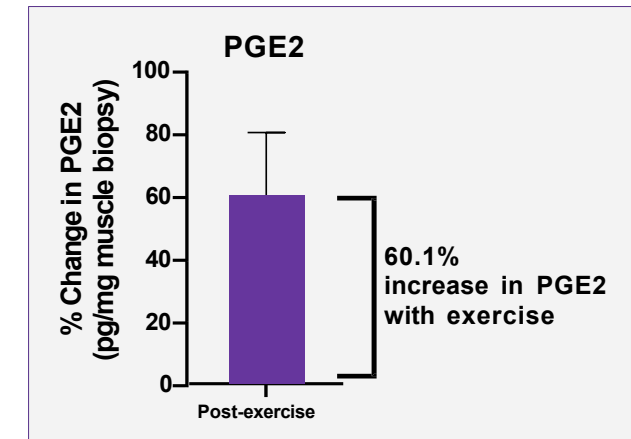
Study 2



Target Engagement Biomarker

- ~50% reduction in PGE-MUM is correlated with
- ~20% improvement in muscle force

PGE₂ in human muscle



Adapted from Trappe TA, et al. J Clin Endocrinol Metab. 2001;86(10):5067-5070

Phase 1 Proof of Mechanism Study

Objectives: Assess the safety, tolerability, pharmacokinetics and pharmacodynamics of MF-300 following single ascending doses (SAD) and multiple ascending doses (MAD)

Populations: Adult healthy volunteers $\geq 18 - \leq 65$ years of age & Healthy older adult cohort $>65 - \leq 75$ years of age

Doses: SAD explored 5 doses ranging from 75mg to 800mg; MAD explored 3 doses of 75mg, 125mg, and 200mg

Part 1a SAD

- N=8 per cohort (2 pbo, 6 MF-300)
- Doses: 75, 125, 250, 500, & 800mg

Single Ascending Dose
5 non-older adult cohorts, 1 older adult cohort

Part 1b Food Effect

- N=12 (all MF-300)
- 500mg MF-300 administered in the fed or fasted state

Food Effect
2 sequence 2 period cross-over

Part 2 MAD

- N=10 per cohort (2 pbo, 8 MF-300)
- Daily dosing for 5 days to achieve steady state PK
- Doses: 75mg, 125mg, 200mg

Multiple Ascending Dose
3 non-older adult cohorts & 1 older adult cohort

- All predefined Phase 1 success criteria across Safety, PK, and PD were achieved
- Enabling advancement into Phase 2b

Safety

- ✓ Safe and well-tolerated
- ✓ No unexpected or dose-limiting findings
- ✓ Majority of adverse events mild and self-limiting
- ✓ No discontinuations due to adverse events

PK

- ✓ Exposure increases predictably with dose
- ✓ Half-life supports once daily dosing
- ✓ Human PK exposures aligned with preclinical efficacy targets

PD

- ✓ Evidence of target engagement (PGE₂ metabolite) w/ substantial proportion of subjects achieving $\geq 50\%$ reduction in PGE-MUM
- ✓ Evidence of mechanism-increased PGE₂ levels
- ✓ Clear dose/response relationship defining therapeutic range, supportive of Phase 2b dose selection

MF-300's Safety Profile Supportive of Continued Development

Safe and well tolerated across the evaluated dose ranges

- No deaths, SAEs, or discontinuations due to AEs
- Maximally tolerated dose not identified up to 800 mg (therapeutic range 75-200mg)
- **Comparable safety profile between older and younger adults**

Adverse Events: No dose-limiting Toxicities

- No maximally tolerated dose identified, majority of adverse events mild, all resolved without intervention
- No dose-response in frequency or severity of AEs
- With repeat daily dosing:
 - **Younger adults:** No difference in incidence of AEs between MF-300 and placebo
 - **Older adults:** Incidence of AEs with MF-300 < placebo
- Most common AE in both populations: Mild diarrhea which was transient (resolving w/in 1-2 days)

Laboratory /Vital Signs / ECGs: No clinically meaningful trends in labs, vital signs, or ECGs

- Fasting glucose remained stable
- No relevant changes in eGFR
- Some fluctuations in blood pressure and heart rate consistent with placebo
- No QTc prolongation or hemodynamic concerns

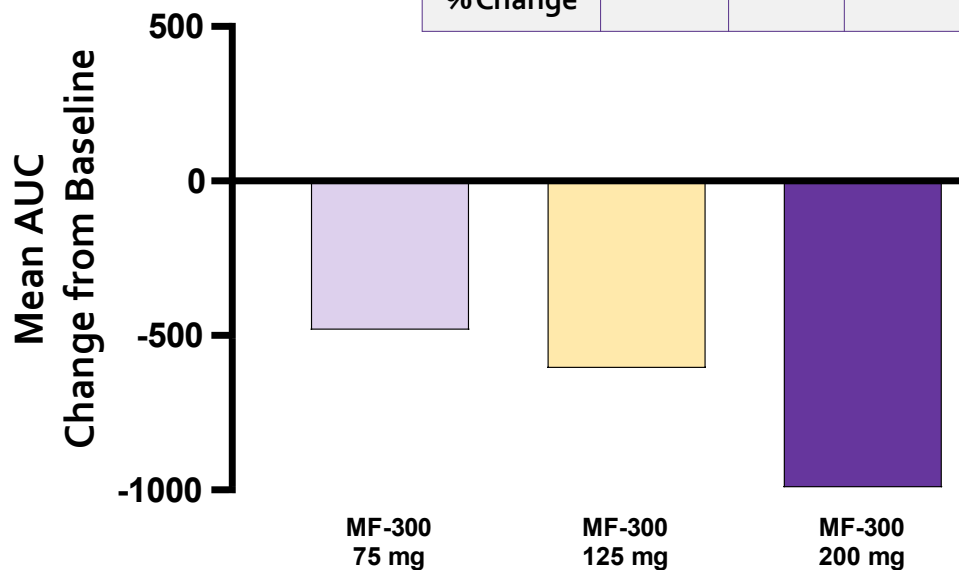
No additional monitoring required beyond standard Phase 2b assessment

Increased PGE₂ Levels with MF-300 Demonstrates Proof of Mechanism

- Targeted reductions in PGE-Major Urinary Metabolite (PGE-MUM) are consistent with those associated with ~20% improvement in muscle force in sarcopenia mice model
- Increases in urinary PGE₂ are consistent with those in muscle following eccentric exercise in humans

Placebo-adjusted PGE-MUM Change from Baseline (95% CI)

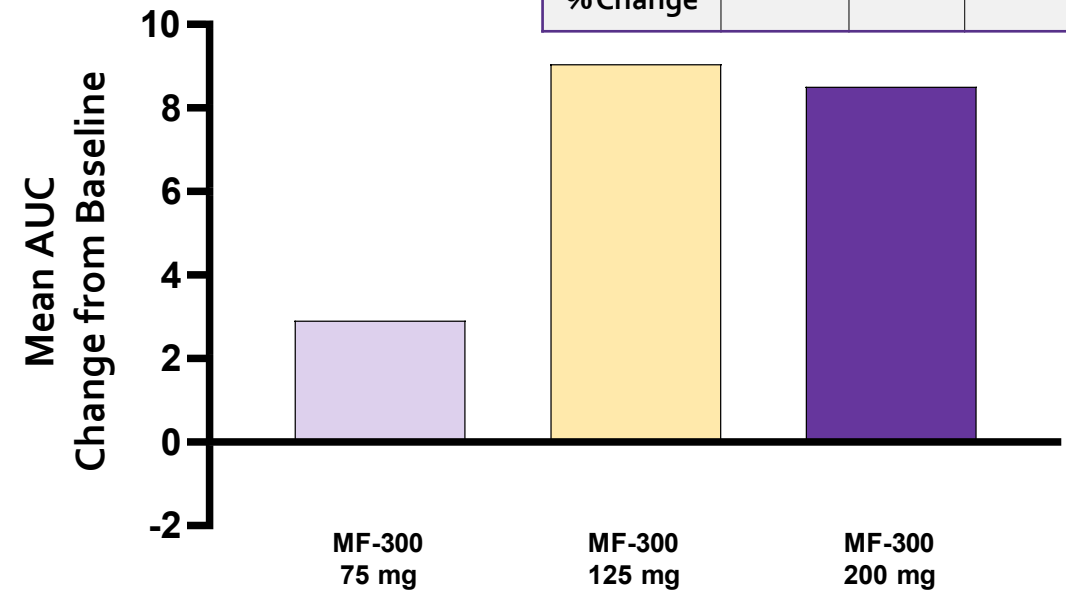
MF-300 (mg)	75	125	200
Placebo Adj. %Change	-64%	-64%	-83%*



*p<0.05 versus placebo (95% CI does not include 0)

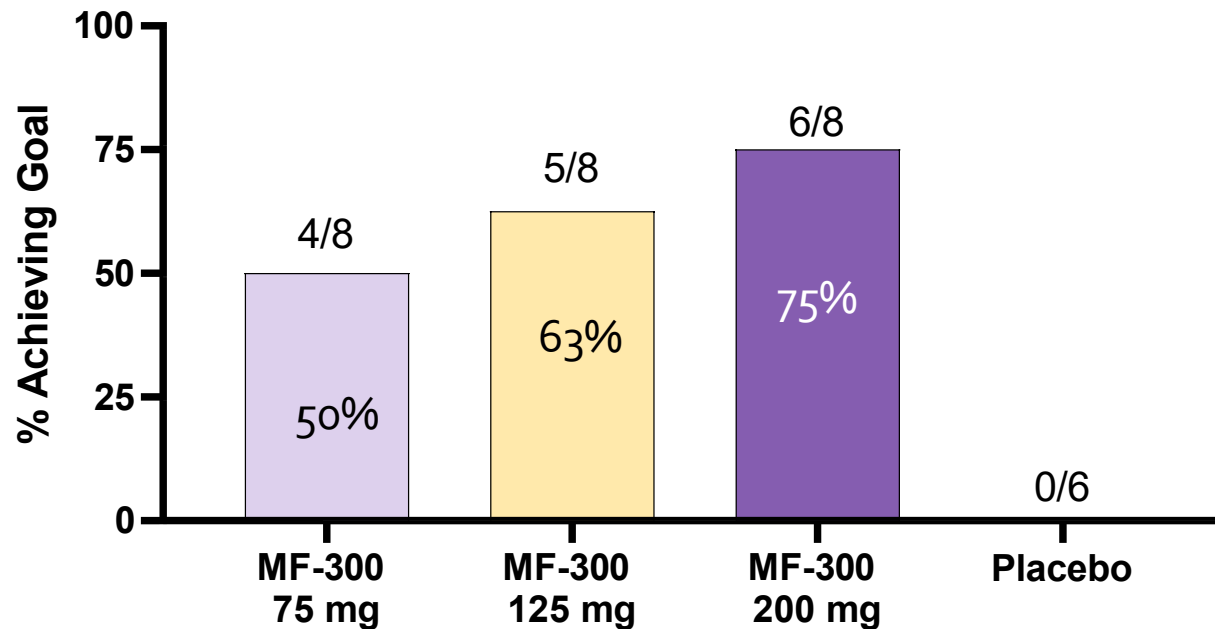
Placebo-adjusted PGE₂ Change from Baseline (95% CI)

MF-300 (mg)	75	125	200
Placebo Adj. %Change	+77%	+116%	+128%



Note: Two outlier subjects in the 75 mg group, with markedly greater PGE₂ responses due to low baseline values were excluded from analysis, including the two subjects = 614% increase in MF-300 75 mg dose group.

Proportion of Subjects Achieving Targeted % decrease in PGE-MUM & 60% Increase in PGE₂



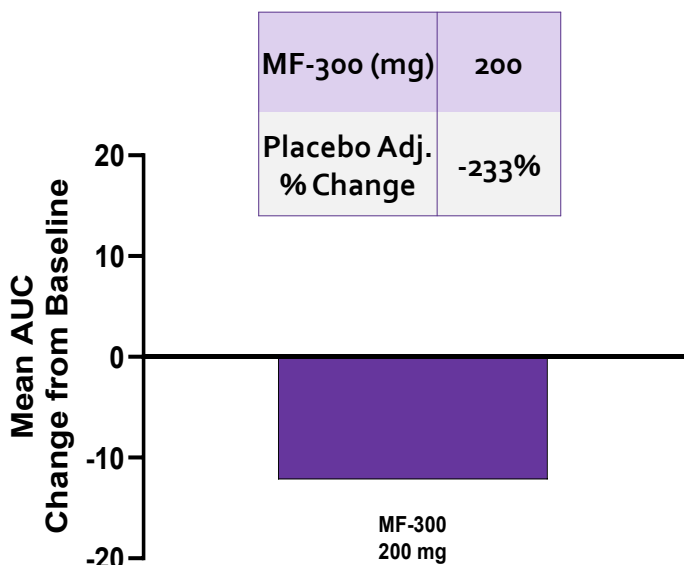
Rationale for targets:

- ~Targeted % reduction in PGE-MUM is associated with ~20% improvement in muscle force
- ~60% increase in muscle following eccentric exercise in humans¹

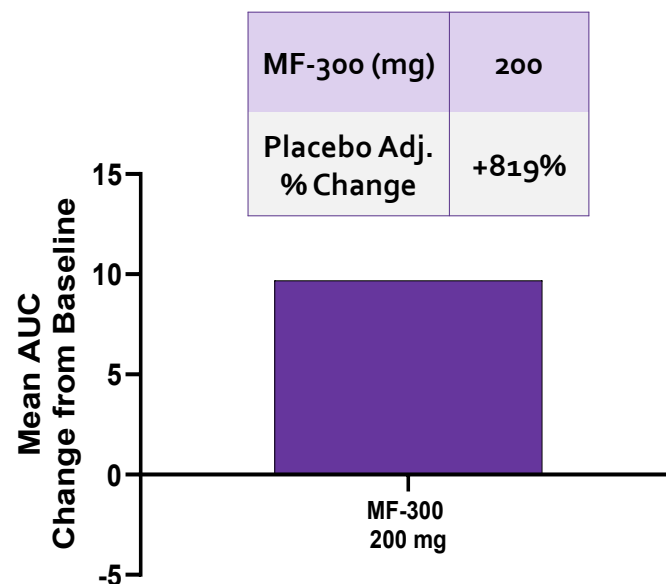
Subjects were counted only once with their maximum improvement at any timepoint (Day 1-5).

¹Trappe et al., *J Clin Endo Met* 2001

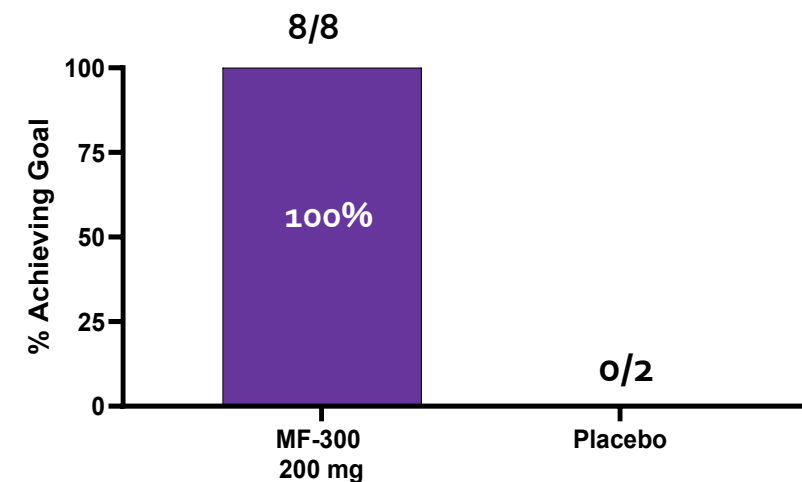
Placebo-adjusted PGE-MUM Change from Baseline



Placebo-adjusted PGE₂ Change from Baseline

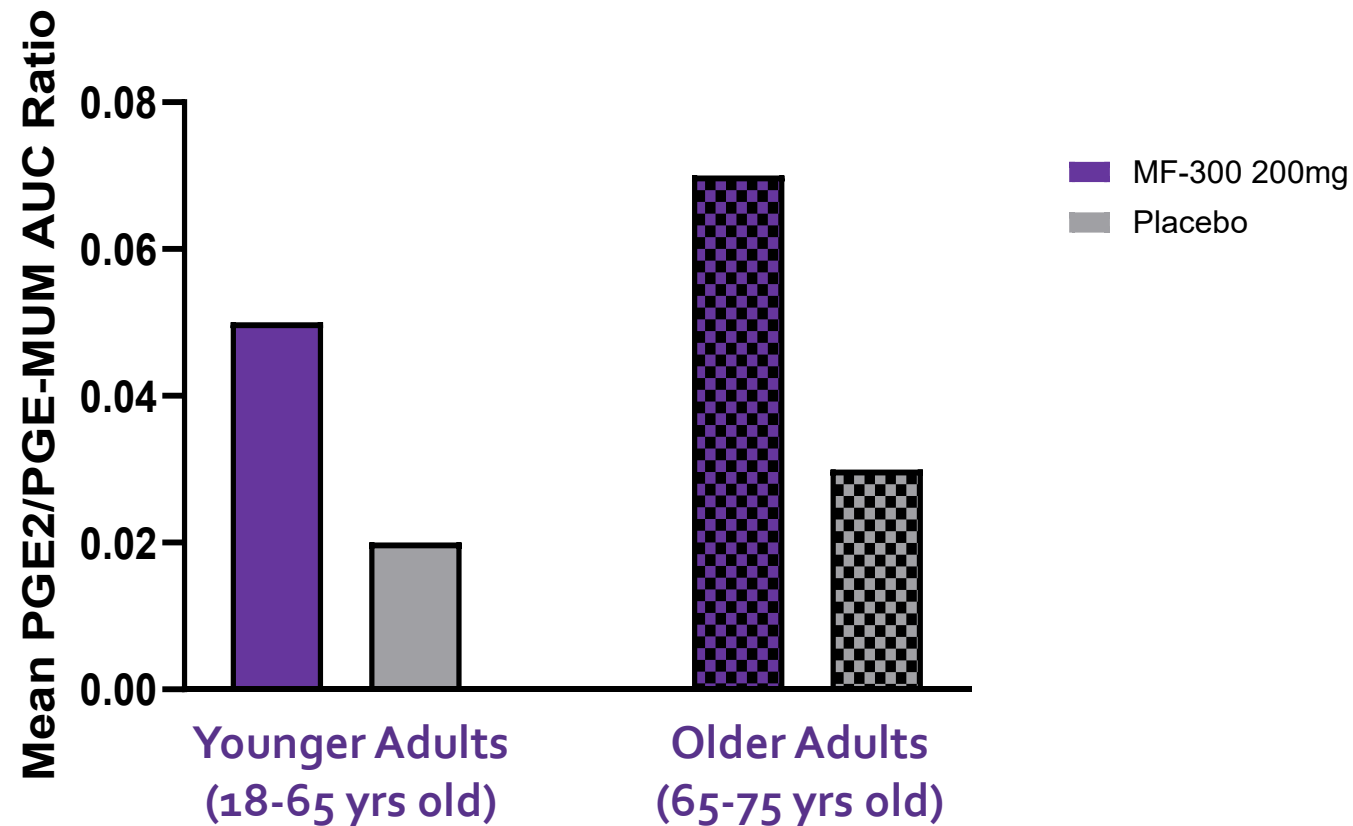


% Subjects with $\geq 50\%$ decrease in PGE-MUM & $\geq 60\%$ Increase in PGE₂

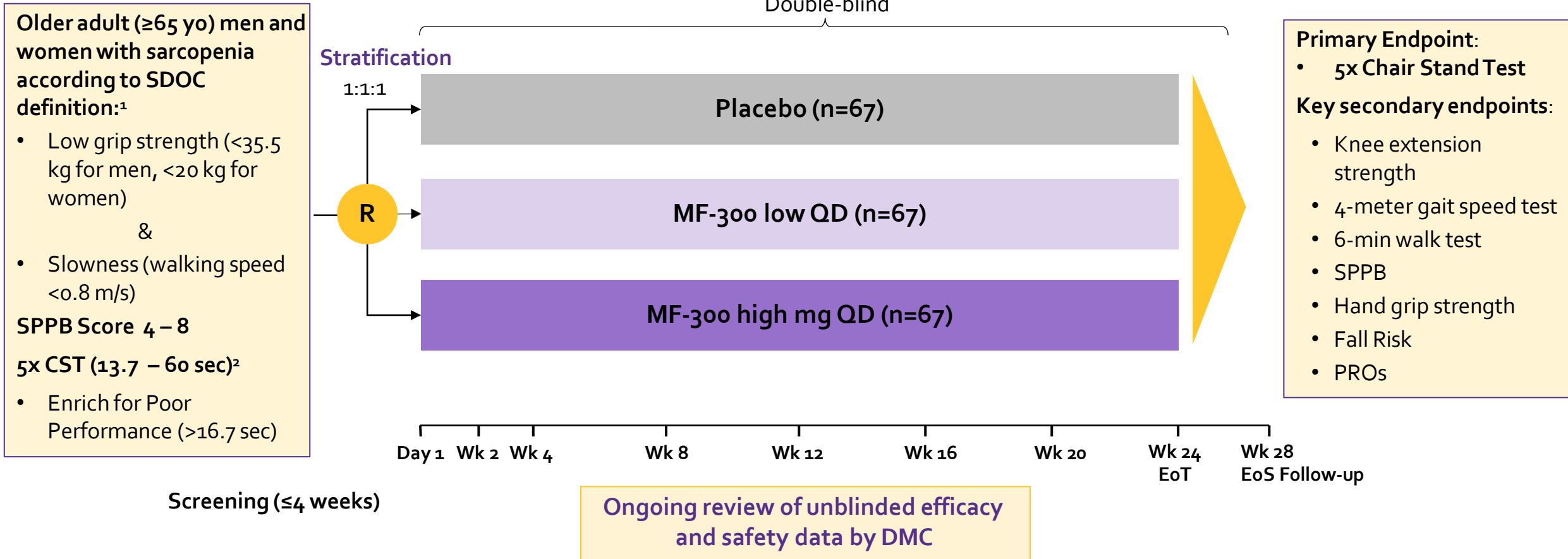


MF-300 Increases the Ratio of PGE₂/PGE-MUM Consistent with Reduced PGE₂ Catabolism in Both Age Groups

2-fold increase in PGE₂/PGE-MUM Ratio in both Age Groups— Consistent Functional Inhibition



Phase 2b: 24-week Randomized, Double-blind, Placebo-controlled Study (N=200)



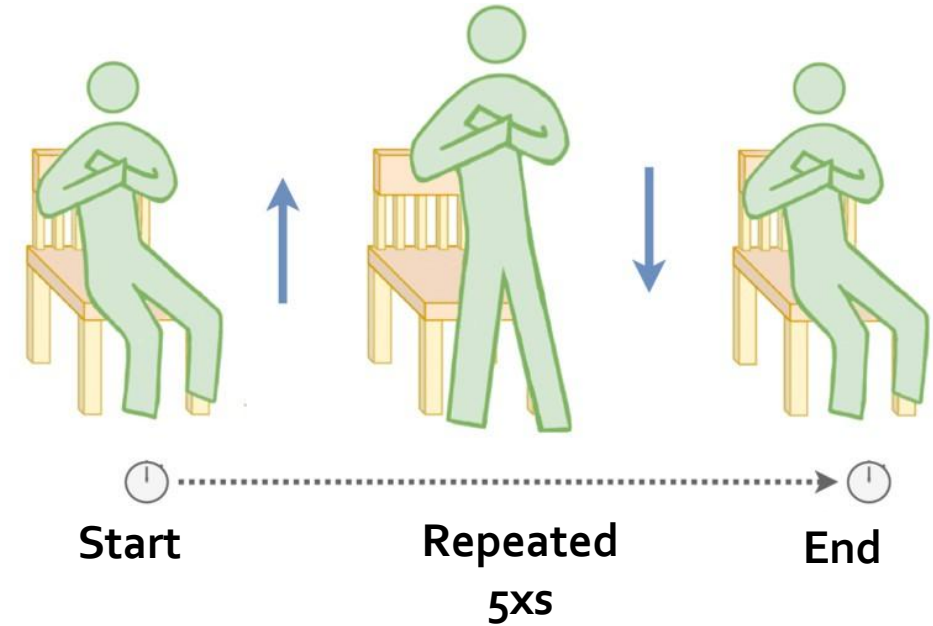
*The study provides ~80% power to detect a 15% difference between the active and placebo groups

DMC=Data Monitoring Committee; EoT=end of treatment; EoS=end of study; R=randomization; SDOC=Sarcopenia Definitions and Outcomes Consortium; SPPB=Short Physical Performance Battery; Wk=week; yo=years old

1. Bhasin S, et al. J Gerontol A Biol Sci Med Sci. 2023;78:S86–S93.

- **Accepted proxy measure of lower limb power and strength**
 - Endorsed by World Health Organization (WHO) ICOPE¹ & EWGSOP²
- **Strong predictor of clinical outcomes**
 - Activities of daily living
 - Fall Risk
 - All-Cause Mortality
- **Loss of 1 second (~10%) per year is accepted as clinically meaningful**
- **Aligns directly with MF-300's mechanism of action**, which targets fast-twitch muscle and primarily lower limb strength
- Limited variability and modifiable within 6 months

5xs Chair Stand Test

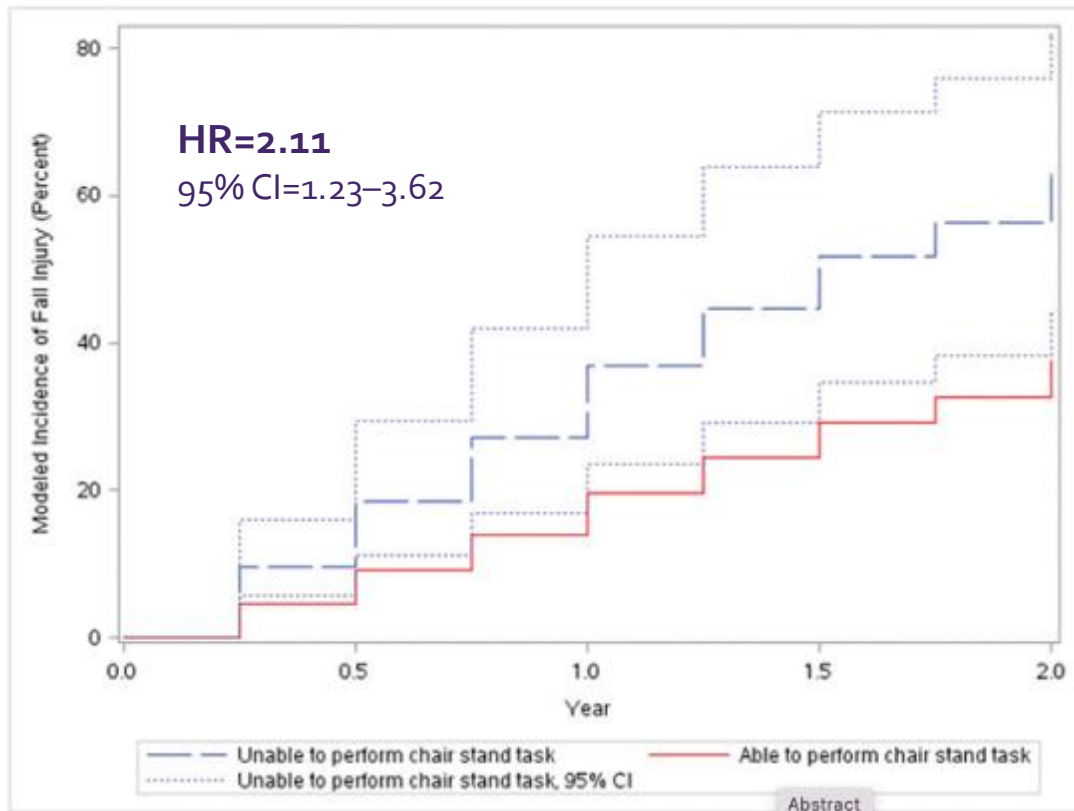


1. ICOPE=Integrated Care for Older People ([9789240103726-eng.pdf](https://www.who.int/publications/i/item/9789240103726-eng.pdf))

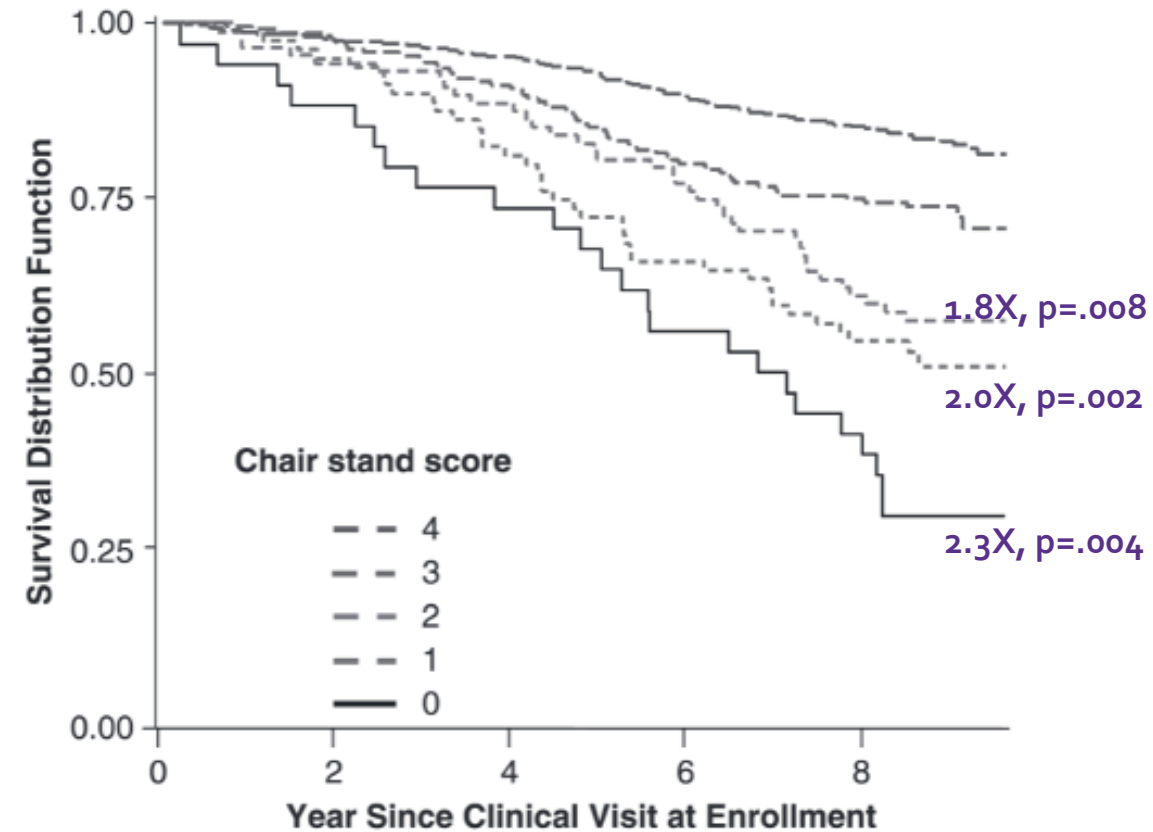
2. EWGSOP2=European Working Group on Sarcopenia in Older People 2 (CRUZ-JENTOFT AJ, et al. Age and Aging. 2019;48:16-31).

Rationale for 5x Chair Stand Test (CST): Strong Predictor of Fall Risk and All-cause Mortality

Cumulative incidence of fall-related injury by the ability to perform 5XCST¹



Survival curves during 9 years of follow-up by time to complete the 5X CST²



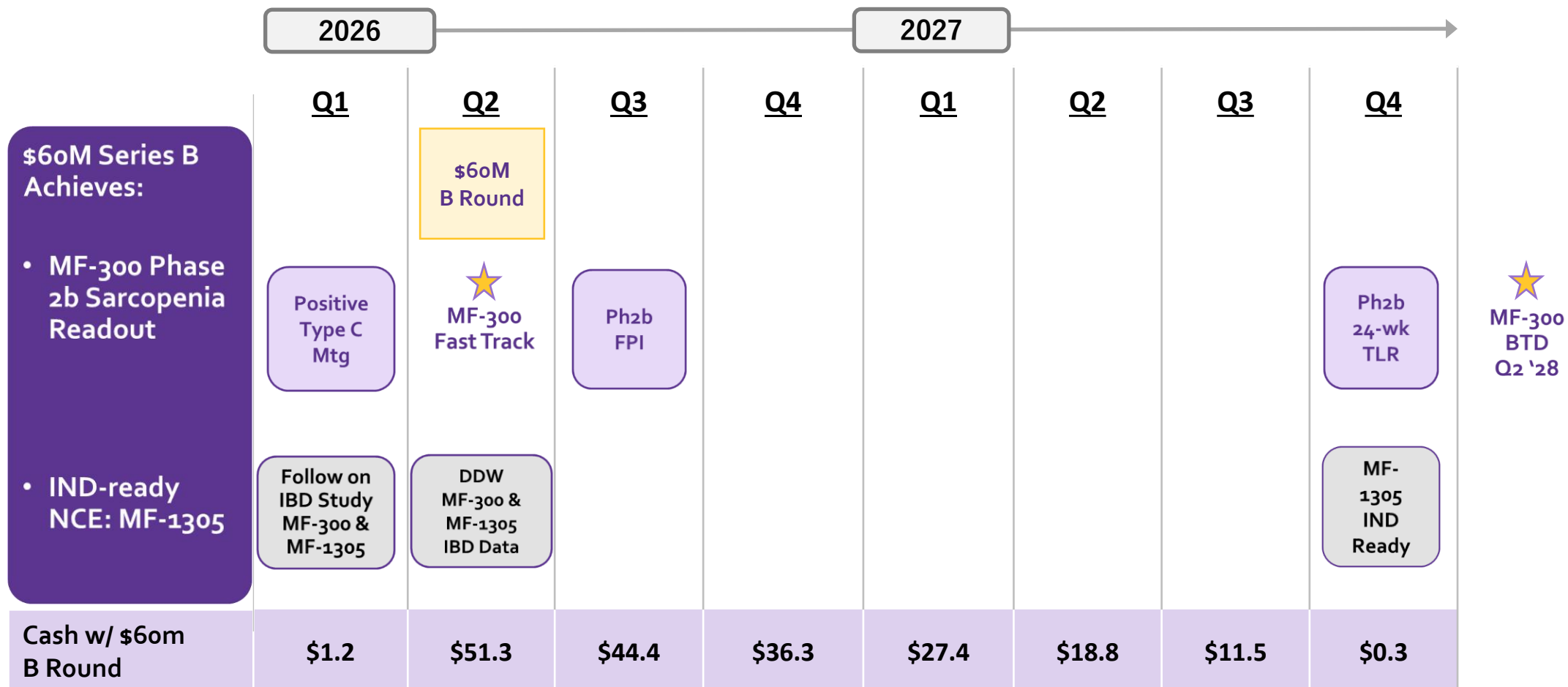
1. Shea et al.; Am J Phys Med Rehabil. 2018; 97(6): 426-432
2. Bandinelli et al., J Am Geriatr Soc. 2009; 57(11): 2172-2173

Key Outcomes

- The FDA's written feedback was overall positive and constructive
- Reached concurrence with FDA on the patient population, primary and secondary efficacy endpoints, treatment duration and dosing regimen of MF-300
- Agreement that the efficacy endpoints evaluated in the Phase 2b study will inform Phase 3 endpoint selection
- Agreement that a Fast Track Designation request may be submitted for MF-300 as a treatment for sarcopenia.

"In the absence of approved pharmacologic therapies or established regulatory pathways for sarcopenia, alignment with the FDA on a Phase 2b trial design represents an important milestone for the field," said Dr. Jose Garcia, M.D., Ph.D., Professor, Department of Medicine, Division of Gerontology and Geriatric Medicine, University of Washington School of Medicine.

Series B Funded Milestones: MF-300 Phase 2b Data Readout & IND Ready NCE

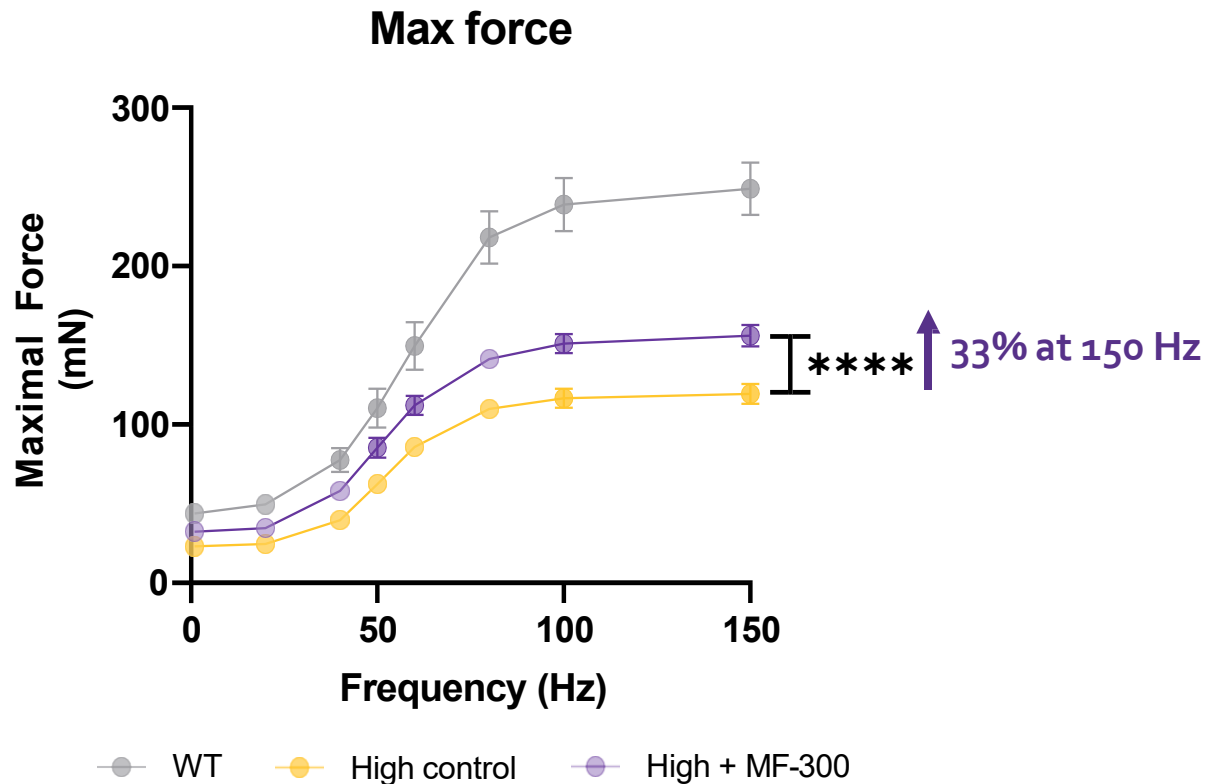


Additional \$30M (\$90M raise) enables Phase 3 CMC commencement bringing forward MF-300 Commercial Launch 6 months to 1H 2032

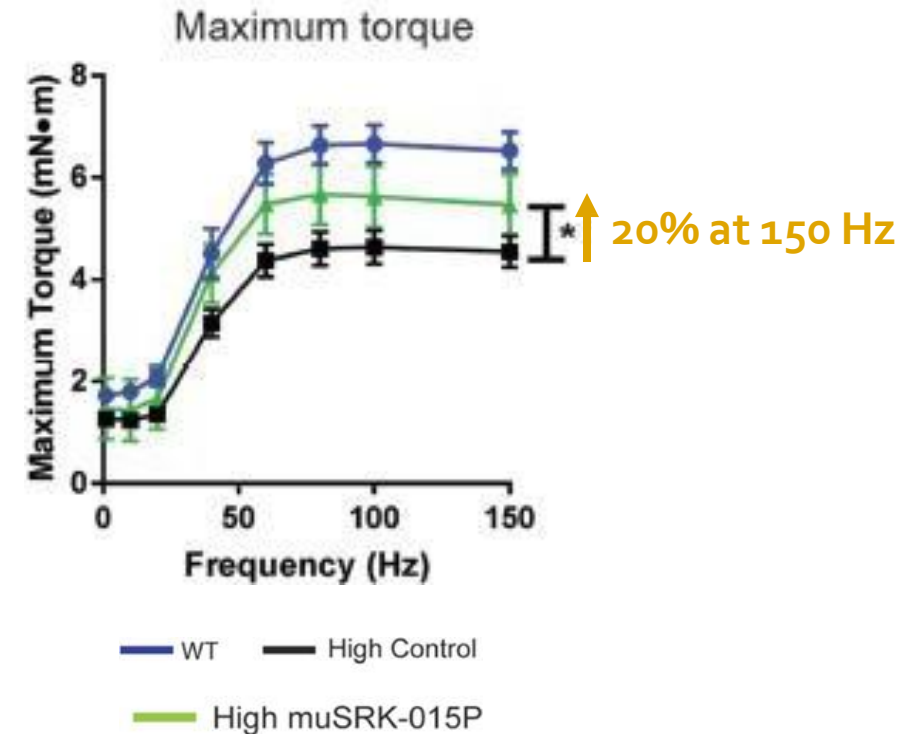
Back-up Section

- MF-300 force improvement comparison to apitegromab in Translational Delta7 SMA Mouse Model
- Epirium's Sarcopenia Development Council

MF-300 in SMN Δ 7 High/High Male mice



mSRK-015P in mouse Δ 7 High/High Male and female mice

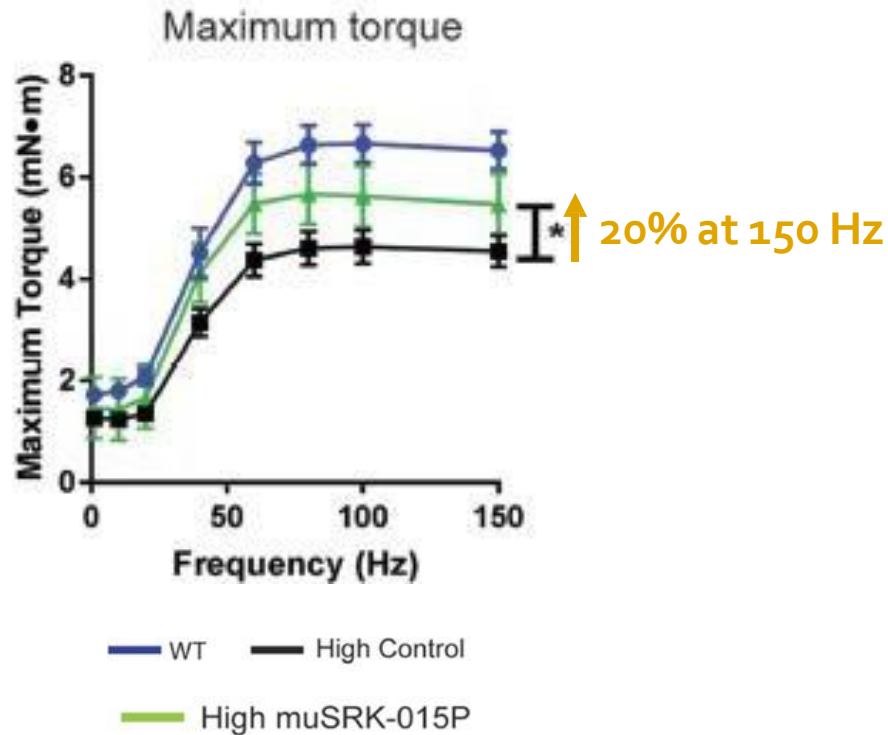


Force = Torque

MYOLOGICA

Demonstrates that a 20% increase in isometric plantar flexor force in mice translates to clinical benefit

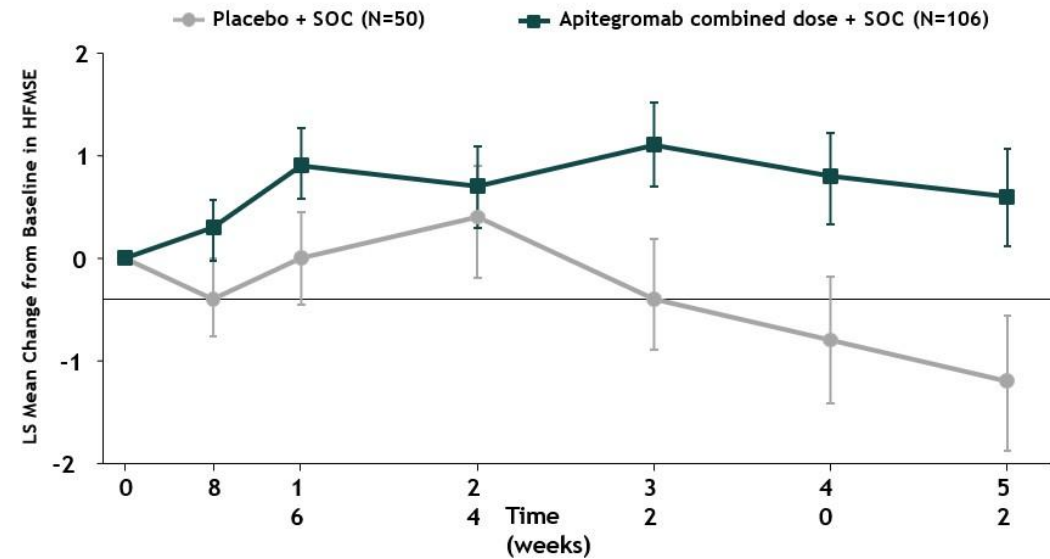
mSRK-015P in mouse $\Delta 7$ High/High



Long et al., *Hum Mol Gen*, 2016

Apitegromab in SMA + SOC (Ph 3 SAPPHERE)

Least Squares Mean (+/- SE) Change from Baseline in HFMS Total Score by Visit (MITT Set)



Change from Baseline in HFMS Total Score

Analysis	n	Results (vs Placebo, n=50)	Unadjusted P-value
Apitegromab 10+20 mg/kg combined	106	1.8	0.0192*
Apitegromab 20 mg/kg	53	1.4	0.1149*
Apitegromab 10 mg/kg	53	2.2	0.0121**

Primary Analysis

Achieved Statistical Significance

Epirium Sarcopenia Clinical Development Advisors



David Cella, PhD

Director, Institute for Public Health and Medicine (IPHAM)

Northwestern University
International leader in PRO;

Key leader in the development of PROMIS® ;

FDA advisor on Care Outcome Set.



Scott Delp, PhD

Founding Chairman of the Department of Bioengineering at Stanford

Stanford, Wu Tsai Center Biomedical Engineering

Stanford engineer pioneering biomechanics, muscle performance, and wearable monitoring technologies.



Jerome Feige, PhD

Adult Health Science Lead & Senior Expert in Musculoskeletal Health

Led drug discovery for muscle diseases at Novartis, contributing to development of new therapies.

Built muscle biology and translational programs leading to commercialization of several products and start-ups.



Roger Fielding, PhD

Co-Director, Boston NIA Center
Tufts University

Researcher studying the underlying mechanisms contributing to the age-associated decline in skeletal muscle mass. Published landmark studies in sarcopenia, frailty and muscle function. Conducted numerous studies examining the roll of skeletal muscle power on physical performance in older adults.



Jose M. Garcia, MD, PhD

Physician-Scientist at the Puget Sound VA Health Care System

University of Washington, Seattle

Directing the Clinical Research Unit and the GRECC. Expert in wasting disorders, leading basic and clinical research on ghrelin, androgens, and other anabolic pathways.



Jack Guralnik, MD, PhD

Professor, Epidemiology & Public Health

U of Maryland, Medical School

Developed the SPPB, a gold-standard functional outcome; expert in disability and mobility trials.



George Kuchel, MD

Professor of Medicine, Travelers Chair in Geriatrics and Gerontology, and Director of the UConn Center on Aging and Pepper Center

University of Connecticut

Researcher studying functional decline, mobility, and cognition, in older adults, with a mission of precision gerontology to tailor interventions to individual variability.



Nathan K. LeBrasseur, PhD

Director, Robert & Arlene Kogod Center on Aging

Mayo Clinic

Noaber Foundation Professor of Aging Research

Department of Physical Medicine & Rehabilitation

Department of Physiology & Biomedical Engineering



Se-Jin Lee, MD, PhD

Presidential Distinguished Professor

University of Connecticut School of Medicine

Professor, The Jackson Laboratory.

Studying the mechanism of action of myostatin and how its activity is regulated.



Naomi Lowy, MD

Principal Drug Regulatory Expert

Hyman Phelps

Fmr. FDA, Deputy Dir. Endocrinology Division

At FDA, provided leadership in drug policy and drug development in sarcopenia.