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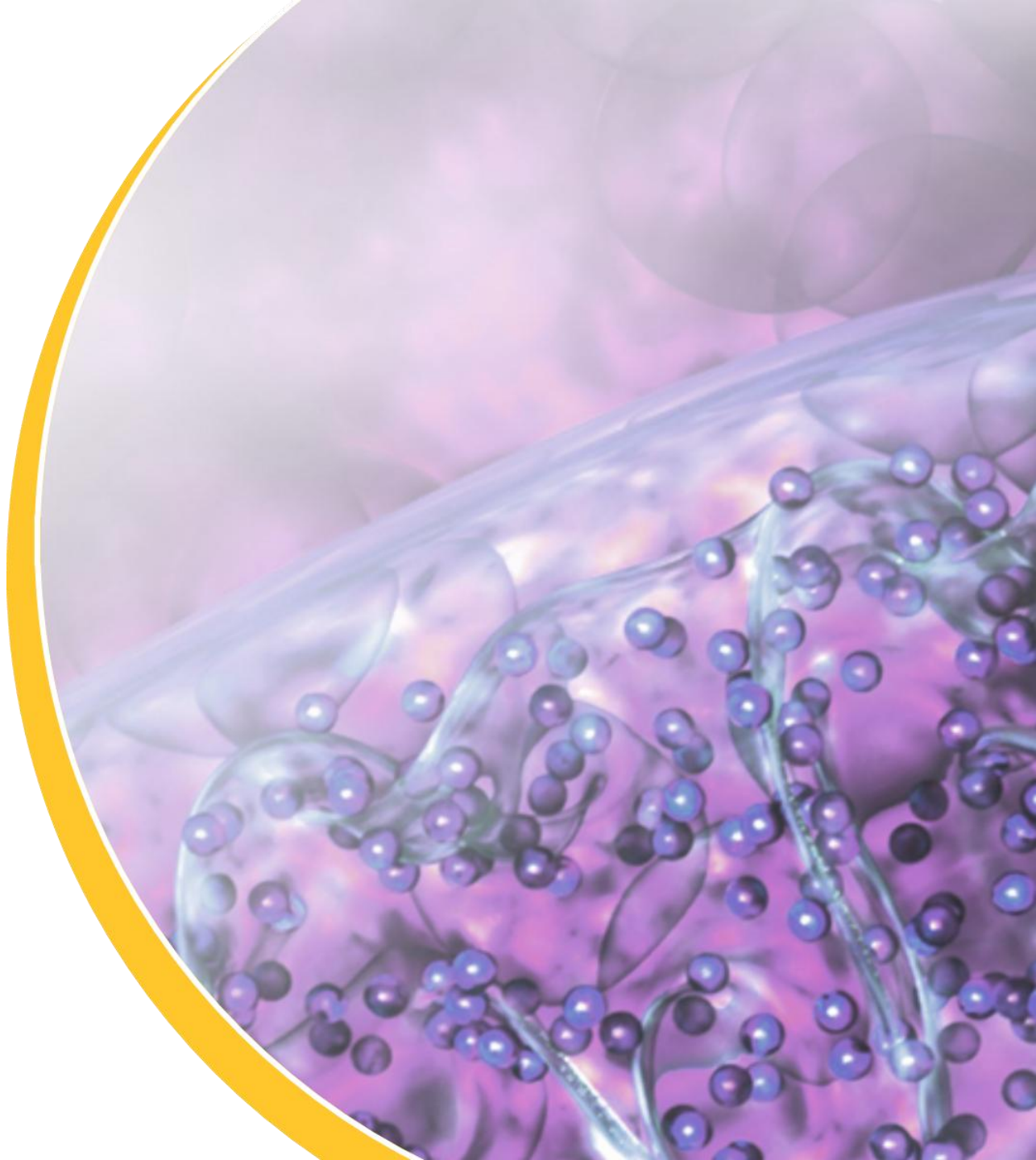
Phase 1 Clinical Evaluation of MF-300 in Older Adults: An Investigational, First-In-Class Oral, Small Molecule in Development for Sarcopenia

ICFSR 2026 – Washington, D.C.

Leigh MacConell, PhD



Disclosures

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- Leigh MacConell is a paid consultant to Epirium Bio.
- MF-300 is an investigational product candidate being evaluated for safety in healthy volunteers. MF-300 has not been approved by any regulatory authority, and its safety and efficacy have not been established.

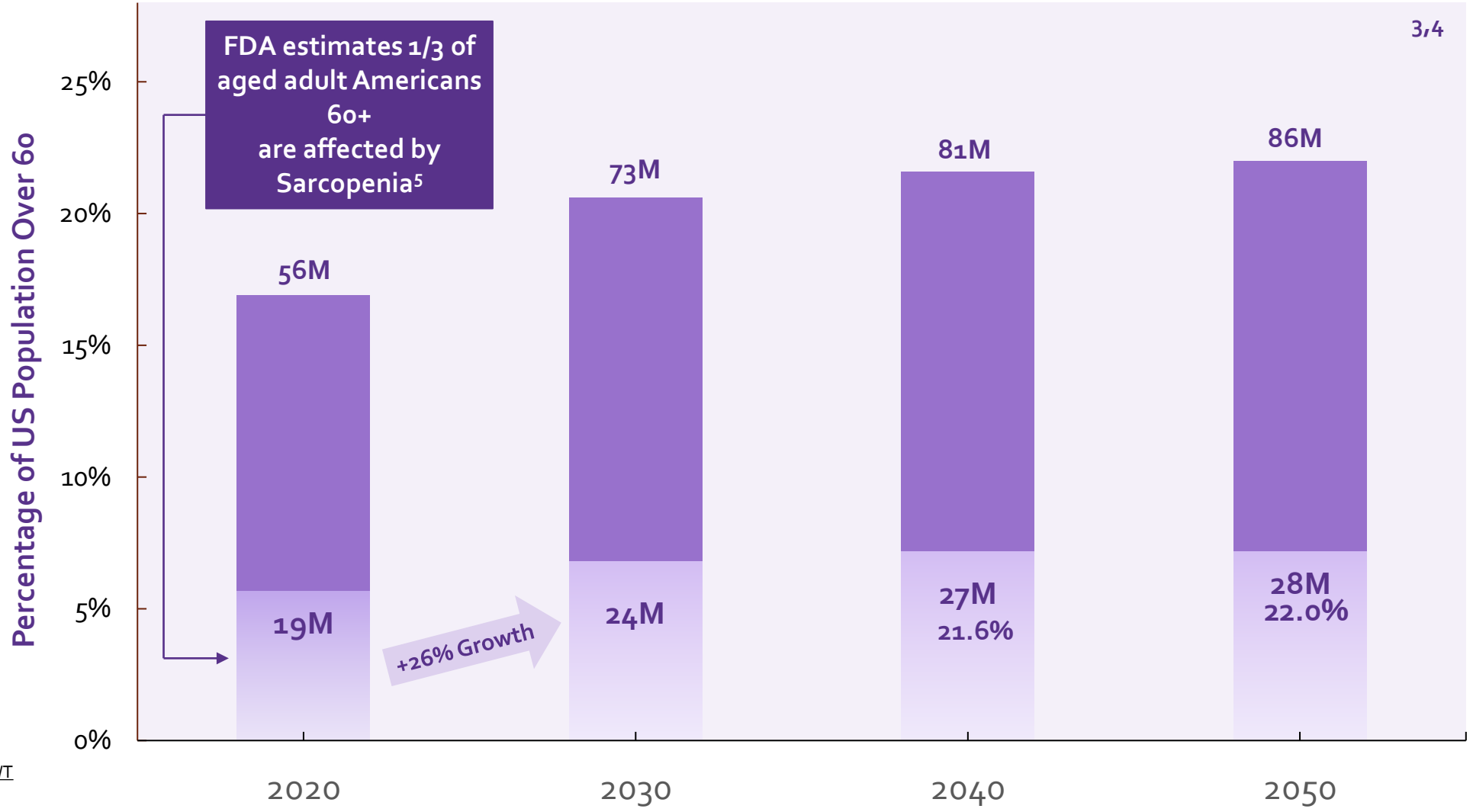
Sarcopenia: Large and Growing Unmet Medical Need

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

Dependence
Increased risk losing independence

Falls
Increased Morbidity & Mortality[2]

Mortality
Increased risk of death[2]

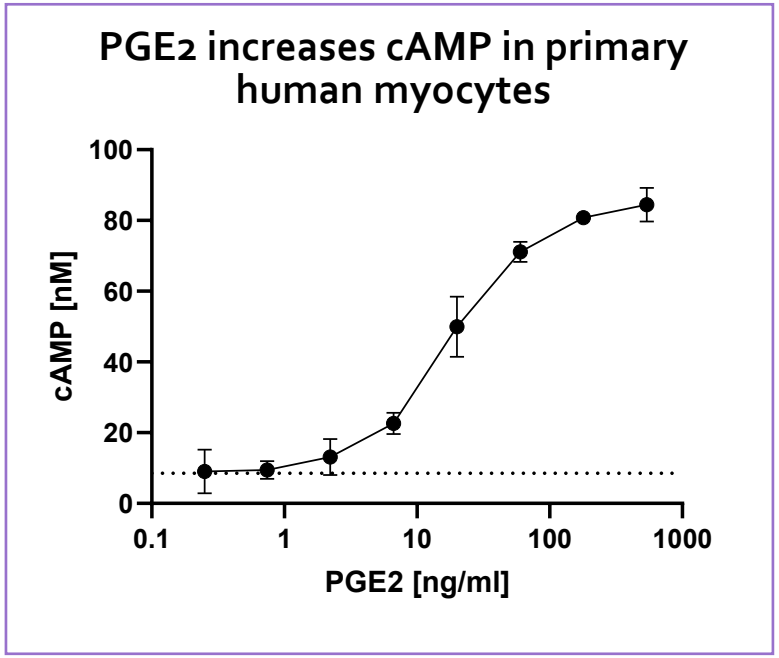


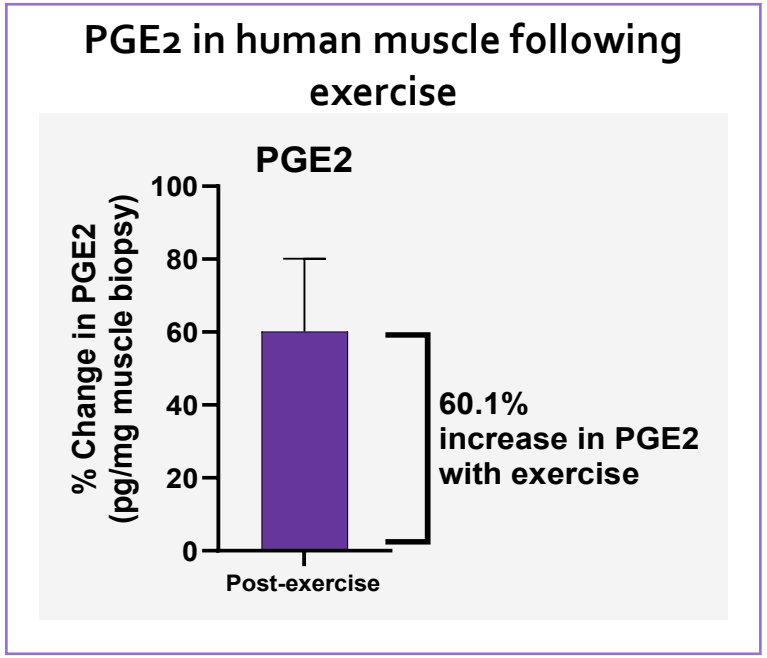
U.S. Population est. 331M

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

Prostaglandin E2–EP4–cAMP Signaling Promotes Muscle Quality

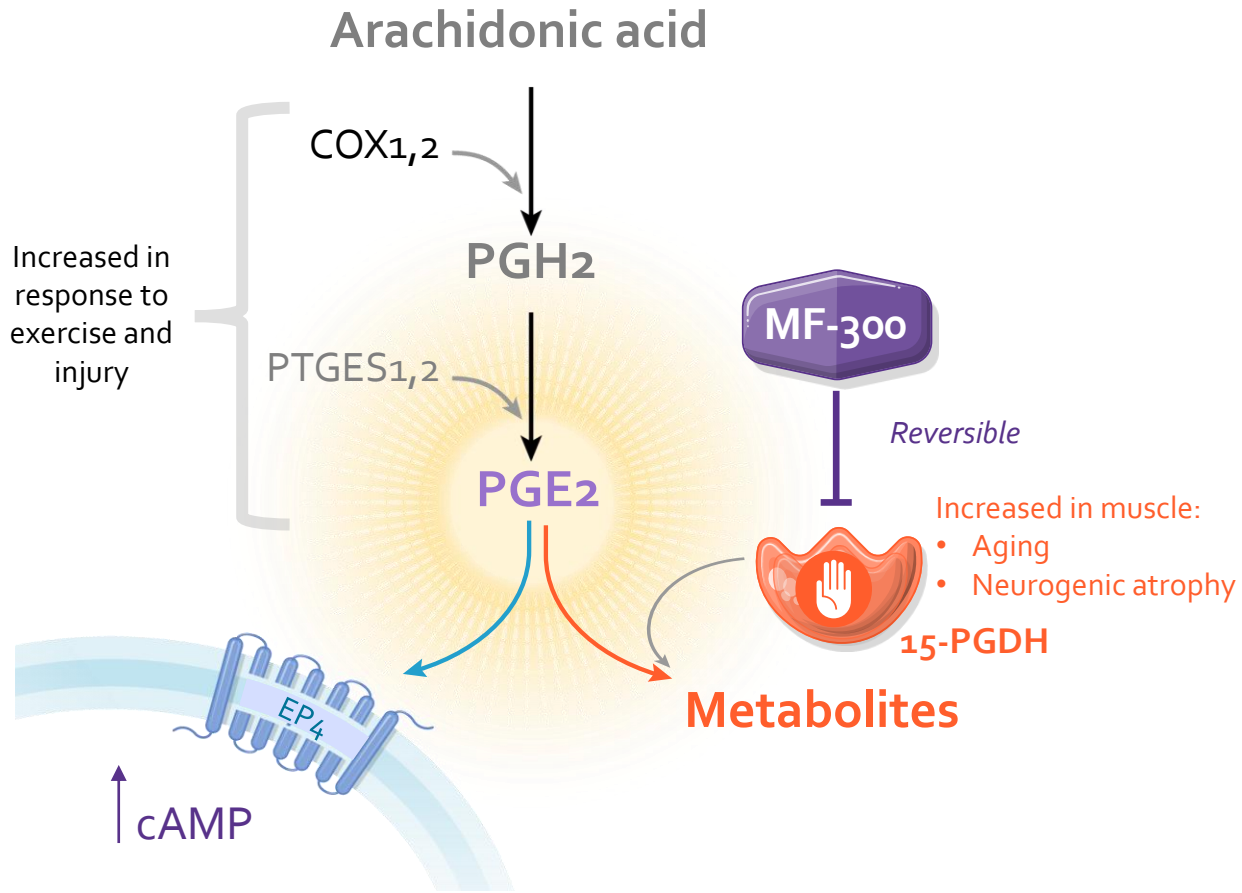
- Targeting the Prostaglandin E2 (PGE2) pathway to improve muscle quality and physical function in patients with sarcopenia.
- PGE2 signaling through the EP4 receptor increases intracellular cAMP, a key regulator of muscle quality that:
  - Supports mitochondrial function, integrity of the neuromuscular junction, and contractile performance
  - Increases proliferation of stem cells (repair/rejuvenation) and improves the adaptive response to exercise and injury





MF-300 Restores PGE2 Levels to Increase cAMP by Inhibiting 15-HydroxyProstaglandin Dehydrogenase

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



- 15-HydroxyProstaglandin Dehydrogenase (15-PGDH) is the principal enzyme responsible for the degradation of PGE2.
  - 15-PGDH gene expression is elevated in aged human muscle.[1,2]
  - Reduced available PGE2 signaling may contribute to the development of age-related muscle weakness.
- MF-300: investigational, first-in-class, small-molecule and a reversible inhibitor of 15-PGDH.
- By inhibiting 15-PGDH, MF-300 blocks PGE2 degradation, restoring endogenous PGE2 / cAMP signaling in muscle.
- In naturally aged mice, oral MF-300 increases muscle force and improves muscle quality[3].

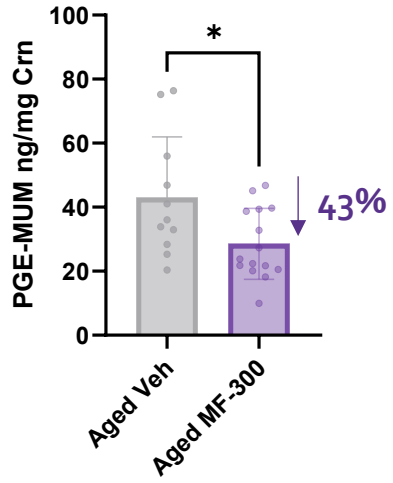
[1] GEO167186,[2] Raue et al., *J Appl Physiol* 2012 (published in Palla et al., *Science* 2021), [3]Epirium data on file

MF-300 Increases Muscle Force with Correlated Reductions in PGE2 Major Urinary Metabolite

Preclinical Sarcopenia Studies

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

Study 1

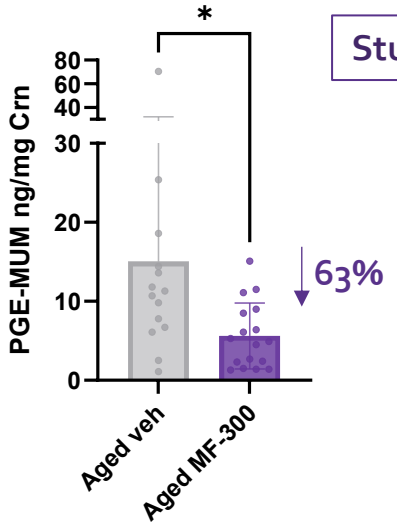


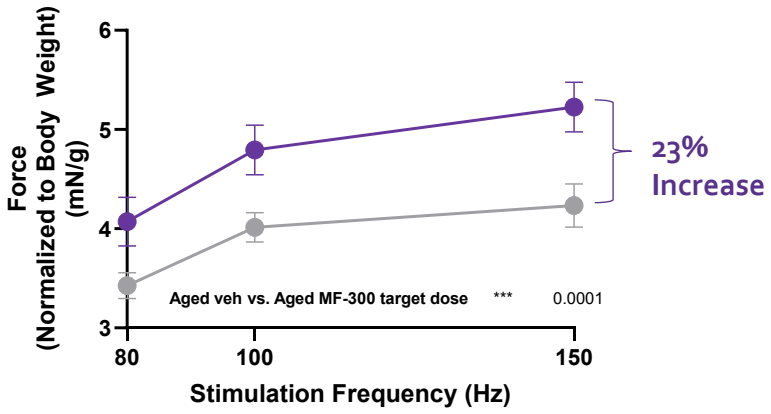
Vehicle
MF-300 target dose mg/kg

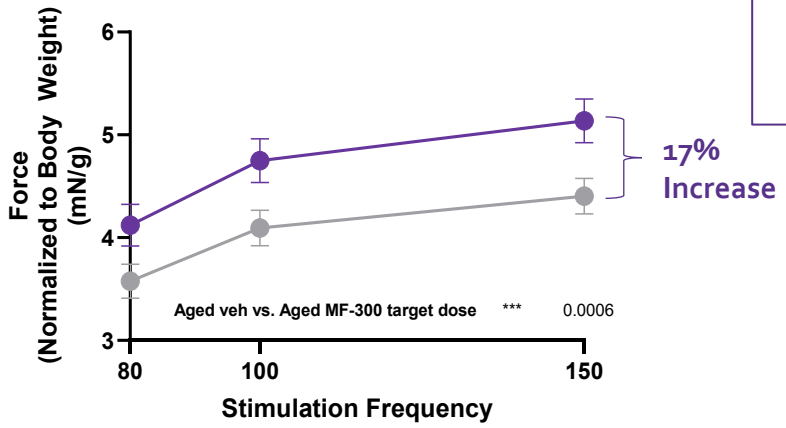
PGE-MUM
↓ ~50% average

Force
↑ ~20% average

Study 2







Treatment of naturally aged mice with MF-300 for 12 weeks demonstrates:

- A ~50% reduction in PGE-MUM consistent with target engagement
- Significantly increases muscle force by ~20%

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

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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

- 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

Part 2 MAD

- 5 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.

Patient Demographics

- **A total of 88 study participants were enrolled across the SAD and MAD study phases.**
  - N = 70 subjects (≥ 18 - ≤ 65)
  - N = 18 subjects (>65 - ≤75 years)
- **Baseline demographics were generally balanced across cohorts and treatment groups.**
  - Predominantly white with overall balanced sex distribution.
  - Mean age: ~37 years in younger cohorts and ~70 years in older cohorts.
  - Mean BMI: 25–28 kg/m² (overweight range), comparable across treatment groups.
  - Renal function: preserved in younger participants (eGFR ~110–114 mL/min) with expected age-related reduction in older cohorts (~82 mL/min).

Safety and Tolerability of MF-300 in Healthy Younger and Older Adults

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Safe and well tolerated across the evaluated dose ranges

- No deaths, serious adverse events, or discontinuations due to adverse events
- Maximally tolerated dose not identified up to 800 mg
- Comparable safety profile between older and younger adults

Adverse Events: No dose-limiting toxicities

- Majority of adverse events mild, resolved without intervention.
  - 3 isolated Grade 2 events (2 MF-300 subjects, 1 placebo subject) considered not-related to study drug
- With repeat dosing: Incidence of adverse events with MF-300 ≤ placebo.
- No dose-response in frequency or severity of adverse events.
- Most common adverse event in both age groups: Mild diarrhea, transient (resolving w/in 1-2 days).

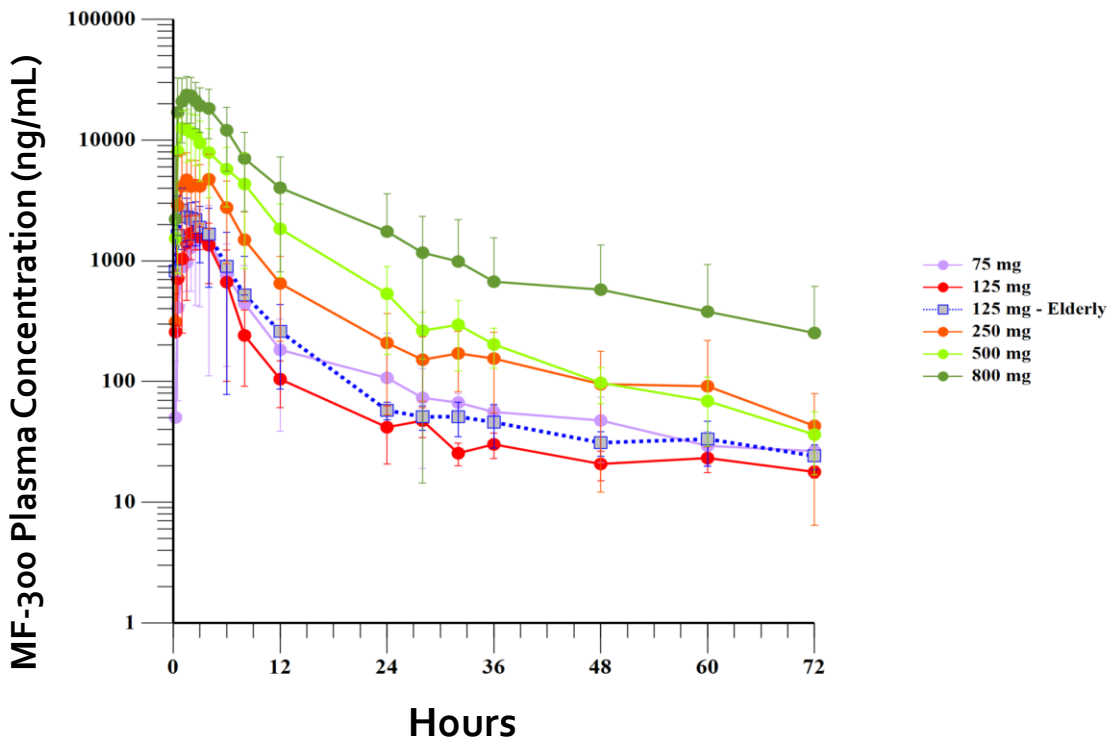
No clinically meaningful trends in labs, vital signs, or ECGs

- Lab parameters remained stable, including glucose, eGFR
- Intrasubject variability in blood pressure and heart rate consistent with placebo
- No evidence of QTc prolongation or hemodynamic concerns

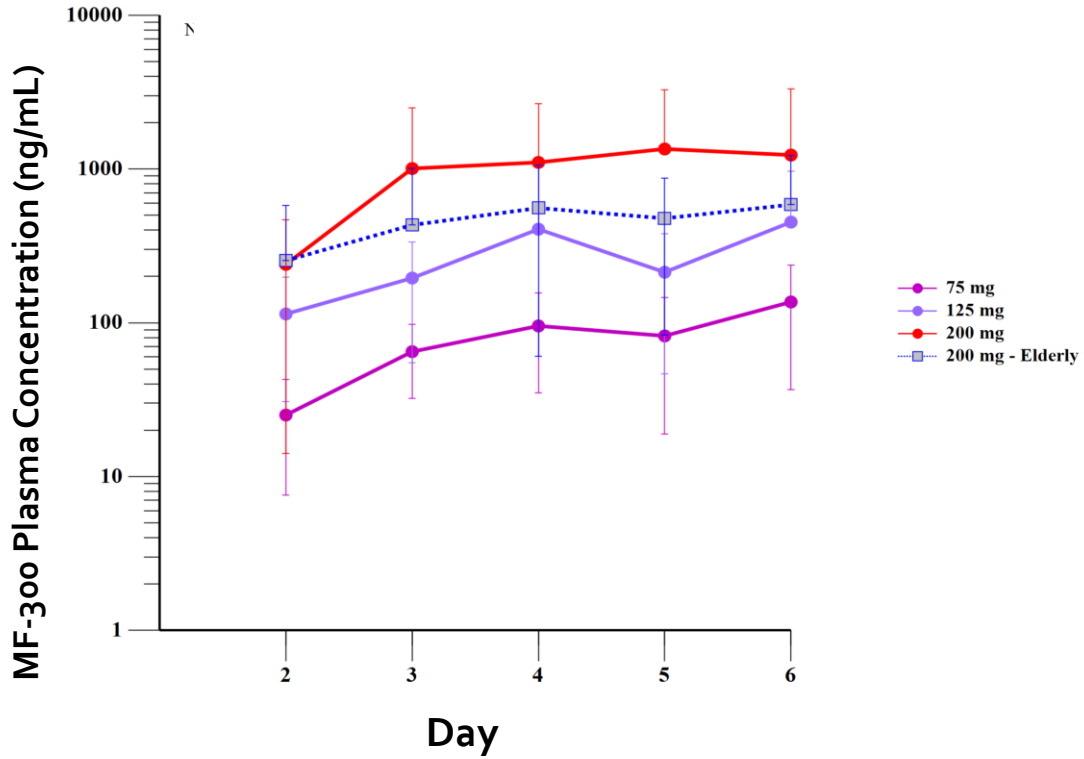
Pharmacokinetics of MF-300 Following Single and Multiple Doses

- Rapid absorption (t_{max} 1.5-2.5 hours) with dose-related increases in systemic exposure.
- Terminal half-life supportive of once-daily dosing.
- Predictable accumulation with time to steady state estimated as within ~3–4 days.
- Similar exposure profiles in younger and older adults; Geometric LSM ratios (older/younger): 81.5% for Cmax and 98 - 102% for AUC parameters

Single Dose PK Profile



Multiple Dose Trough PK Profile



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

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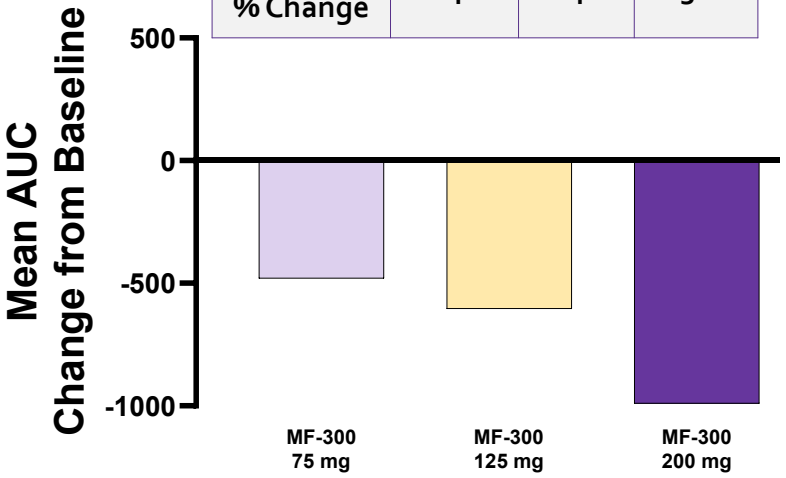
Placebo-adjusted PGE-MUM Change from Baseline

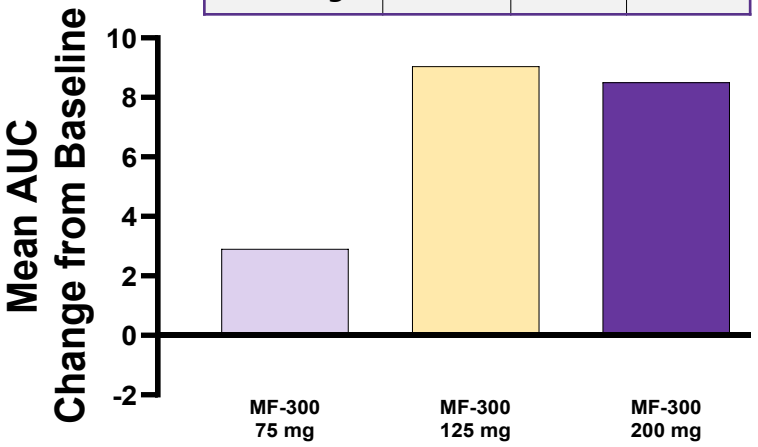
MF-300 (mg)	75	125	200
Placebo Adj. % Change	-64%	-64%	-83%*



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

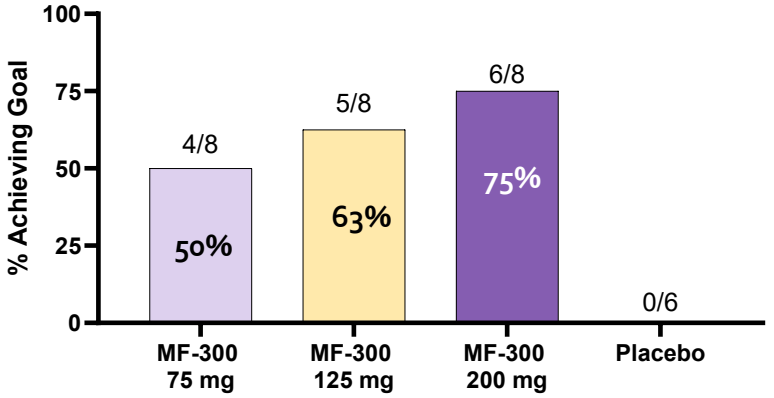
Placebo-adjusted PGE2 Change from Baseline

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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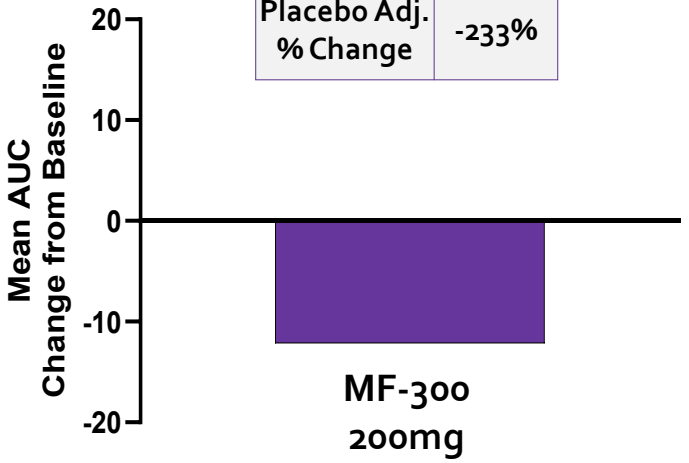
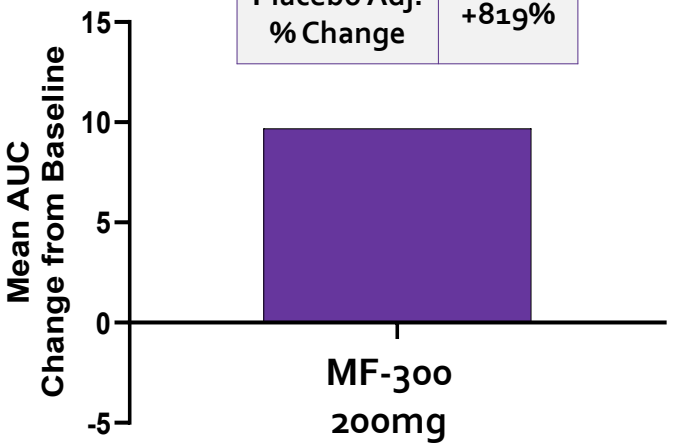
Placebo-adjusted PGE-MUM Change from Baseline

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

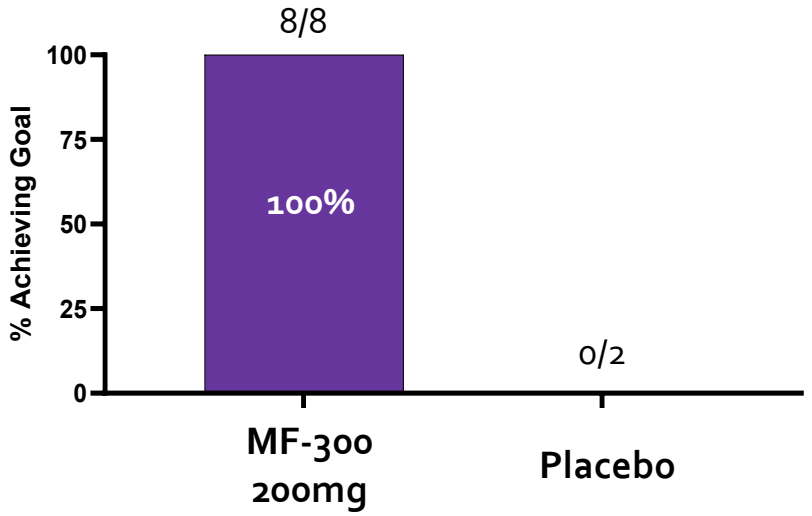


Placebo-adjusted PGE2 Change from Baseline

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



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



Conclusions

- **MF-300 was safe and well tolerated at single doses up to 800 mg and repeat doses up to 200 mg QD.**
  - Adverse events were predominantly mild and not dose-related.
  - Comparable safety in younger and older adults.
- **MF-300 demonstrated rapid absorption and dose-proportional increases in exposure with a half-life supportive of once-daily dosing.**
  - Similar systemic exposures in younger and older adults.
- **Biomarker evidence supports MF-300's muscle preservation mechanism**
  - Increased urinary PGE2 with corresponding reductions in inactive metabolites in younger and older adults.
- **Overall, these data support continued development of MF-300 for the treatment of sarcopenia.**
  - A 6-month Phase 2b study is planned to evaluate MF-300 on functional performance and muscle strength in age-related sarcopenia.

Acknowledgements

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THANK-YOU!

Epirium Bio

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