

SRK-439 Selectively Inhibits Myostatin to Promote Healthy Body Composition During Metformin Therapy

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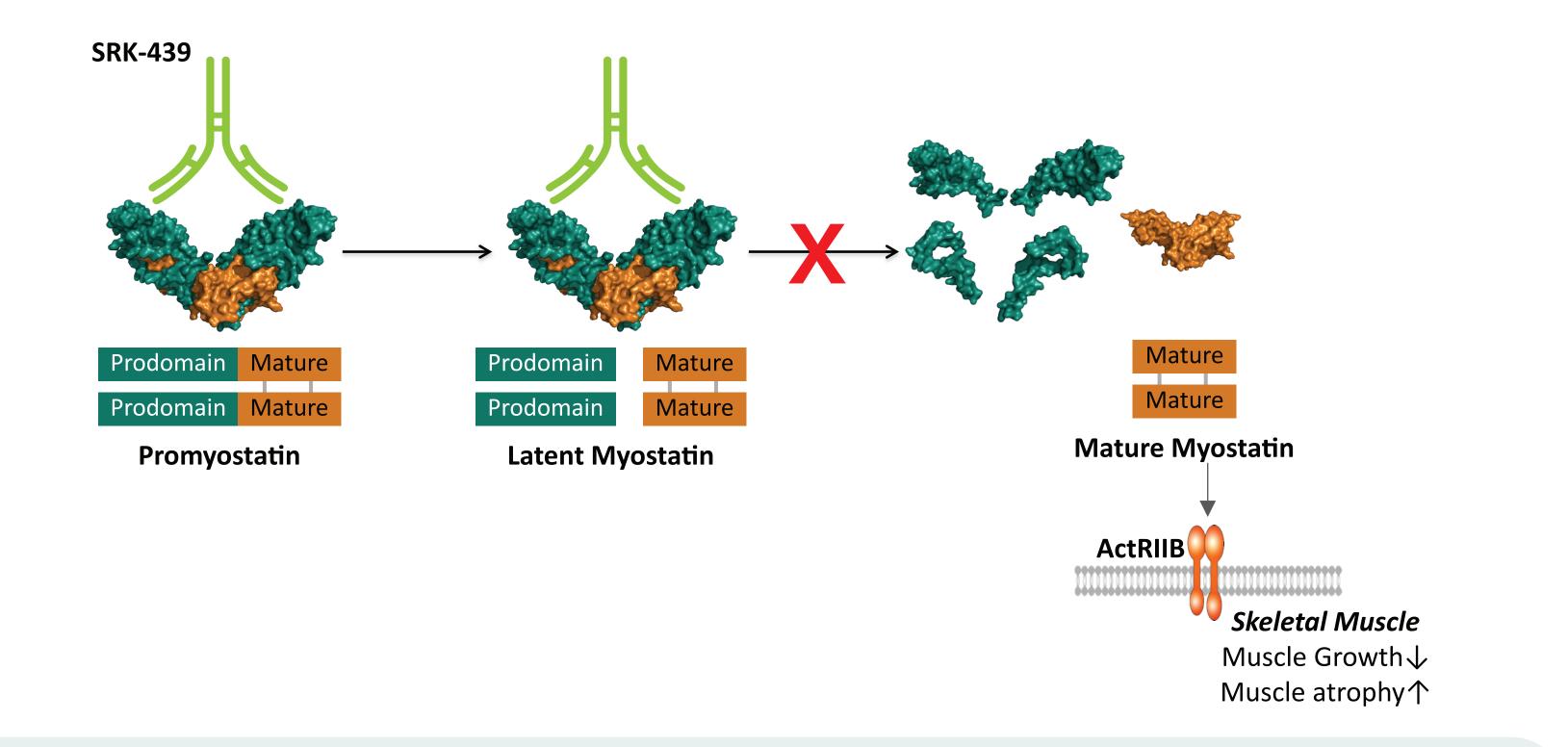
Hypothesis

The increase in the use of pharmacological weight loss interventions highlights the need to maintain a healthy body composition. Up to 40% of total weight lost is lean mass which may diminish long-term health benefits and make maintaining weight loss challenging. Safe and durable complementary therapies are needed to preserve lean mass. Myostatin is a growth factor expressed in skeletal muscle which restricts muscle mass. SRK-439 is a highly selective anti-pro and latent myostatin antibody that increases lean mass in mice. We have previously shown that a mouse chimera of SRK-439 administered with GLP-1 receptor agonists preserves lean mass and enhances fat mass loss in diet-induced obesity (DIO) mice. Clinical work using a related, less-specific mechanism demonstrated weight loss in participants with type 2 diabetes and obesity who were on metformin. We hypothesized that inhibiting myostatin during metformin treatment would maintain lean mass and improve body composition, which may have long-term metabolic benefits.

Background

Metformin is a commonly prescribed anti-diabetic drug which has been suggested to have both positive and deleterious effects on skeletal muscle. A clinical trial evaluating an ActRIIA/B-specific antibody in participants with type 2 diabetes and obesity demonstrated increased lean mass during weight loss; 87% of the total participants were taking metformin (Heymsfield 2021). However, non-selective targeting of the receptor has many potential safety liabilities and we believe selectively targeting myostatin is the preferred strategy.

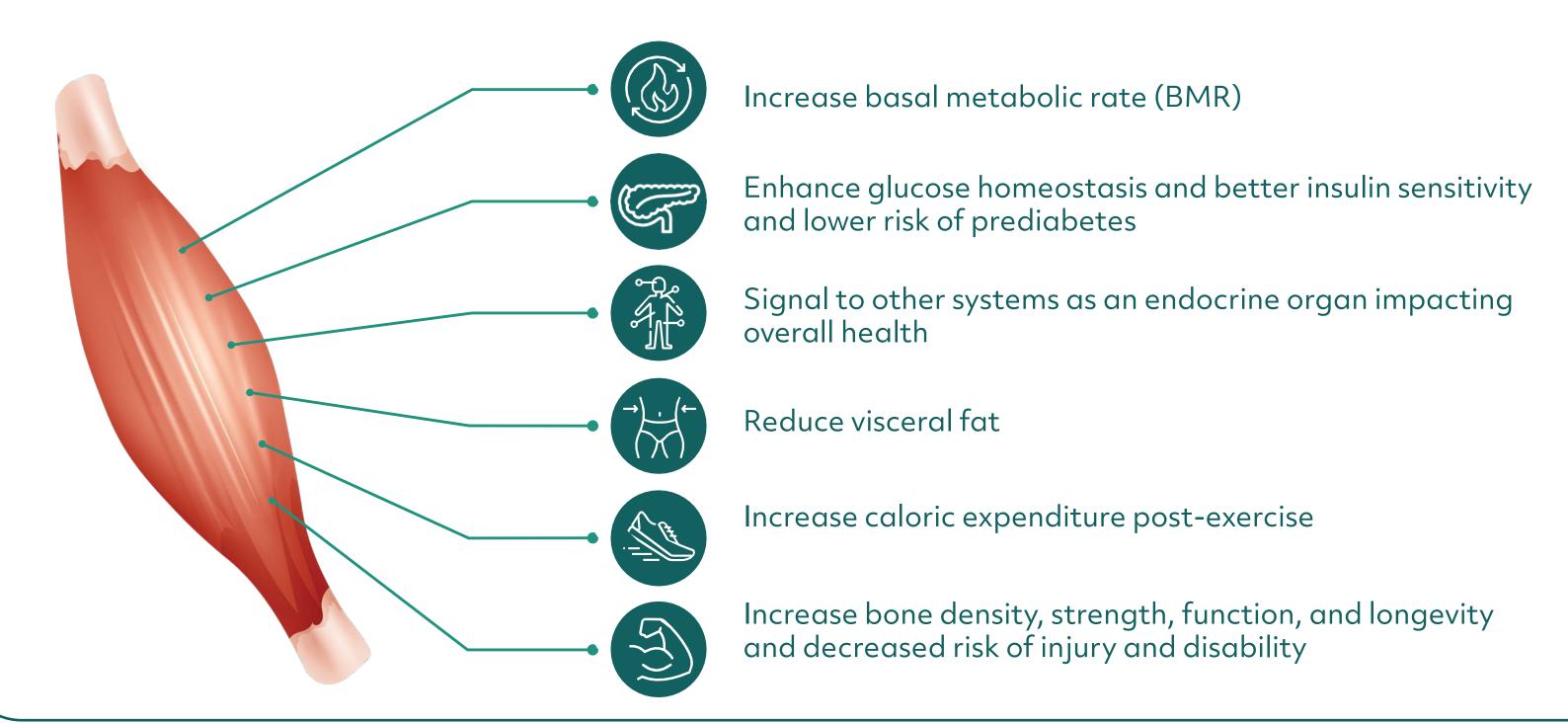
SRK-439 binds to pro- and latent myostatin to prevent activation and enable muscle growth

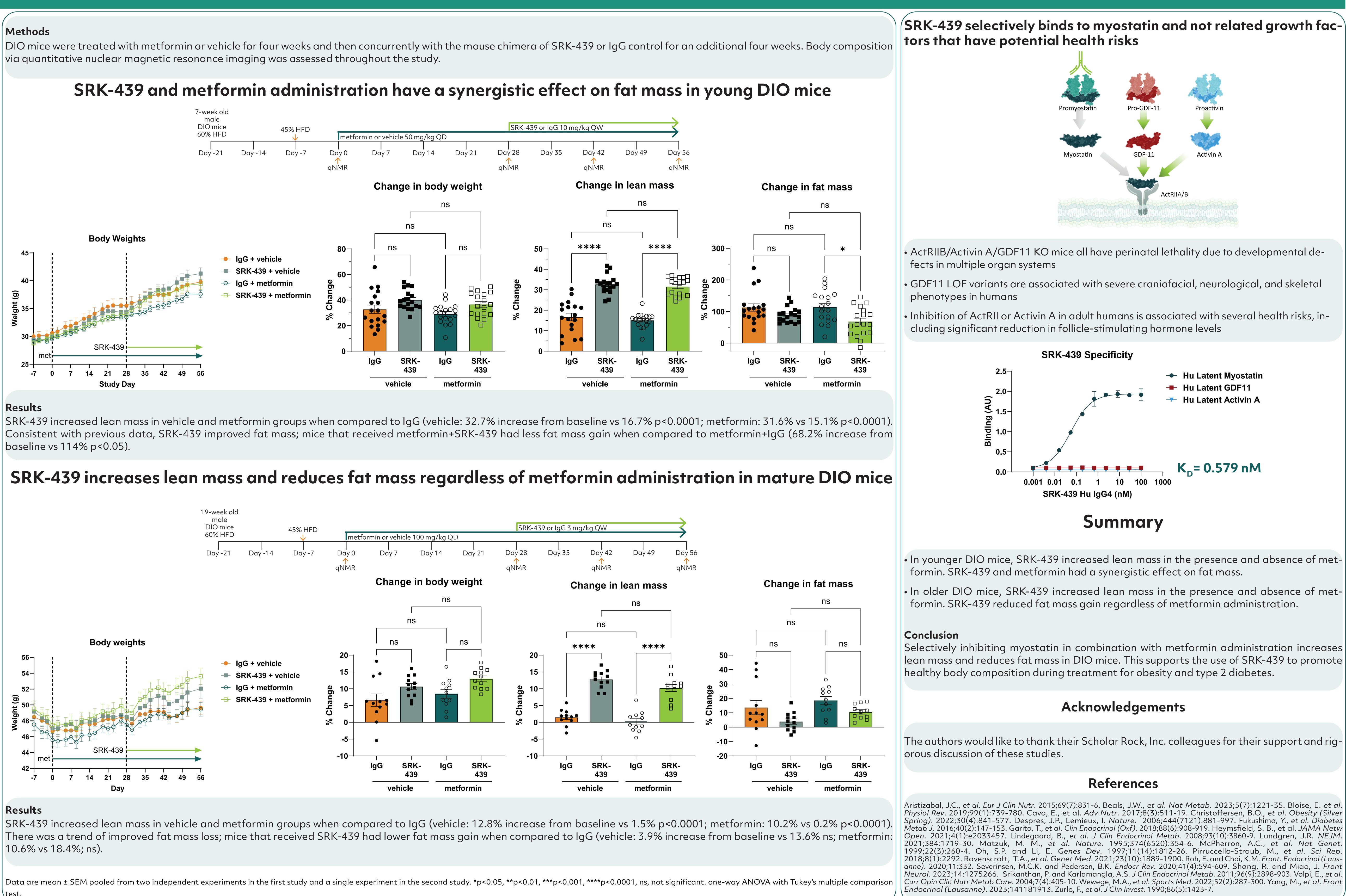


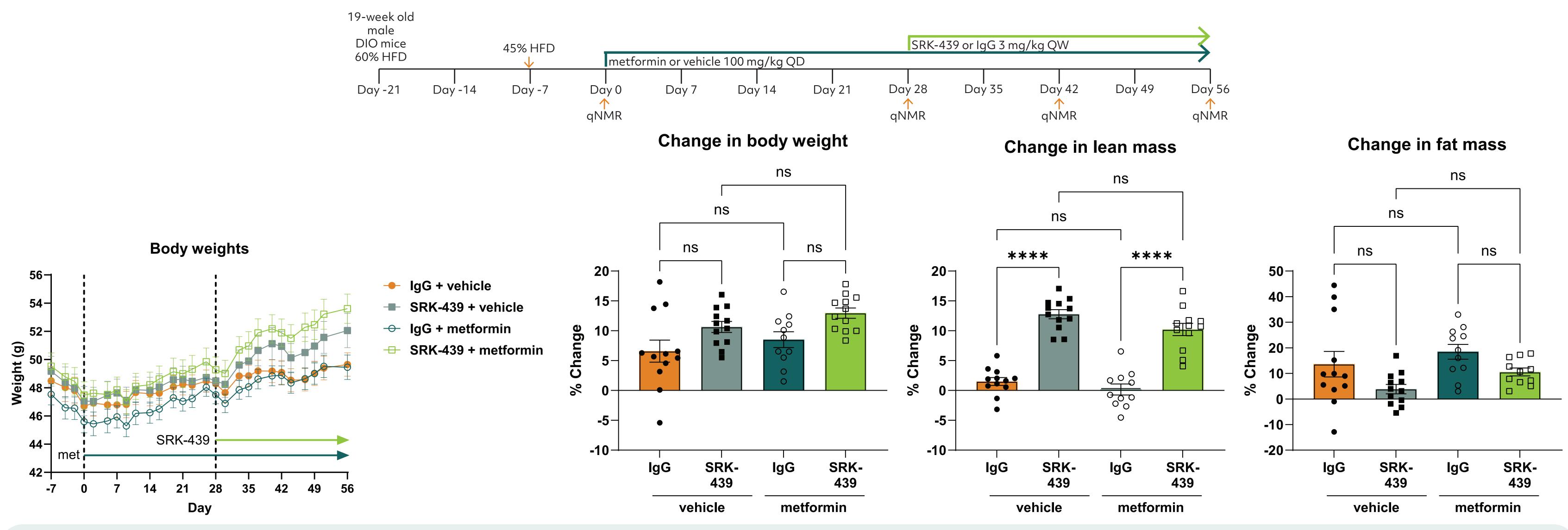
• SRK-439 binds to pro- and latent myostatin and blocks the conversion of the latent form to mature myostatin

• By inhibiting the release of mature myostatin, SRK-439 prevents myostatin from interacting with receptors which results in the inhibition of signaling and promotes muscle growth

Muscle is critical for overall health







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