Ridgeline
Therapeutics

Age stronger,
live longer…

Stan Watowich, PhD
Founder & CEO

Disclosures

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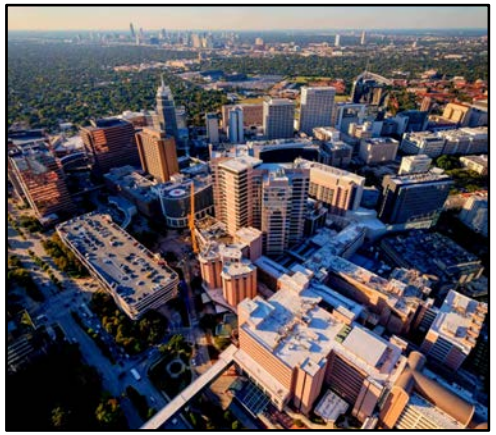
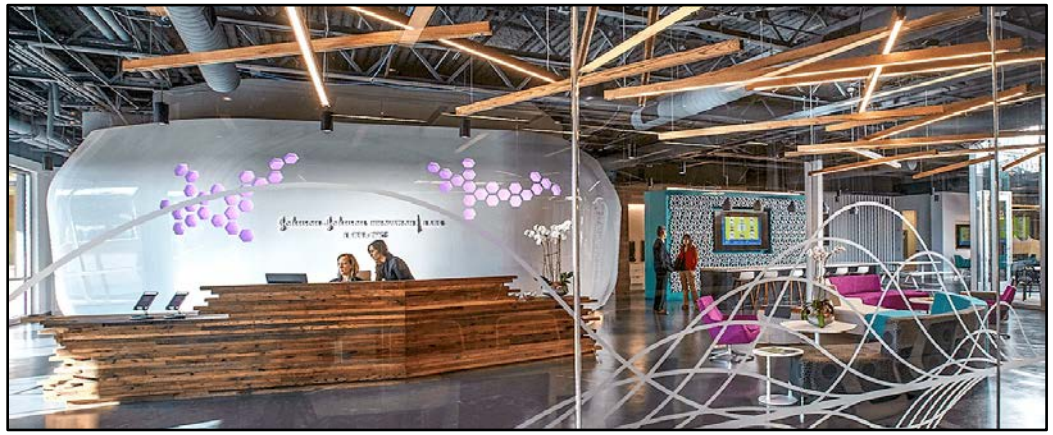
Ridgeline overview

- Biotech company based in the Texas Medical Center (Houston, TX)
- Part of Johnson & Johnson Innovation (JLABS) network
- Focused on novel targets to treat
  - ✓ sarcopenia, frailty, muscle repair
  - ✓ obesity & obesity-linked diseases
  - ✓ weight loss-induced muscle dysfunction
- Healthy Longevity Catalyst awardee (US Nat. Academy of Medicine)
- Raised >$10M in non-dilutive funding


CATALYST
AWARD
This certificate is proudly presented to
Stan Watowich
for their bold, new, and innovative idea supporting the aims of the NAM Healthy Longevity Global Competition to extend health and function as people age.
VICTOR J. DZAU
PRESIDENT
NATIONAL ACADEMY OF MEDICINE
NATIONAL ACADEMY of MEDICINE
Healthy Longevity


Houston, TX


Texas Medical Center


JLABS@TMC

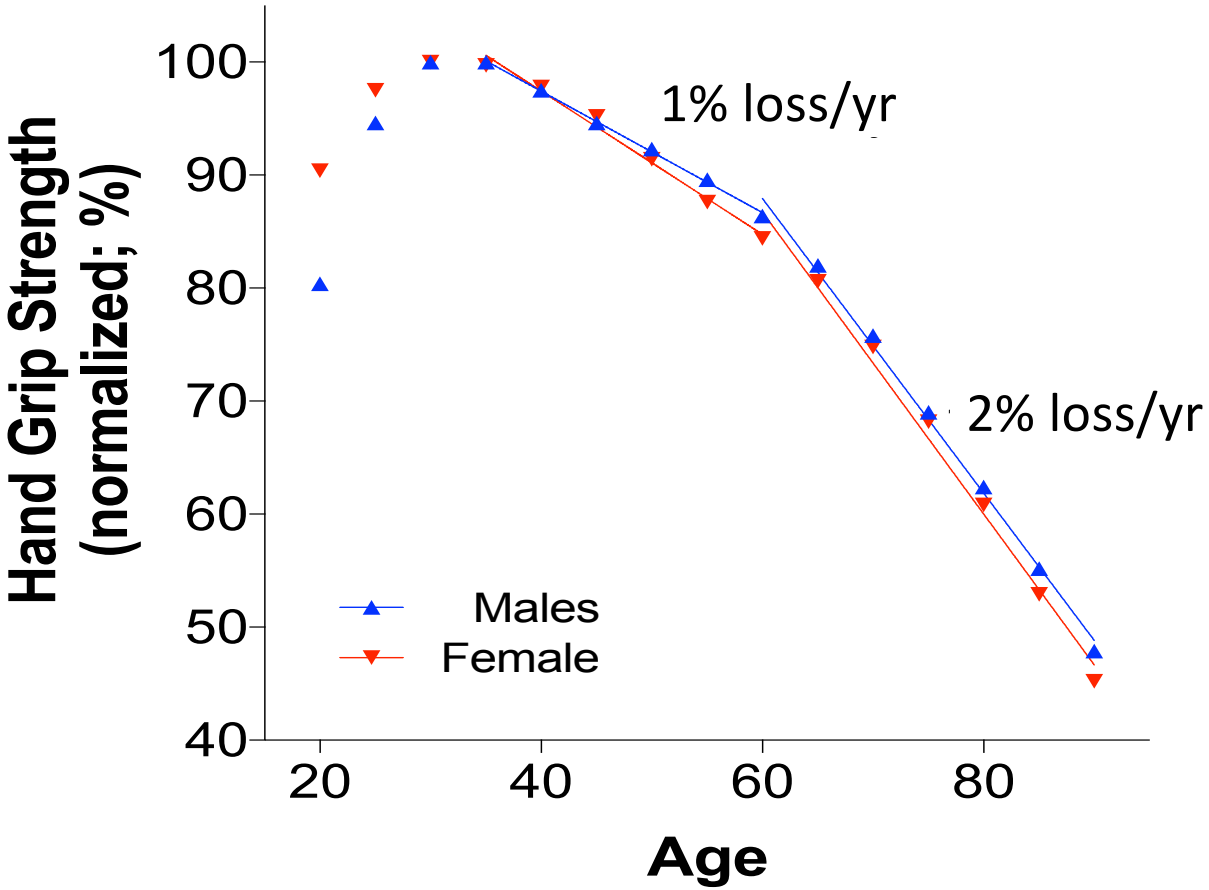
Muscle strength relentlessly declines with age

All adults become

- 25% weaker by age 60
- 50% weaker by age 80

(compared to age 35)

Loss of muscle strength*



*Dodds et al. (2014) Grip Strength across the Life Course: Normative Data from Twelve British Studies. PLoS ONE 9

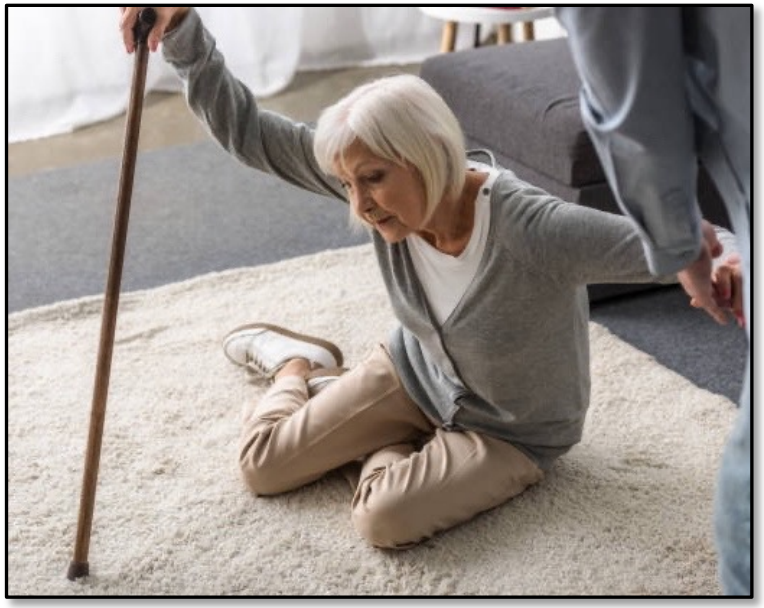
Age-linked muscle decline leads to…

Loss of

- quality of life
- mobility
- independent living
- cognitive function

Increase in

- heart & pulmonary diseases
- falls & fractures
- metabolic disease (e.g., diabetes)
- all-cause mortality



There are no FDA-approved therapies to reverse age-linked muscle decline

Our solution: RT-002 daily pill to restore muscle

- Will be the first FDA-approved oral drug to reverse age-linked muscle decline & weakness
- First-in-class oral drug to build muscle mass & strength in aging individuals
- Targets a novel mechanism of action
- Reactivates muscle stem cells to repair and regenerate aging muscles
- Strategic clinical path to accelerate FDA approval

THIS

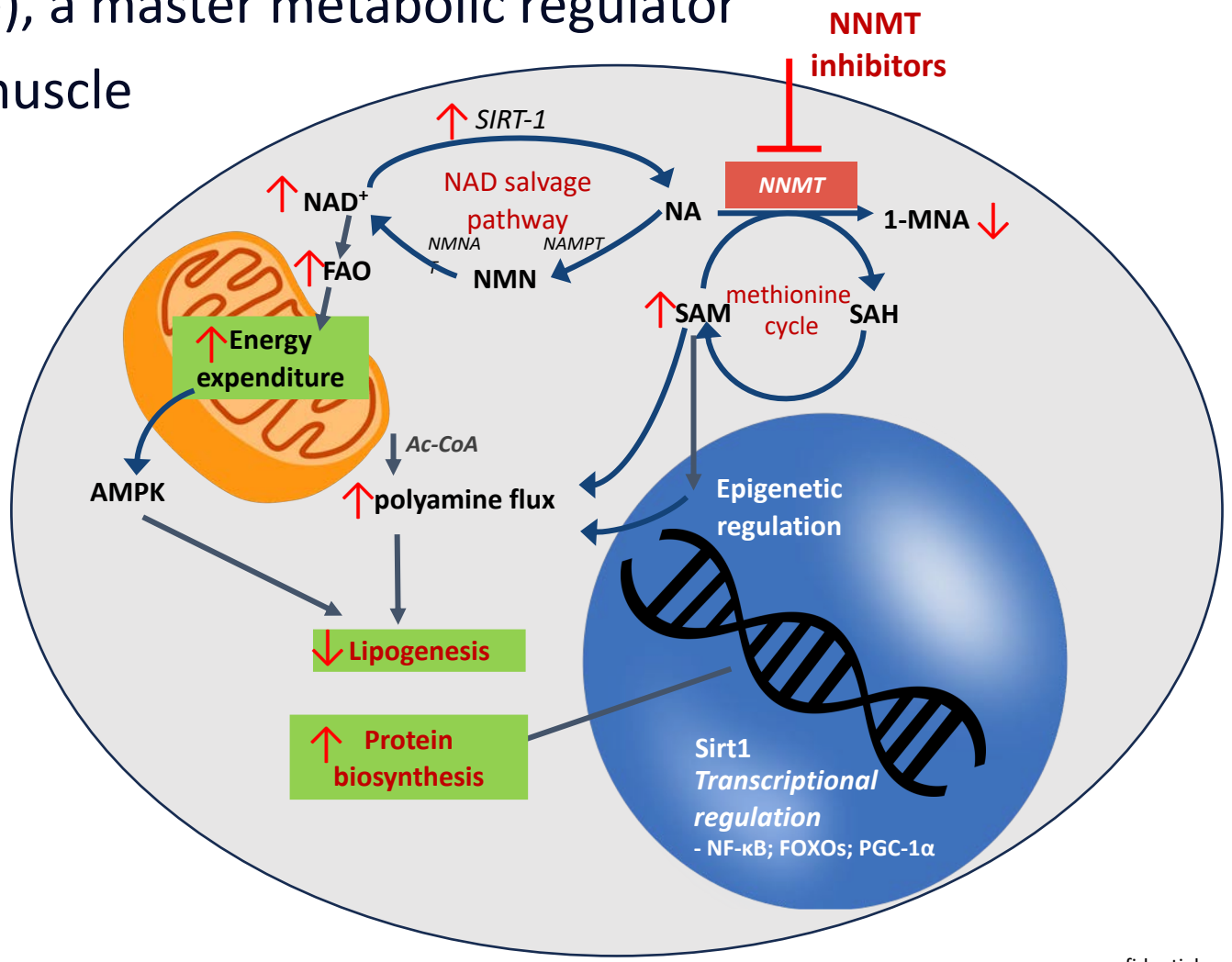
NOT THIS

RT-002 inhibits a novel cellular target

- NNMT (nicotinamide N-methyltransferase), a master metabolic regulator
- Selectively upregulated in aging skeletal muscle

NNMT inhibitors

- ✓ increase muscle function
- ✓ promote muscle hypertrophy
- ✓ accelerate muscle regeneration
- ✓ reduce intramyocellular lipids
- ✓ enhance mitochondrial bioenergetics
- ✓ decrease insulin resistance

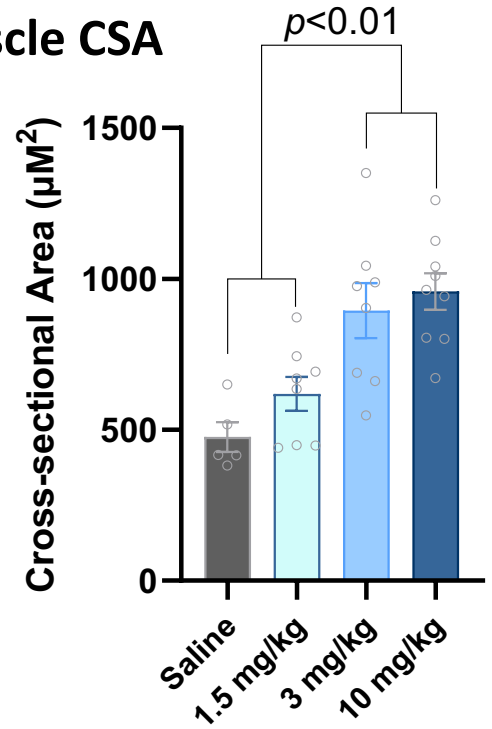


Muscle repair: drug increased muscle size

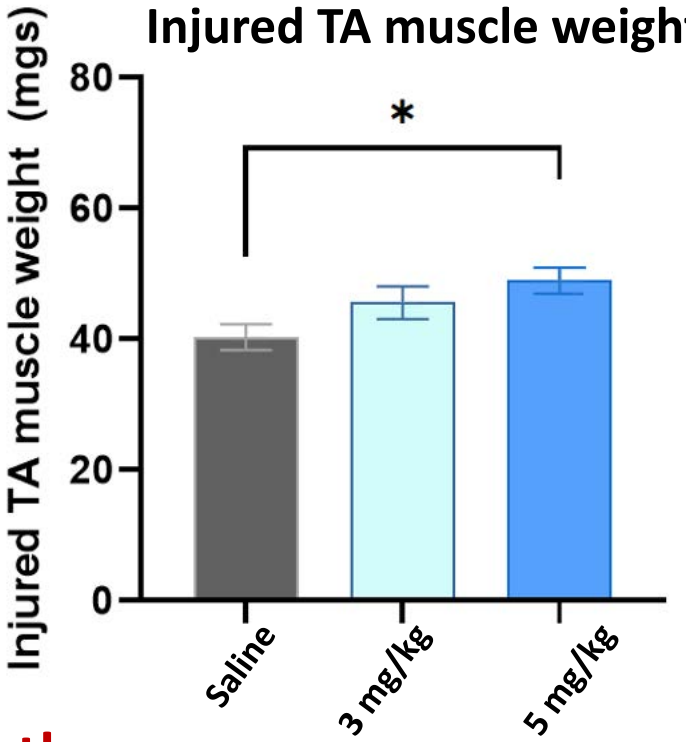
Aged mouse muscle injury model

- >100% increased fiber cross-sectional area (CSA), showing increased muscle repair & growth
- 33% increased muscle mass, indicating increased muscle regeneration & growth

Injured TA muscle CSA



Injured TA muscle weight



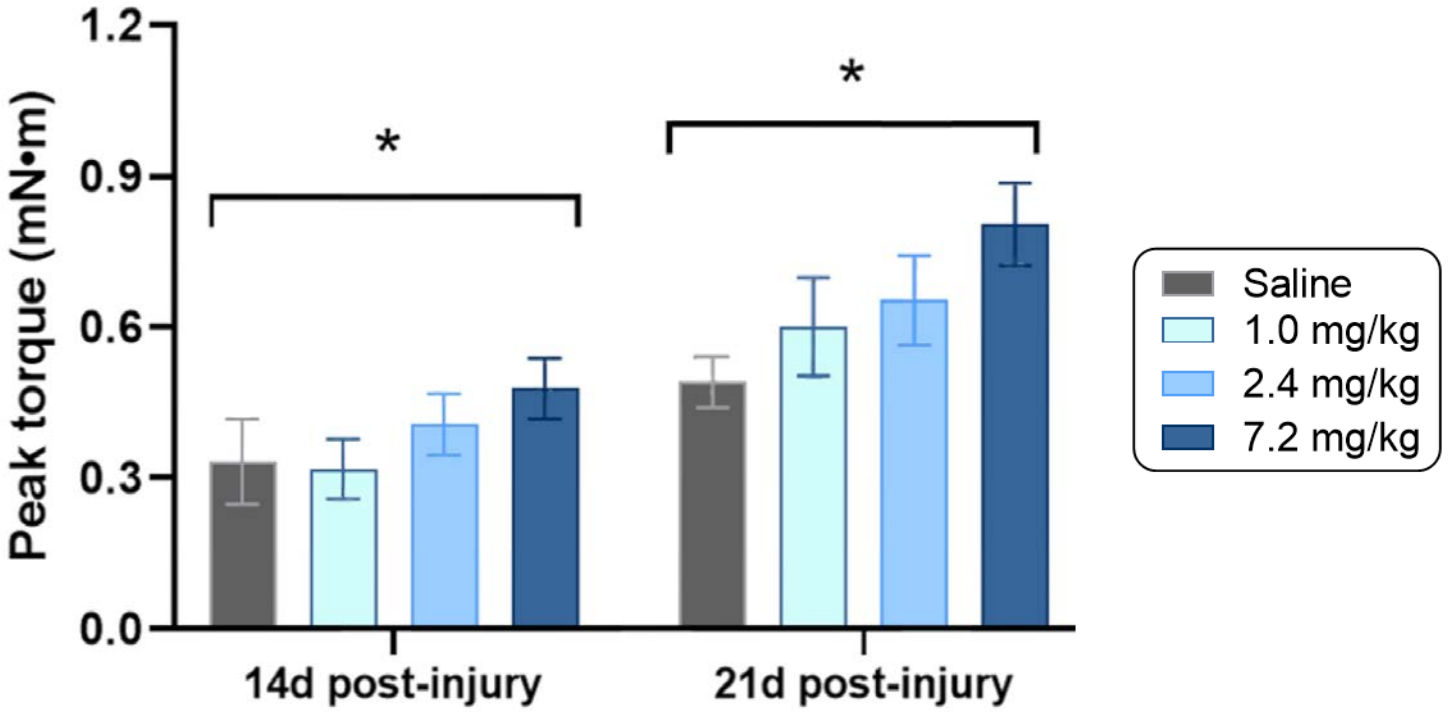
NNMT drug greatly increased muscle repair & growth

nonconfidential

Muscle repair: drug increased muscle strength

Aged mouse muscle injury model

- Muscle strength increased ~2-fold at 14- and 21-d post-injury
- Recovered >85% of strength by 21d



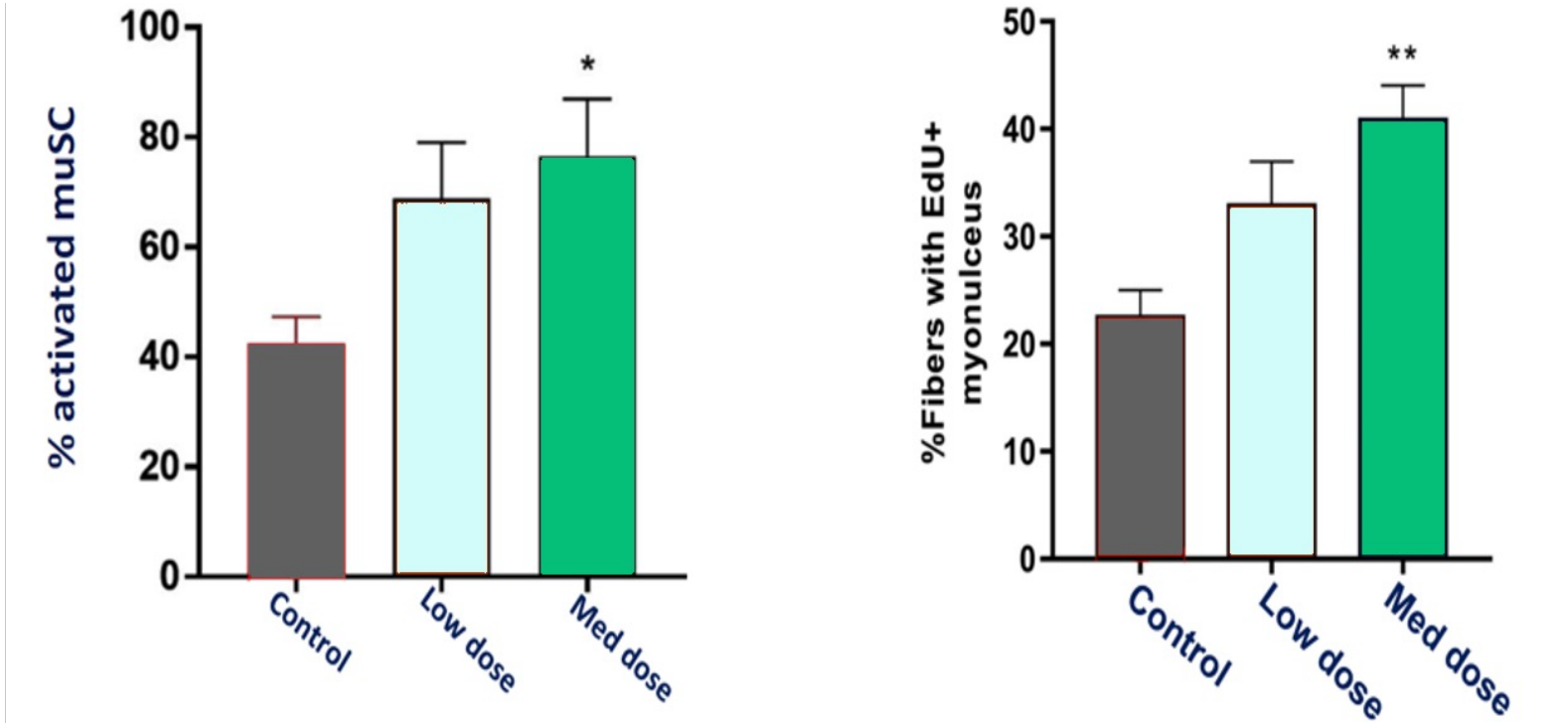
NNMT drug greatly accelerated and increased recovery of muscle strength

nonconfidential

Muscle repair: drug increased muSC activation

Aged mouse muscle injury model

- muSC (muscle stem cell) proliferation increased ~50%
- muSC myofiber fusion index increased ~2-fold

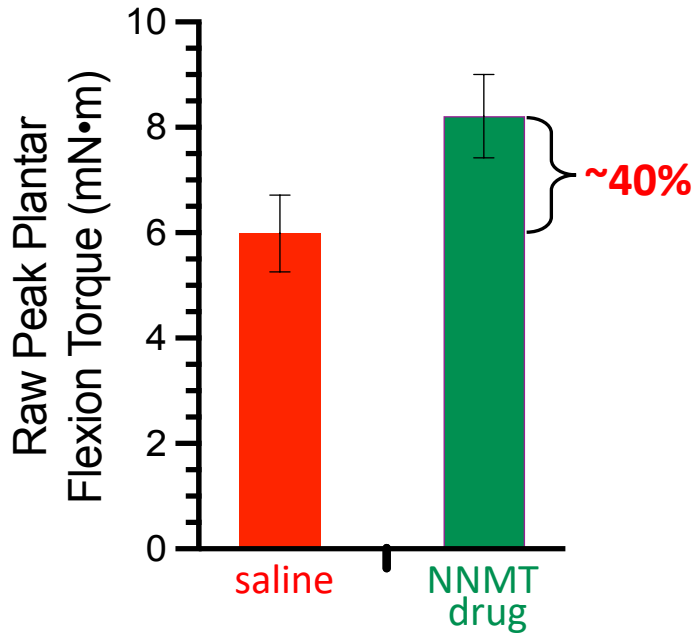


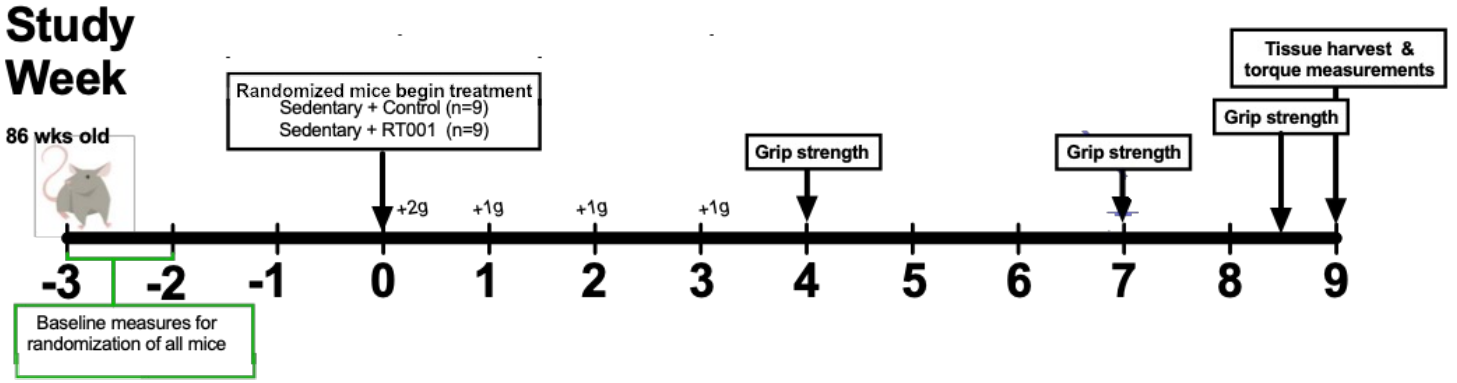
NNMT drug greatly increased muscle regeneration by reactivating muscle stem cells

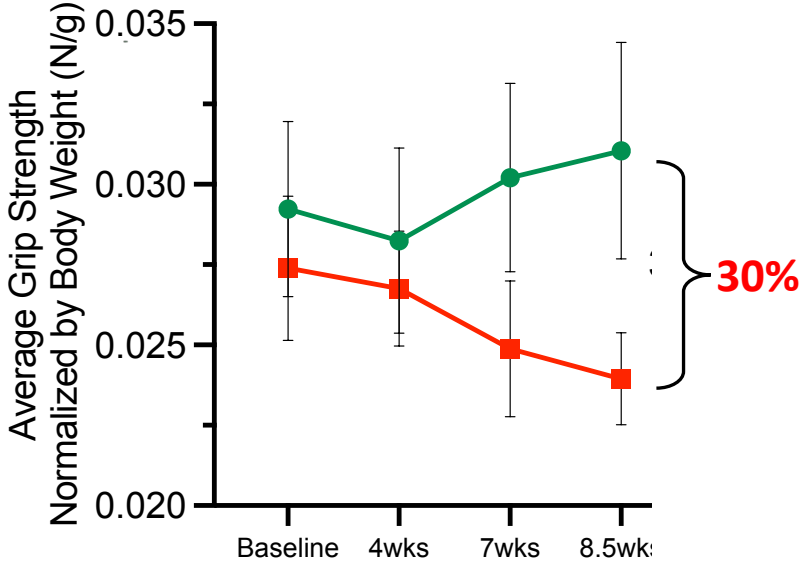
Neelakantan et al, Biochem. Pharmacol. 163, 481, 2019

Muscle aging: drug builds muscle strength

Aged sedentary mouse model



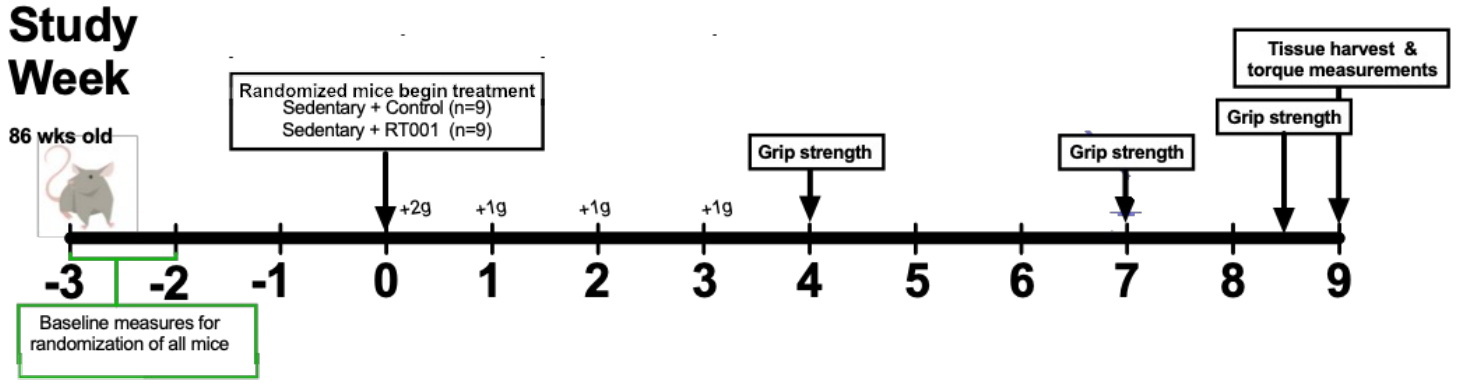




NNMT drug increased peak muscle strength 40%; prevented age-linked muscle weakness

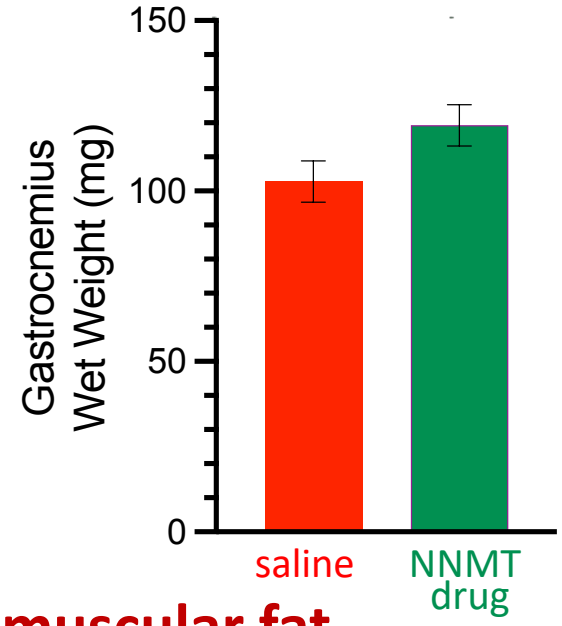
Muscle aging: drug builds muscle mass & quality

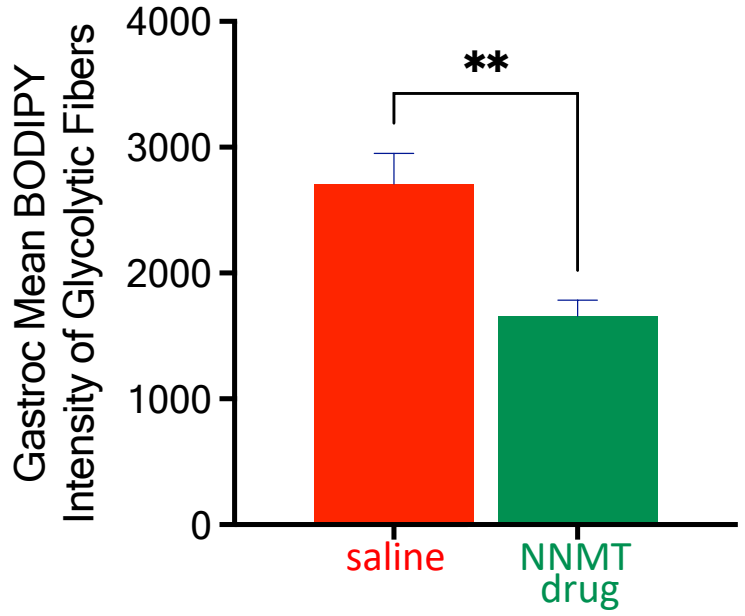
Aged sedentary mouse model



NNMT drug

- increased muscle mass ~20%
- increased bone density
- reduced intramuscular fat* ~40%





NNMT drug greatly reduced intramuscular fat

*intramuscular fat linked to increased death, heart failure risk, visceral fat deposits, muscle weakness

RT-002: on track to begin human testing

Completed

- ✓ AMES genotoxicity studies; no concerns
- ✓ Unremarkable off-target profile; no activity against cardiac ion channels
- ✓ GLP safety/tox studies in rodents; no concerns
- ✓ Non-GLP safety/tox studies in mini-pigs; no concerns
- ✓ Pre-IND meeting with FDA; cleared for IND submission
- ✓ GLP safety/tox studies in minipigs

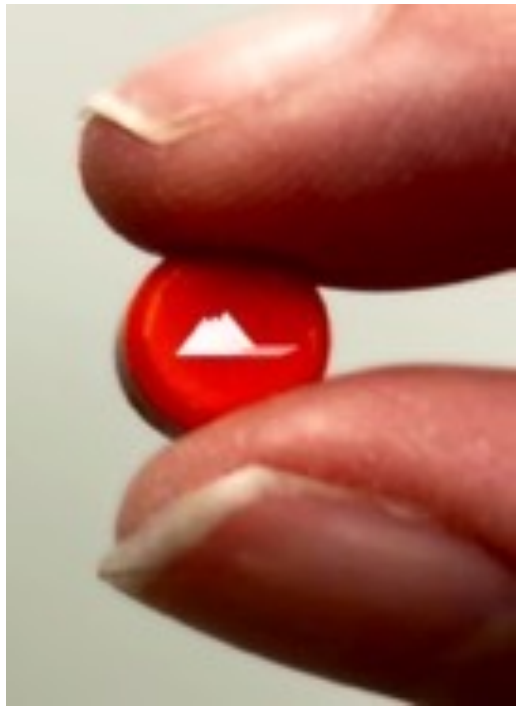
In progress

- GLP cardiovascular study in minipigs
- IND submission to FDA
- First-in-human Phase 1 trial (SAD/MAD)

RT-002: low cost, high-yield, & scalable synthesis

Completed

- ✓ Stable RT-002 API polymorph identified
- ✓ High-yield 3-step synthesis established with US CDMO
- ✓ Consistent, reproducible high-purity API with CDMO
- ✓ Scale-up of 4 kg API for GLP studies
- ✓ GMP manufacturing process established for drug substance
- ✓ Excipients established for drug product



In progress

- 9 kg drug product under GMP conditions for Phase 1 & stability studies

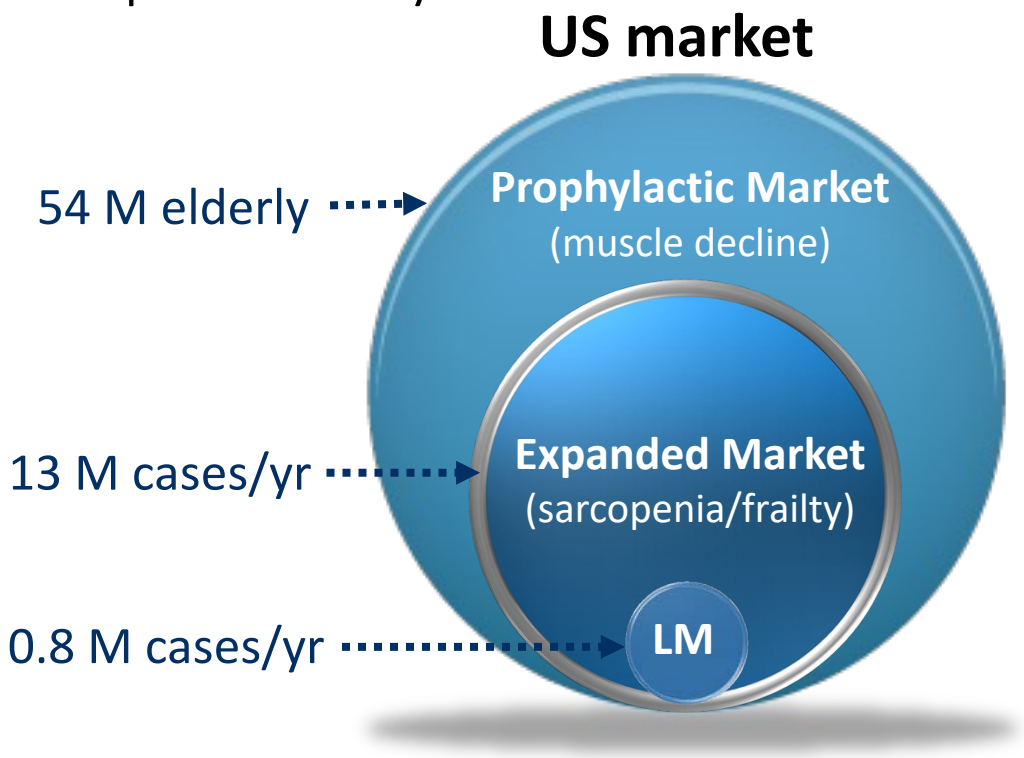
Rapid & strategic path to large markets

Launch market (LM)

- recovery from knee replacement surgery

Expanded market

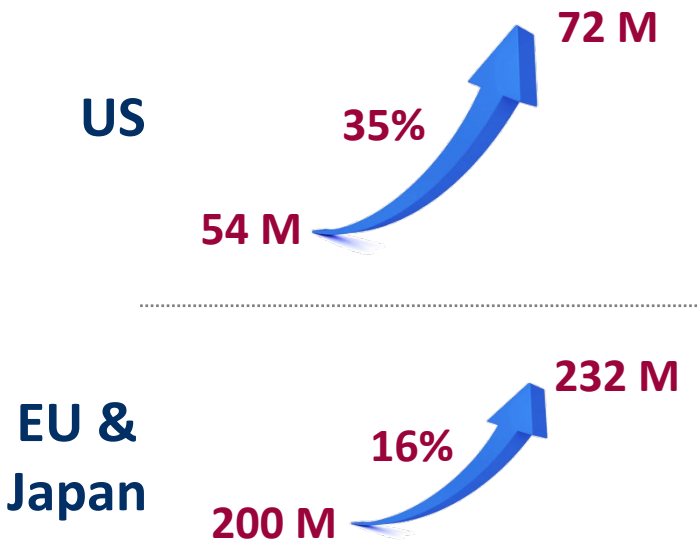
- sarcopenia & frailty



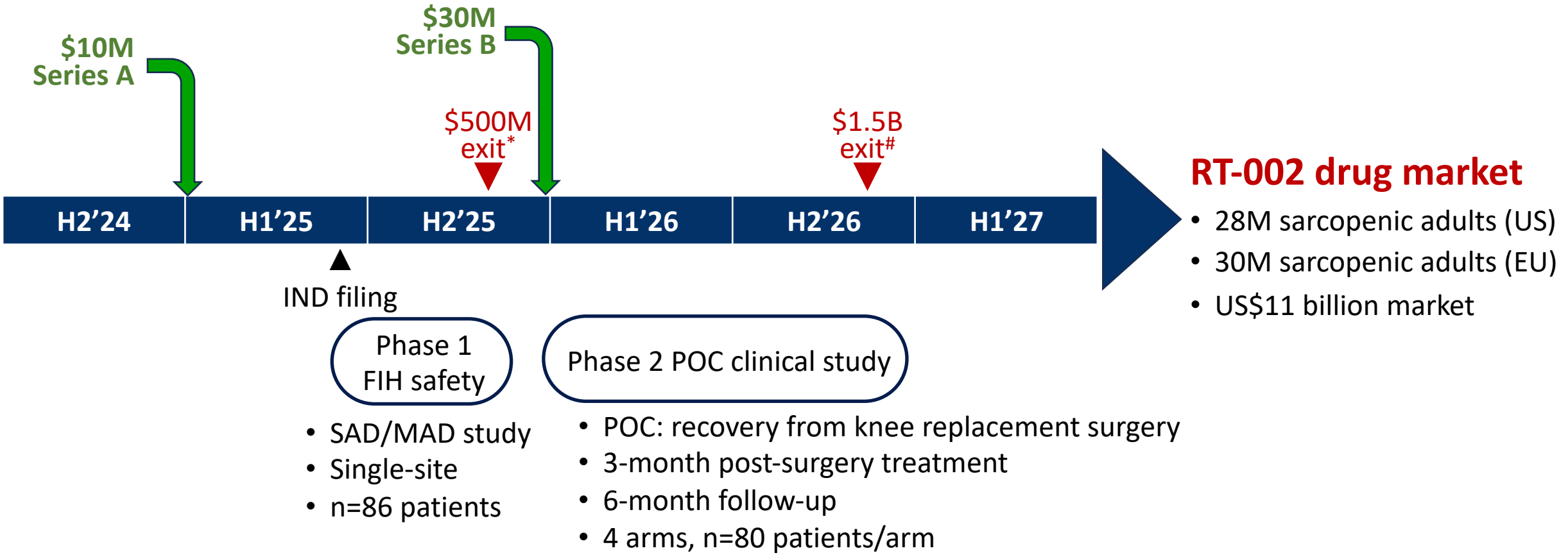
Market growth

- driven by growing elderly populations

Elderly population (2022 – 2023)



Rapid clinical milestones & high ROI exits



*Novo Nordisk paid $532M for Omega (Jan'24) (BioPharmaDive)

#Eli Lilly paid $1.9B for Versanis (7/23); Novo Nordisk paid $1.1B for Inversago (8/23) (BioPharmaDive)

RT-002: superior product profile

	NOVARTIS	CHUGAI	astellas	biophytis	BIOAGE	Ridgeline Therapeutics
Asset	Bimagrumab (activin receptor -mAb)	GYM3290 (activin receptor -mAb)	Stem cells	BIOS 101 (oral steroid)	BGE-105 (apelin receptor agonist)	RT-002
Phase	3	1	IND	3	1B	IND
Oral drug	✗	✗	✗	✓	✓	✓
Increases muscle size	✓	✓	?	✓	✓	✓
Increases muscle strength	✗	✓	✗	✗	?	✓
Reduces muscle fat	✗	✗	✗	✗	?	✓

Funding & strategic partnerships

Seeking $10M strategic investment to accelerate clinical trials

- $$ to complete first-in-human Phase 1 trials (6-mo, single-site trial design)
- High-value out-licensing to pharmaceutical giants
  - end of Phase 1 clinical trial (SAD/MAD safety readout)
  - end of Phase 2a clinical trial (POC efficacy)

Seeking strategic partnerships to accelerate clinical trials

- Collaborate on clinical trial design & execution
- Collaborate on EU regulatory approval
- Out-licensing opportunities

Experienced leaders & renowned advisors

Leadership

Stan Watowich, PhD
Founder & CEO

Harshini Neelakantan, PhD
Executive Director of Research

Suzanne Tomlinson, PhD, MBA
Director, Finance & Operations

Neil Warma, MBA
Executive Chair

Scientific Advisors

Quintin Anstee, PhD
Professor & Chair, Experimental Hepatology
Newcastle University, England

Johan Auwerx, PhD
Professor
Ecole Polytechnique (Switz.)

Ellen Binder, MD
Professor, Geriatric Medicine
Washington Univ (St. Louis)

Charles Brenner, PhD
Chair, Diabetes & Cancer Metabolism
City of Hope, CA

Michael Charlton, MBBS
Professor of Medicine, Dir. Ctr for Liver Diseases
Univ Chicago

Christopher Fry, PhD
Assoc Professor, Dept Clinical Nutrition
Univ Kentucky

Zbigniew Gugala, MD
Assoc Professor, Orthopedic Surgery
Univ Texas Medical Branch

David Halsey, MD
Past President. Am. Acad. Ortho. Surgeons
Univ Vermont

Jay Magaziner, PhD
Chair, Epidemiology & Public Health
Univ Maryland School of Medicine

Stan McHardy, PhD
Director, Ctr for Innovative Drug Discovery Univ Texas San Antonio

James Pacala, MD
Past President, Am. Geriatric Soc.
Univ Minnesota

Phillip Scherer, PhD
Director, Touchstone Diabetes Ctr
Univ Texas SouthWestern

Elena Volpi, MD, PhD
Director, NIH Pepper Ctr
Univ Texas Medical Branch

Robust pipeline of early-stage assets

Indication	Discovery	Preclinical	Phase 1	
Muscle regeneration				
Muscle damage recovery				RT-002
Frailty & sarcopenia				RT-002
ACL injuries				RT-003
Metabolic diseases				
Obesity				RT-004
NASH				RT-004
Chronic kidney disease				RT-004

Funding & accomplishments

2018

- $0.25M NIH NIA
- $0.25M NIH NIDDK
- Diabetes Innovation Challenge (Finalist)
- Top 100 Science Spinoffs

2019

- $4.2M DoD
- $0.25M NIH NIAMS
- Top-100 science discoveries (Curiosity Stream)

2021

- $4.1M NIH NIA
- Global Longevity Innovator Award (US Nat'l Academy of Medicine)

2023-24

- $0.6M NIH NIA
- $0.3M NIH NIAMS

Ridgeline Therapeutics

RT-002: age stronger, live longer

- Oral drug to restore & maintain muscle strength
- CMC, safety, & efficacy studies have significantly derisked IND filing
- Superior characteristics compared to competing therapeutics
- Rapid & strategic regulatory path to market approval
- Experienced leadership and renowned scientific advisors
- Strong composition-of-matter IP portfolio

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