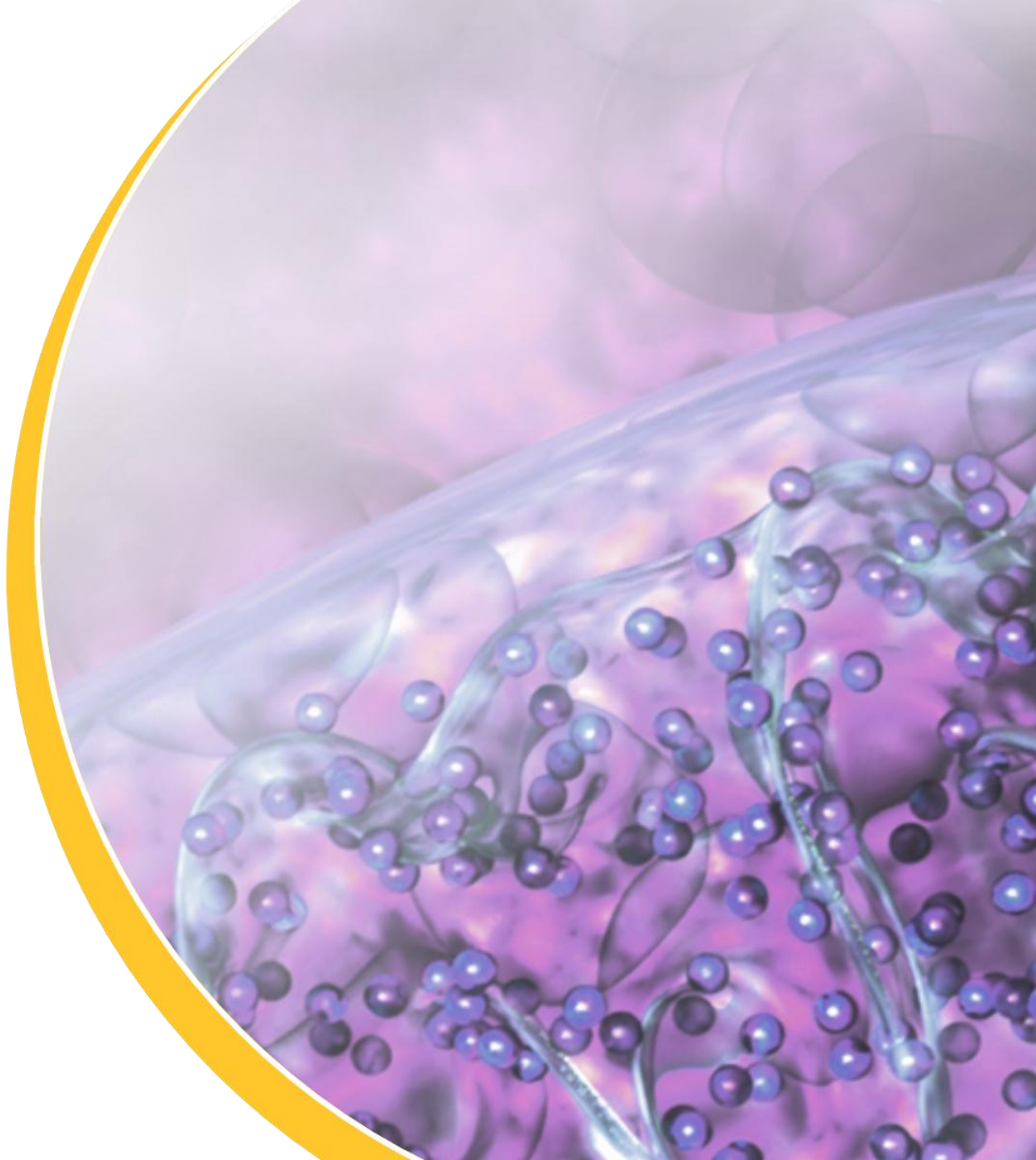
Epirium Bio

Oral 15-PGDH Inhibitor Platform:

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

- **MF-300 in Phase 2b Start-up for 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)

Leigh MacConell, Ph.D. Chief Development Officer

25 years drug development, primarily in metabolic and liver disease

Led multiple drug approvals including first in class forT2DM (GLP-1) and primary biliary cholangitis (PBC)

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

Eric Miller, CFO

Head Finance, Synthorx (acquired by Sanofi)

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

Cadence Pharm. (acquired by Mallinckrodt)

Consultant Advisors

Daniel Cooper, M.D. Medical Lead

Over 20 years in drug development

Formerly VP Pharmacovigilance Orexigen, Affymax; Clinical and Safety Scientist roles at Roche, Johnson & Johnson

Multiple successful NDAs supporting pre- and post-marketing approvals

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

Pipeline in a Mechanism: Unifying Biology Addressing Blockbuster Markets

Epirium Bio

Inhibiting 15-PGDH to leverage the potential of PGE_2 to promote tissue function

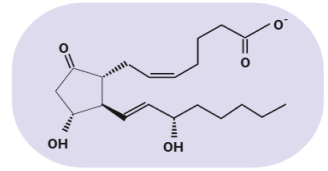
Imbalance Associated with Inflammation and disease

Oral Small Molecule Inhibitors

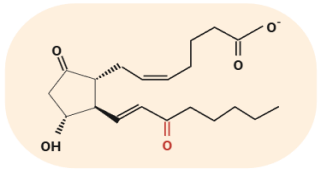
MF-300
MF-1305

15-PGDH

PGE2

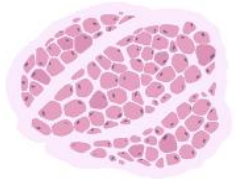
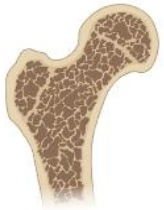
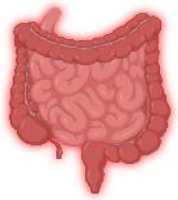
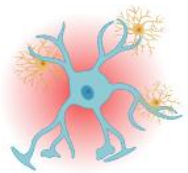
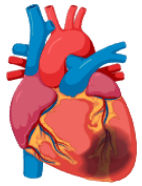


PGE2 Metabolite (Inactive)



EP2, EP4

15-PGDH inhibition resolves aberrant inflammation, promoting tissue repair

Musculoskeletal	Inflammatory & Fibrotic			Cardiovascular
					
✓ **Sarcopenia** Sarcopenic Obesity ✓ **Rare Neuromuscular**	✓ **Osteoporosis** OA/cartilage	✓ **Ulcerative Colitis** Crohn's Disease	✓ **IPF**	Neuro-Inflammation	Heart Failure

✓ = **POC Achieved**

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

Epirium Bio

Therapeutic Area		15-PGDH INHIBITOR (Oral)	PRECLINICAL / IND ENABLING / PHASE 1 / PHASE 2
Musculoskeletal	**Sarcopenia** *Potential label expansion: Sarcopenic obesity*	MF-300	Phase 2b in start-up
Musculoskeletal	**Osteoporosis***	MF-300	Phase 2 ready
Musculoskeletal	**Spinal Muscular Atrophy**	MF-300	Phase 2 ready
Inflammatory / Fibrotic	**IBD**	MF-300	Phase 2 ready
		MF-1305	Preclinical Efficacy
Inflammatory / Fibrotic	**Idiopathic Pulmonary Fibrosis**	MF-300	Preclinical Efficacy

Key Milestones – Sarcopenia

- ✓ Phase 1 completed Q4 '25
- ✓ Positive End-of-Phase 1 Type C Meeting Q1 '26
- **FDA Fast Track** Q2 '26
- **Phase 2b FPI** 2H '26
- **Phase 2b TLR** H2 '27

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

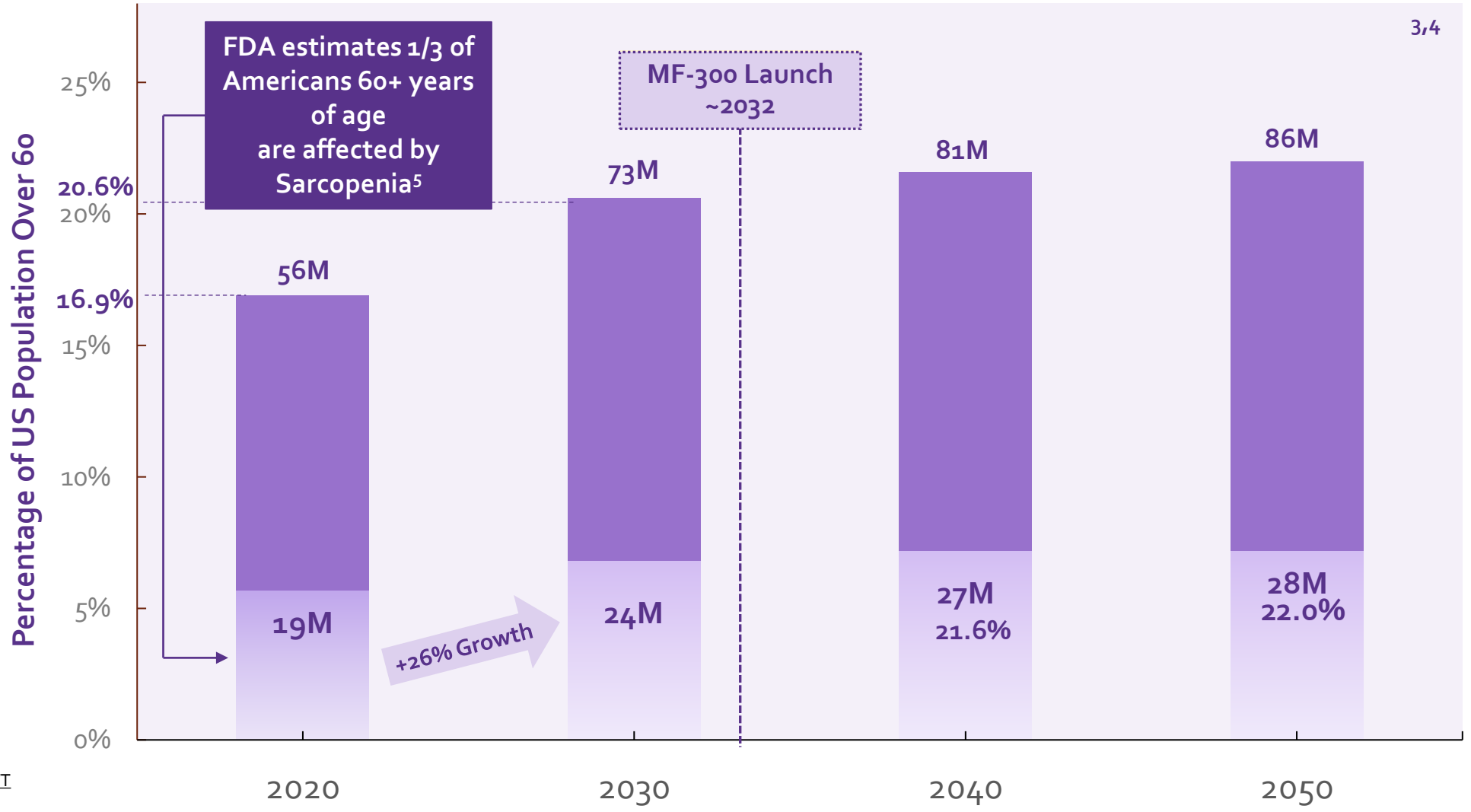
Sarcopenia: Large and Growing Unmet Medical Need w/ No FDA Approved Therapy

Current U.S. Healthcare Sarcopenia Spending Estimated >$40 Billion Annually[1]

Dependence
Increased risk losing independence

Falls
Increased fracture risk & hospitalization, >2-fold greater cost[2]

Mortality
2-fold Increased risk of death[2]



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%20fda/published/The-Voice-of-the-Patient--Sarcopenia.pdf

PGE2–EP4 Signaling Elevates cAMP to Promote Muscle Function

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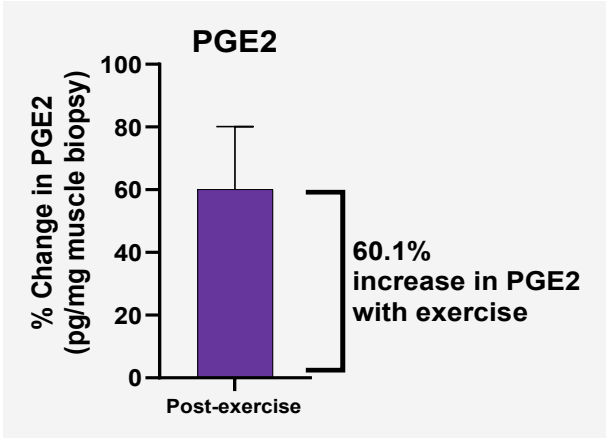
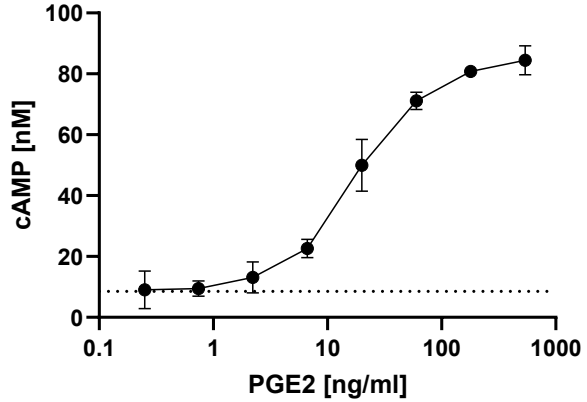
PGE2 in human muscle following exercise

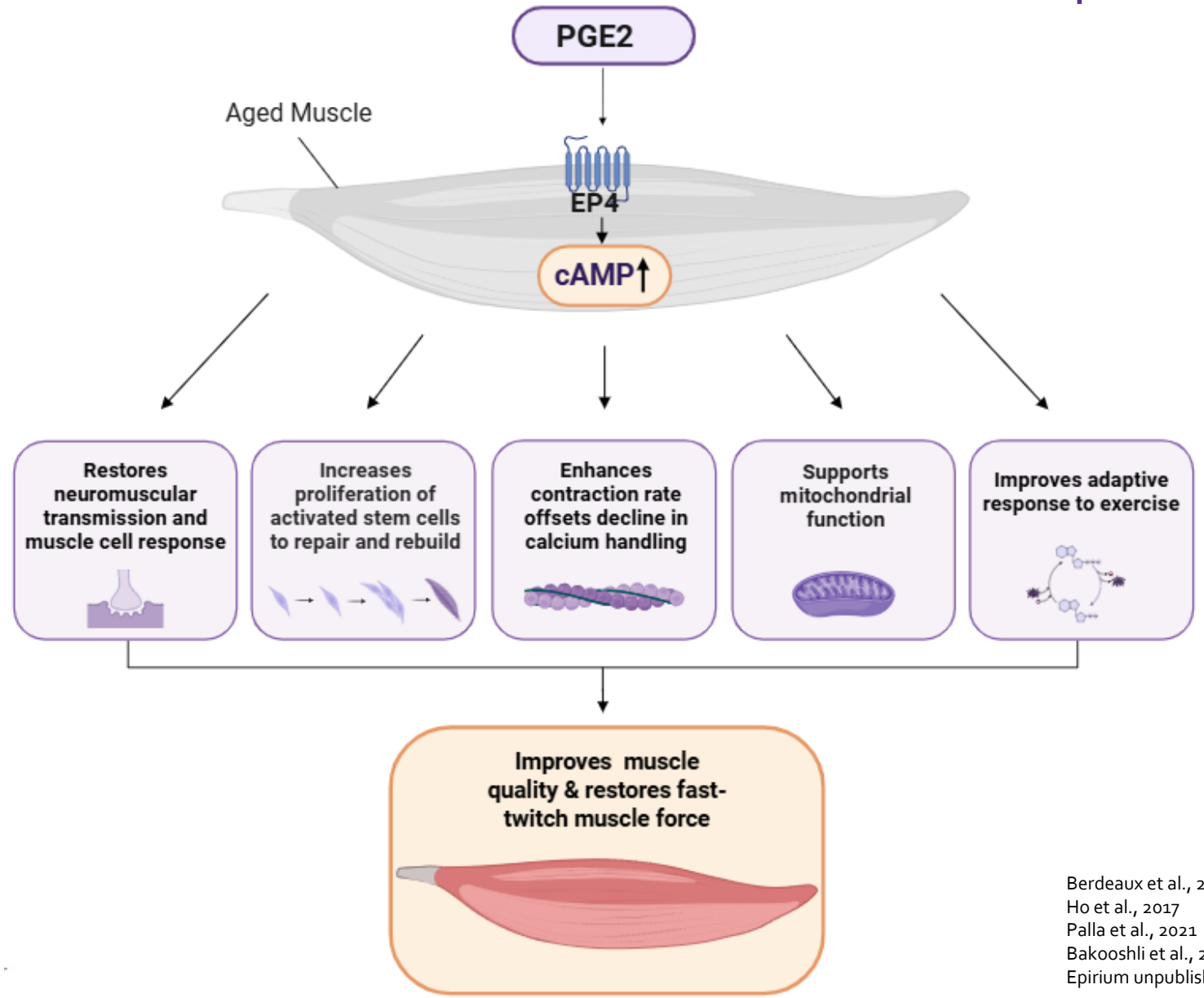


Adapted from Trappe TA, et al. J Clin Endocrinol Metab. 2001;86(10):5067-5070

PGE2 increases cAMP in primary human myocytes



Epirium unpublished data



Berdeaux et al., 2012
Ho et al., 2017
Palla et al., 2021
Bakooshli et al., 2023
Epirium unpublished data

15-PGDH, an Enzyme that Degrades PGE2, is Upregulated in Aged Muscle

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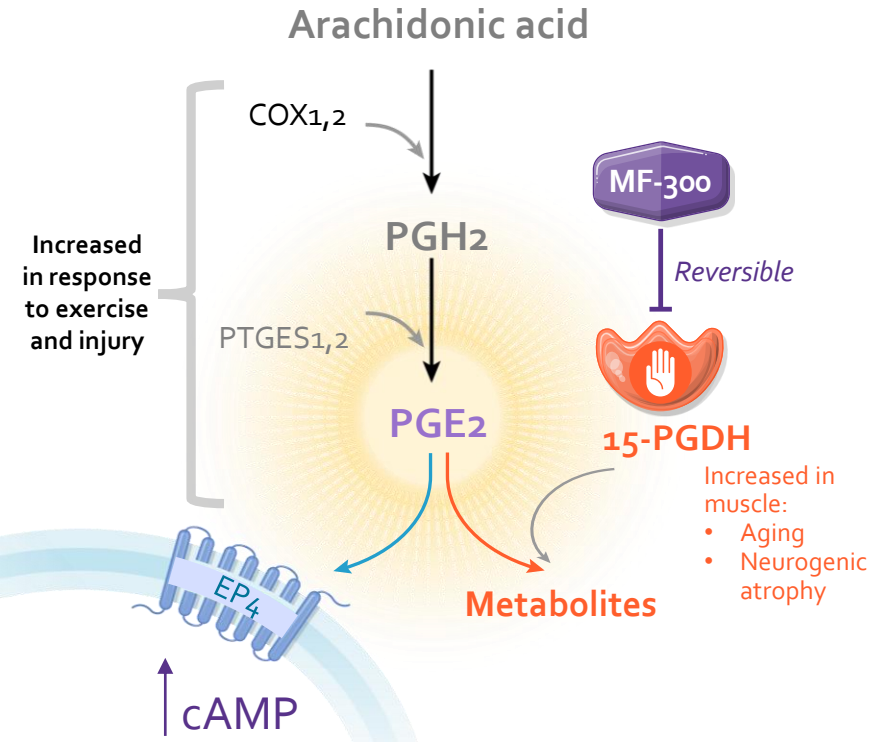
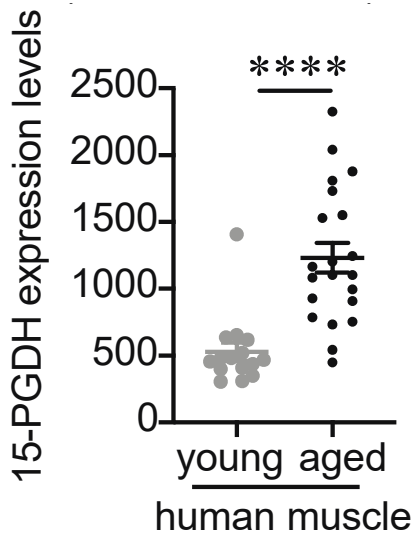
15-Hydroxyprostaglandin Dehydrogenase (15-PGDH) Reduces levels of PGE2

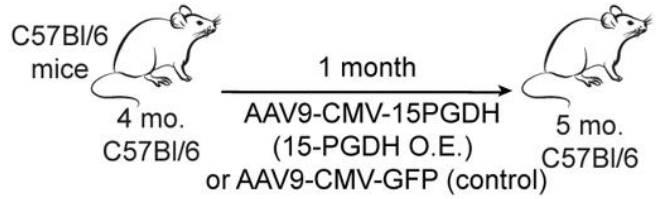


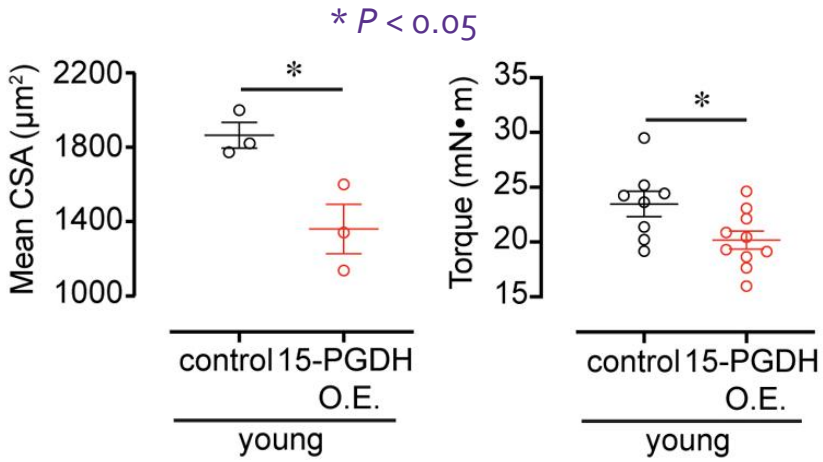
15-PGDH expression Elevated in aged human muscle[1]



- Vastus lateralis (microarray)
- Younger, N=15 (**25±3 y.o.**)
- Older, N=21 (**78±6 y.o.**)
- **** $P < 0.0001$

15-PGDH overexpression (O.E.) Reduces myofiber cross-sectional area (CSA) and muscle force[2]





cAMP, cyclic adenosine monophosphate; COX1,2, cyclooxygenase enzymes 1 and 2; PGE2, prostaglandin E2; PGH2, prostaglandin H2; PTGES1, 2, prostaglandin E synthase 1,2; y.o., years old

[1] Raue et al., *J Appl Physiol* 2012 (published in Palla et al., *Science* 2021), [2] Palla et al., *Science 2021*

Improving Muscle Quality (Intrinsic Strength) Addresses High Unmet Need in Sarcopenia

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Sarcopenia pathology		MF-300 therapeutic effects	
Age-related ↓ muscle-specific force	→	↑ specific force in aged muscle	✓
Fast-twitch muscle disproportionally lost → ↓ muscle power	→	↑ fast twitch muscle contractility	✓
Age-related deficits in protein synthesis and proteostasis	→	↑ ribosomes ↓ DNA damage response proteins ↓ muscle structural proteins	✓
Neuromuscular junction degradation	→	↑ post-synaptic scaffold proteins ↑ pre-synaptic transmission proteins	✓
Age-related expansion of cortical bone and porosity → frailty and falls	→	Slows age-related expansion of cortical bone and porosity	✓

↑ urinary PGE_2 levels and ↓ PGE-MUM demonstrates target engagement and use as translational biomarkers

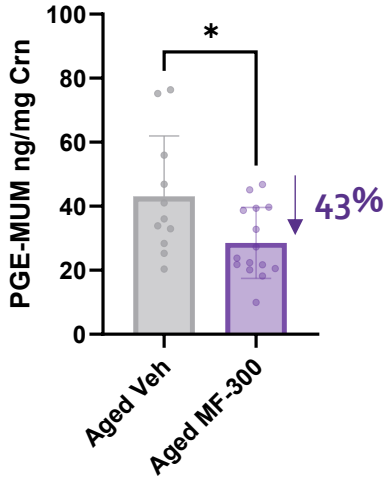
PGE_2, prostaglandin E_2; PGE-MUM, prostaglandin E major urinary metabolite

MF-300 Increases Muscle Force with Correlated Reductions in PD Biomarker

Preclinical Sarcopenia Studies

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

Study 1

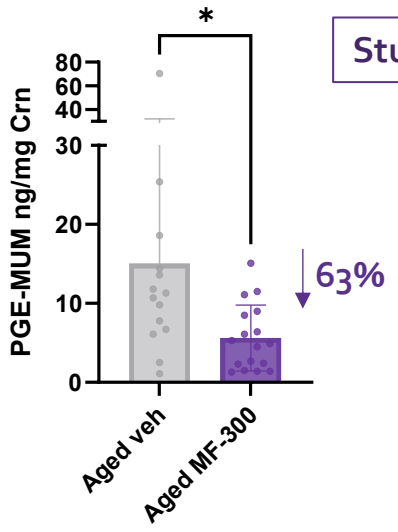


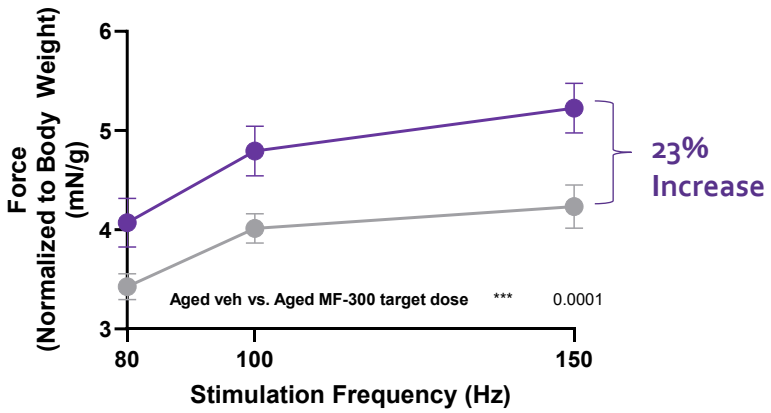
Vehicle
MF-300 target dose mg/kg

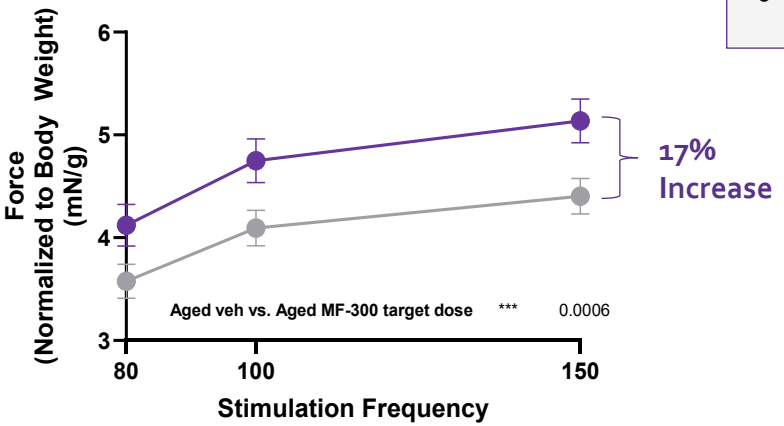
PGE-MUM
↓ ~50% average

Force
↑ ~20% average

Study 2







Target Engagement Biomarker

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

MF-300 Increased Many of the Ribosomal Proteins Reduced in Aging Skeletal Muscle

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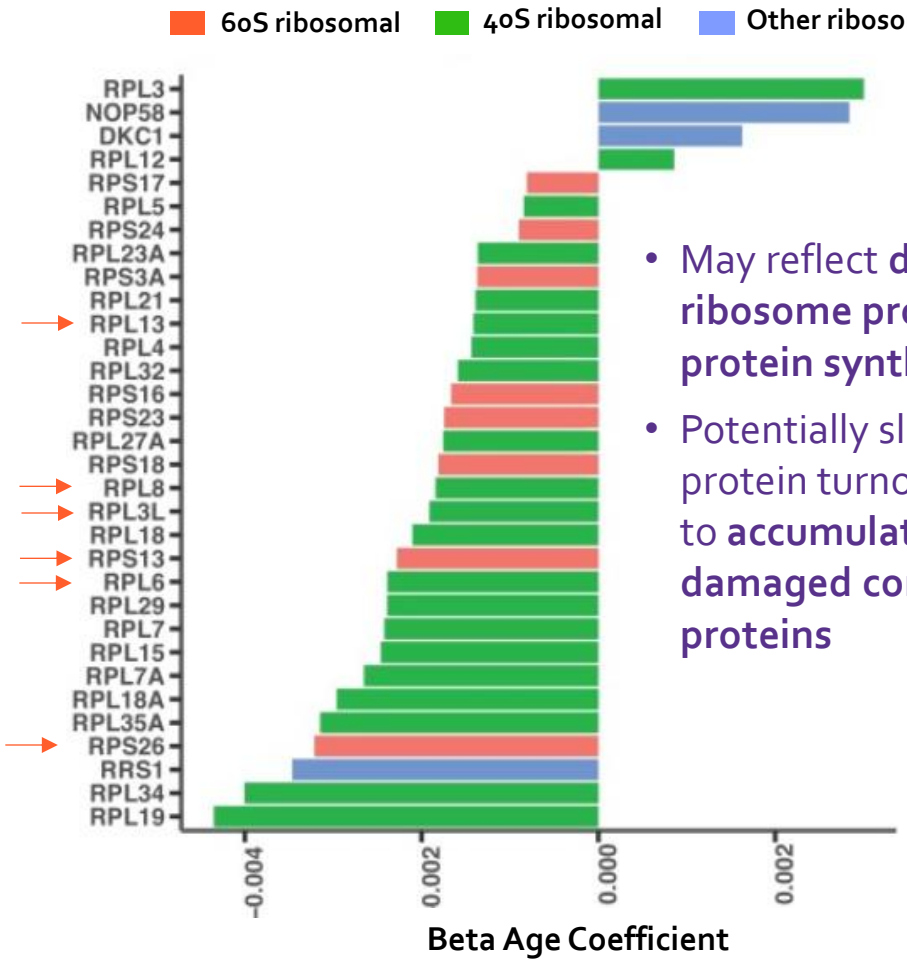
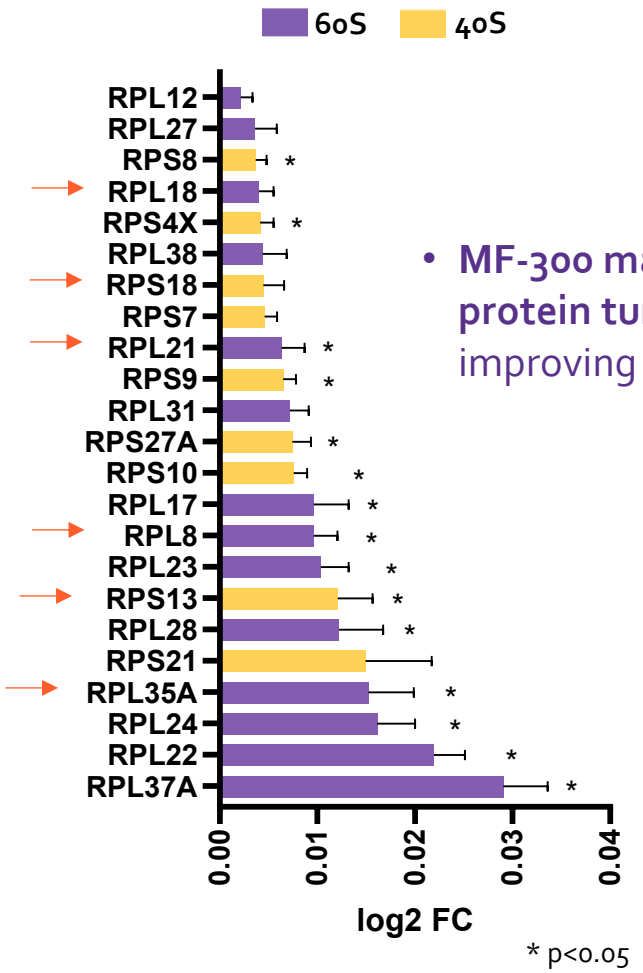
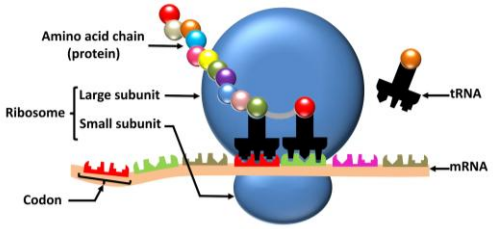
Reduced ribosomal protein abundance in muscle correlates with aging in human



- May reflect **decreased ribosome production and protein synthesis**
- Potentially slowing protein turnover, leading to **accumulation of damaged contractile proteins**

MF-300 increased abundance of large and small ribosomal proteins





- **MF-300 may increase protein turnover rate,** improving muscle quality

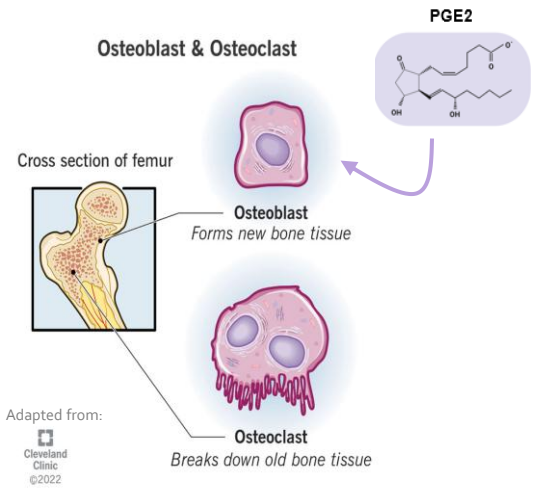
Ubaida-Mohien et al., *eLife*, 2019

Proteomic analysis by Tandem Mass Tagging of Gastrocnemius Muscle

MF-300 Delays Age-Related Alterations in Bone Micro-Architecture

- Cortical bone increases in perimeter and develops pores with aging in rodents and humans
- More porous cortical bone is strongly linked to hip and wrist fractures, vertebral fragility
- PGE2 supports bone remodeling by balancing bone formation and resorption

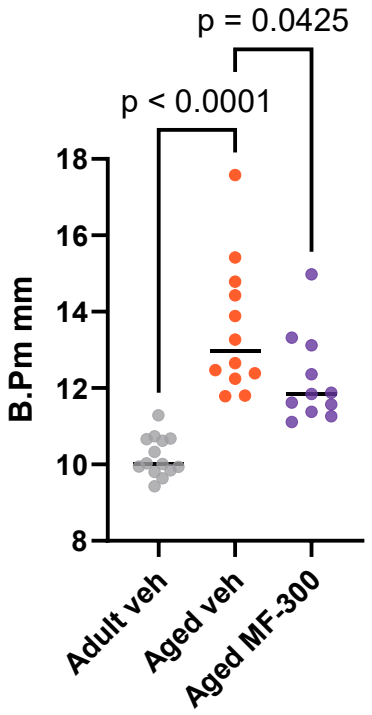
PGE2 can Promote Osteoblast Activity



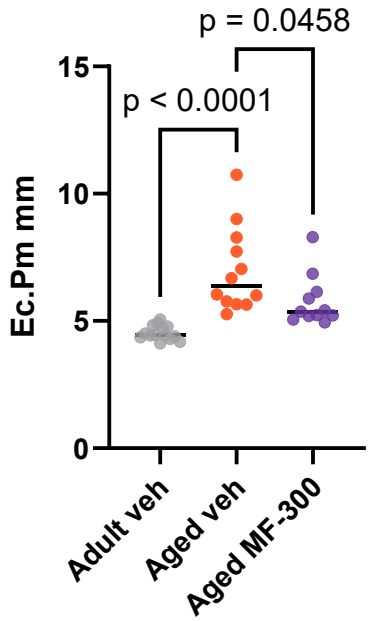
Mouse cortical bone

Micro-Computed Tomography (µCT)

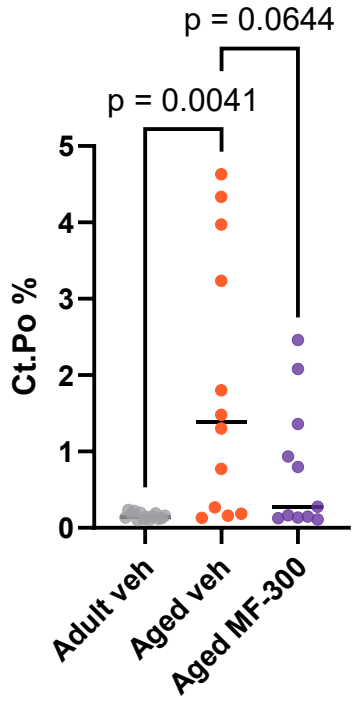
Bone Perimeter



Endocortical Perimeter

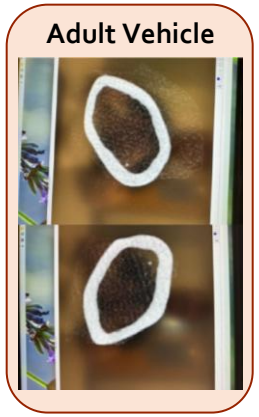


Porosity



12 weeks MF-300 Oral Administration

Cortical porosity by µCT



Data generated by: Myologica

Phase 1 Clinical Study: Evaluating the Safety, Pharmacokinetics and Pharmacodynamics of MF-300 in Younger and Older Adults

Design: Double-blind, randomized, placebo-controlled

Objectives:

- Assess safety and tolerability of MF-300
- Characterize MF-300 pharmacokinetics and pharmacodynamics (PGE2, PGE-MUM)

Populations:

- Younger adults ≥ 18 - ≤ 65 years; Healthy volunteers
- Older adults >65 - ≤75 years; Controlled chronic conditions and stable concomitant medications permitted

Single Ascending and Multiple Ascending Dose Cohorts:

- Single Ascending Dose (SAD): 5 dose levels (75–800 mg), older adults received 125 mg
- Multiple Ascending Dose (MAD): 3 dose levels (75, 125, 200 mg) administered once daily (QD) for 5 days, older adults received 200 mg

Part 1a SAD	Part 2 MAD
• 5 younger adult cohorts, 1 older adult cohort • N=8 per cohort (2 pbo, 6 MF-300) • Single dose • Doses: 75, 125, 250, 500, & 800mg	• 3 younger adult cohorts, 1 older adult cohort • N=10 per cohort (2 pbo, 8 MF-300) • QD dosing for 5 days • Doses: 75mg, 125mg, 200mg

[1] Older adults received MF-300 125mg in the SAD phase and MF-300 200mg in the MAD phase.

Phase 1 Clinical Success Criteria to Enable Phase 2b

Epirium Bio

- All predefined Phase 1 success criteria across Safety, PK, and PD were achieved
- Comparable clinical profile between younger and older adults
- Study results enable 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

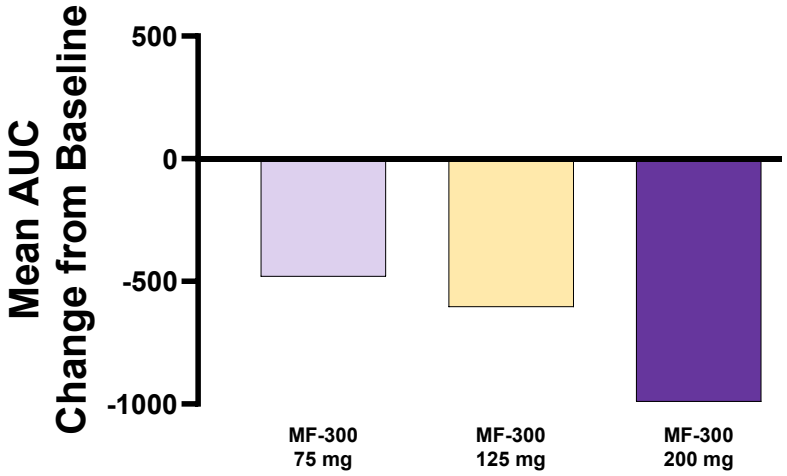
- ✓ Evidence of target engagement (15-PGDH) w/ substantial reductions in PGE_2 metabolites
- ✓ Proof of mechanism: Clear evidence of mechanism with dose-related increases in PGE2 levels
- ✓ Clear dose-response relationship defining therapeutic range, supportive of Phase 2b dose selection

Biomarker Data Provides Proof of Mechanism for MF-300 in Younger Adults

- PGE-MUM Reductions Consistent with ~20% improvement in muscle force in sarcopenia mouse model
- PGE2 Increases consistent with that following eccentric exercise in humans (~60%)

Placebo-adjusted PGE-MUM Change from Baseline

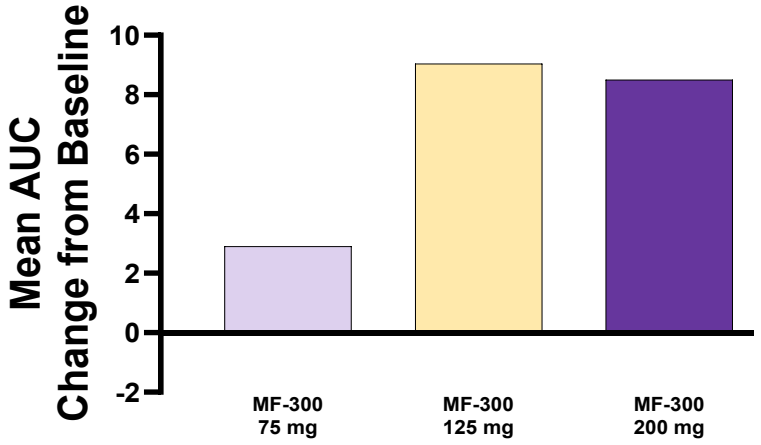
MF-300 (mg)	75	125	200
Placebo Adj. % Change	-64%	-64%	-83%*



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

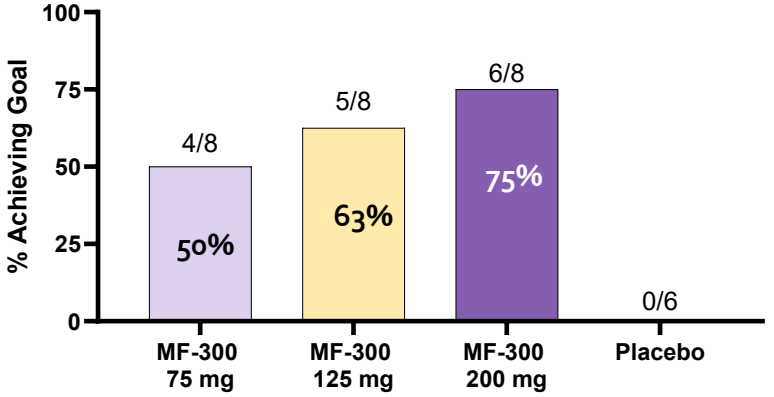
Placebo-adjusted PGE2 Change from Baseline

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.

% Subjects with ≥50% decrease in PGE-MUM & ≥60% Increase in PGE2



Biomarker Modulation in Older Adults Consistent with that Observed in the Younger Population

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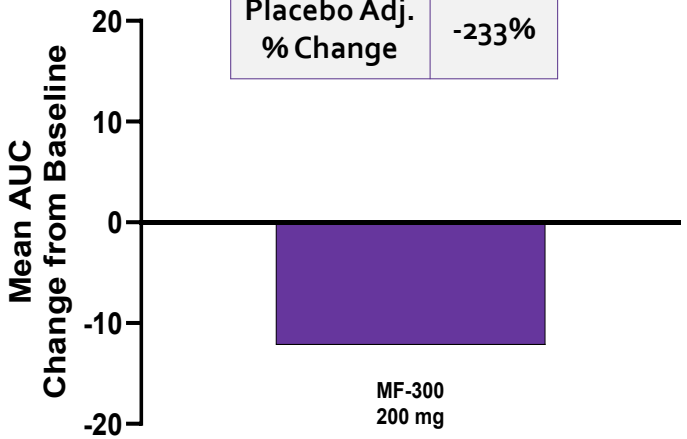
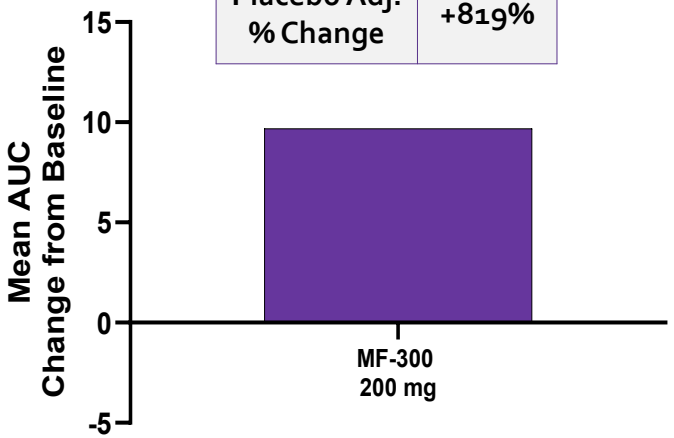
Placebo-adjusted PGE-MUM Change from Baseline

MF-300 (mg)	200
Placebo Adj. % Change	-233%

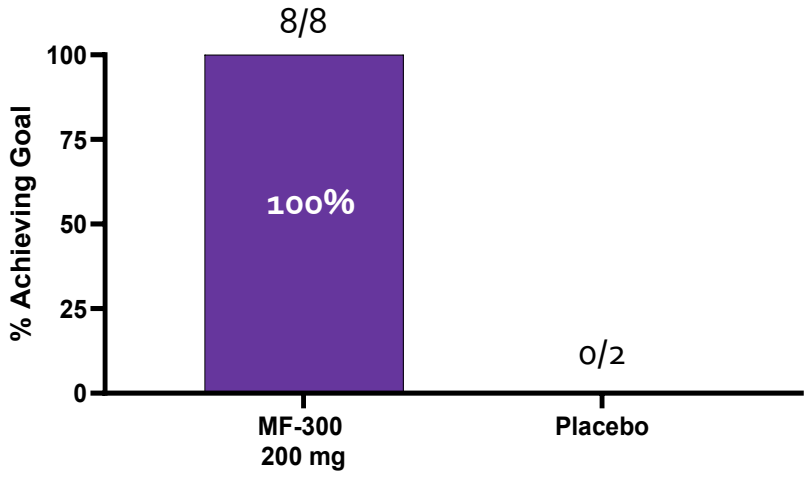


Placebo-adjusted PGE2 Change from Baseline

MF-300 (mg)	200
Placebo Adj. % Change	+819%

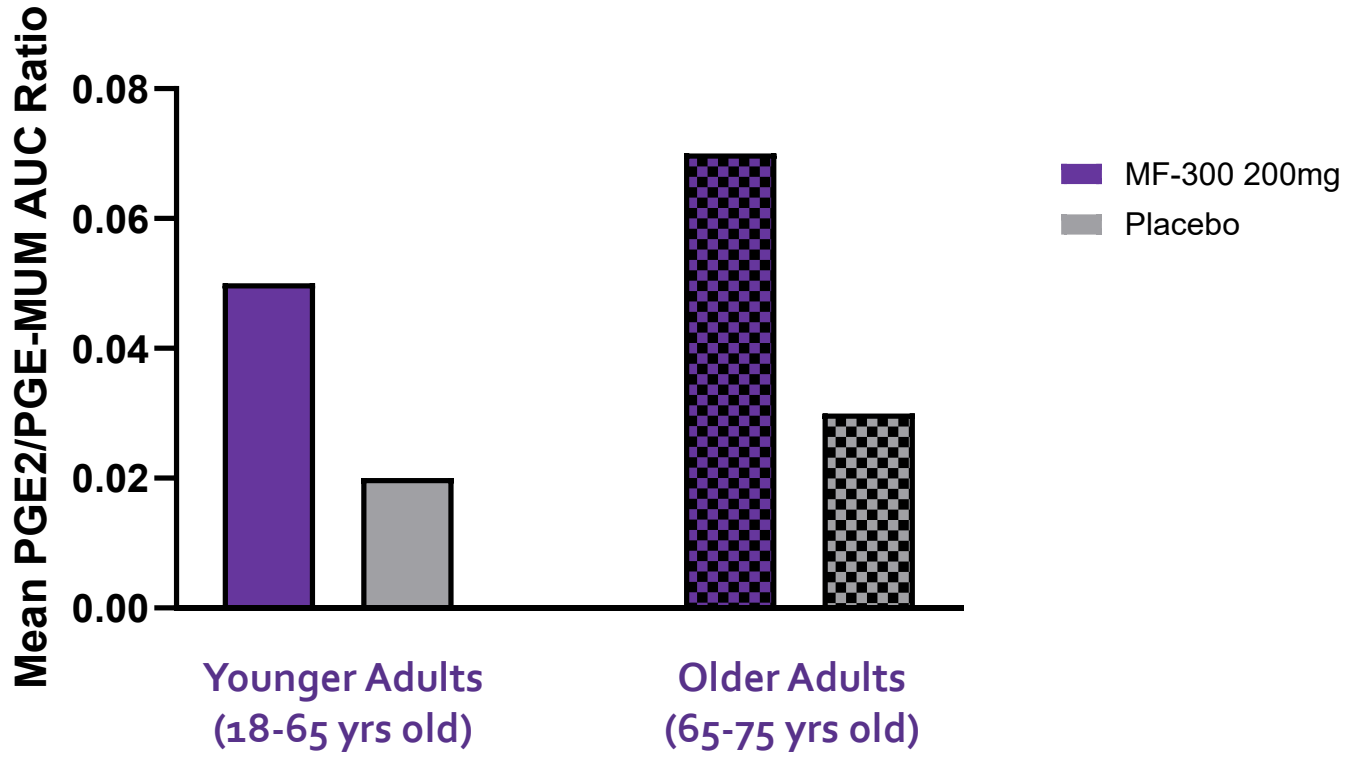


% Subjects with ≥50% decrease in PGE-MUM & ≥60% Increase in PGE2



MF-300 Increases the Ratio of PGE_2/PGE-MUM Consistent with Reduced PGE_2 Catabolism in Both Age Groups

2-fold increase in PGE_2/PGE-MUM Ratio in both Age Groups – Consistent Functional Inhibition



Two-Part Phase 2 Study Design

Part A: Open-label (Exploratory, Hypothesis Generating)

~20 patients (≥65 yrs) diagnosed with sarcopenia[1]

MF-300 75 mg QD (n=20)

Wk 0 (Day 1) — Wk 12 — Wk 24

Functional Endpoints:
- 5x Chair Stand Test, SPPB, Grip strength, 4-meter gait speed

Imaging (DXA)
Bone biomarkers
QoL Measures

Part B: Double-blind Randomized Placebo Controlled

~200 patients (≥65 yrs) diagnosed with sarcopenia[1]

Stratification
1:1:1

R

- **Placebo (n=67)**
- **MF-300 75 mg QD (n=67)**
- **MF-300 200 mg QD (n=67)**

Wk 0 (Day 1) — Wk 2 — Wk 6 — Wk 12 — Wk 18 — Wk 24 EoT — Wk 28 Follow-up/EoS

Primary Endpoint:
- 5x Chair Stand Test

Secondary Endpoints:
- SPPB
- Hand grip strength
- Knee extension
- 4-meter gait speed
- Imaging (DXA, CT)
- Bone biomarkers
- Incidence of falls
- QoL Measures

EoT=end of treatment; EoS=end of study; R=randomization; SPPB=Short Physical Performance Battery; Wk=week

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

Positive Type C (End-of-Phase 1) FDA Meeting Supports Advancement of MF-300 to a Phase 2b Study in Sarcopenia

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Key Outcomes

- The **FDA's written feedback was overall positive and constructive**
- **The Phase 2b study design was endorsed,** including FDA agreement to the patient population, primary and secondary efficacy endpoints, treatment duration and dosing regimen of MF-300
- **FDA agreed that the efficacy endpoints evaluated in the Phase 2b study will inform Phase 3 endpoint selection**
- **FDA supports pursuing Fast Track Designation,** signaling that they consider Sarcopenia a serious condition and that MF-300 has the potential to address an unmet need

Strategic Implications

- Supports advancement of MF-300 to a Phase 2b study
- Phase 3 endpoint strategy is conditionally endorsed – regulatory risk around endpoints is reduced
- Fast Track, if accepted, will allow greater access to FDA during development and enable priority review, potentially accelerating development timelines

$60M Series B Achieves Phase 2 Readouts – Multiple Value Inflection Points

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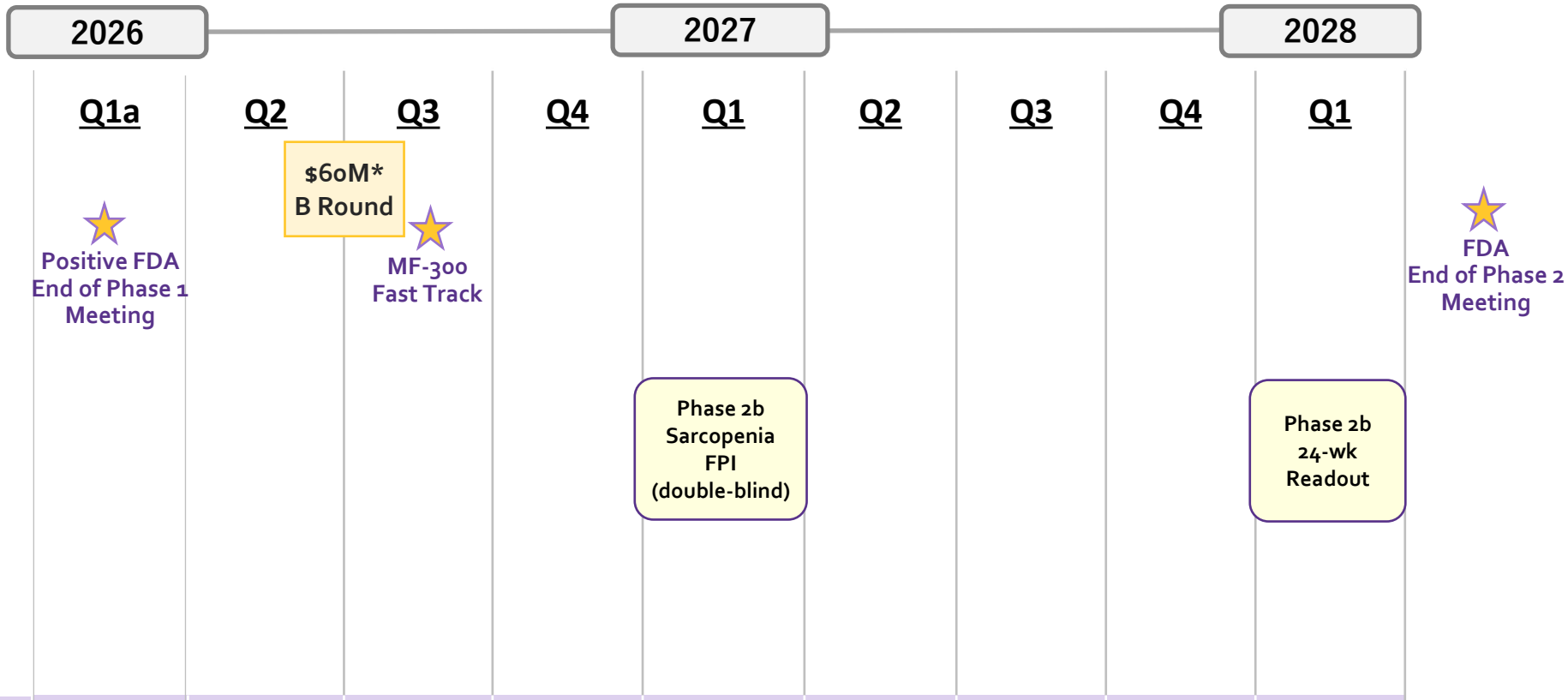
$60M Series B

Achieves Phase 2 Readouts:

- Fast-Track Designation – Q3 '26
- Phase 2b Readout – Q1 '28
- End of Phase 2 FDA meeting – Q2 '28



	Q1a	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1
Cash w/ $60m B Round	$1.4	$4.0	$59.6	$55.0	$43.1	$33.0	$22.6	$11.9	$1.8

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End of Presentation

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.