Targeting the TGF-Beta Superfamily for the Treatment of Obesity

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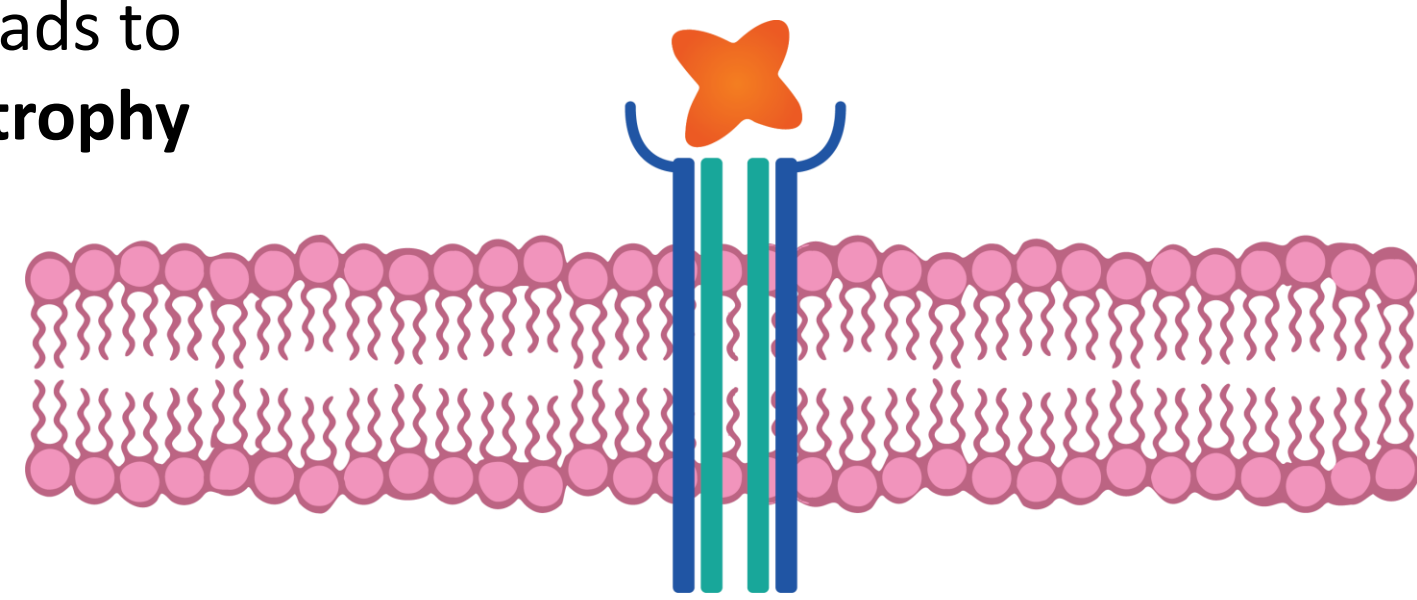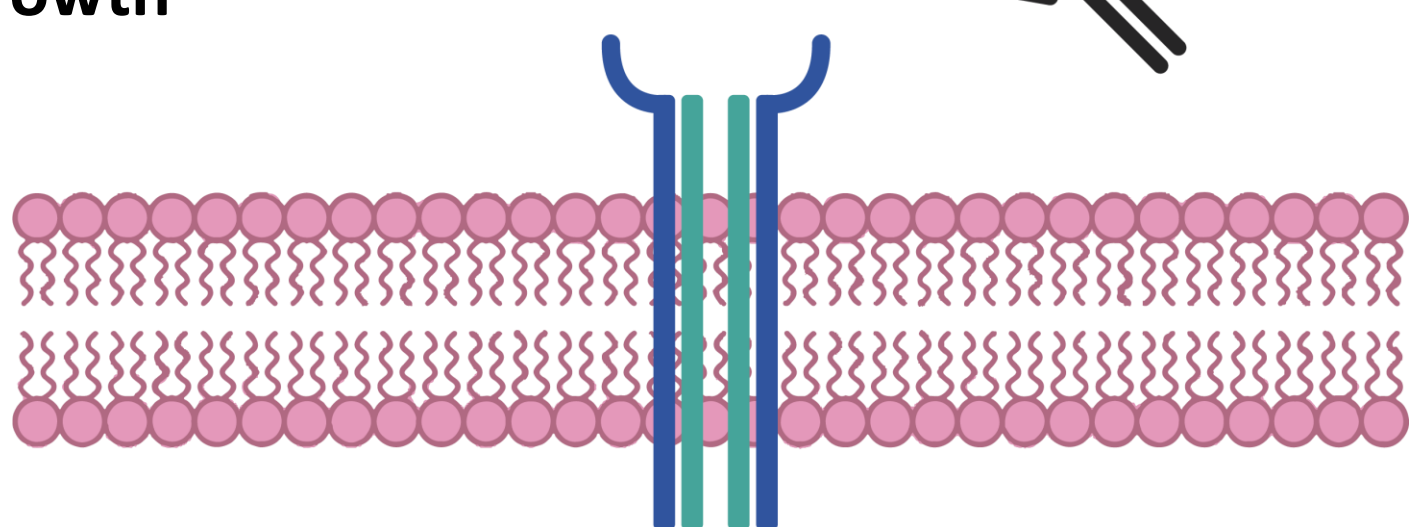
IBIO-600: Long-Acting Anti-Myostatin Antibody

Why target myostatin?

Binding of Myostatin to cells leads to **muscle atrophy**

Blocking of Myostatin leads to **muscle growth**

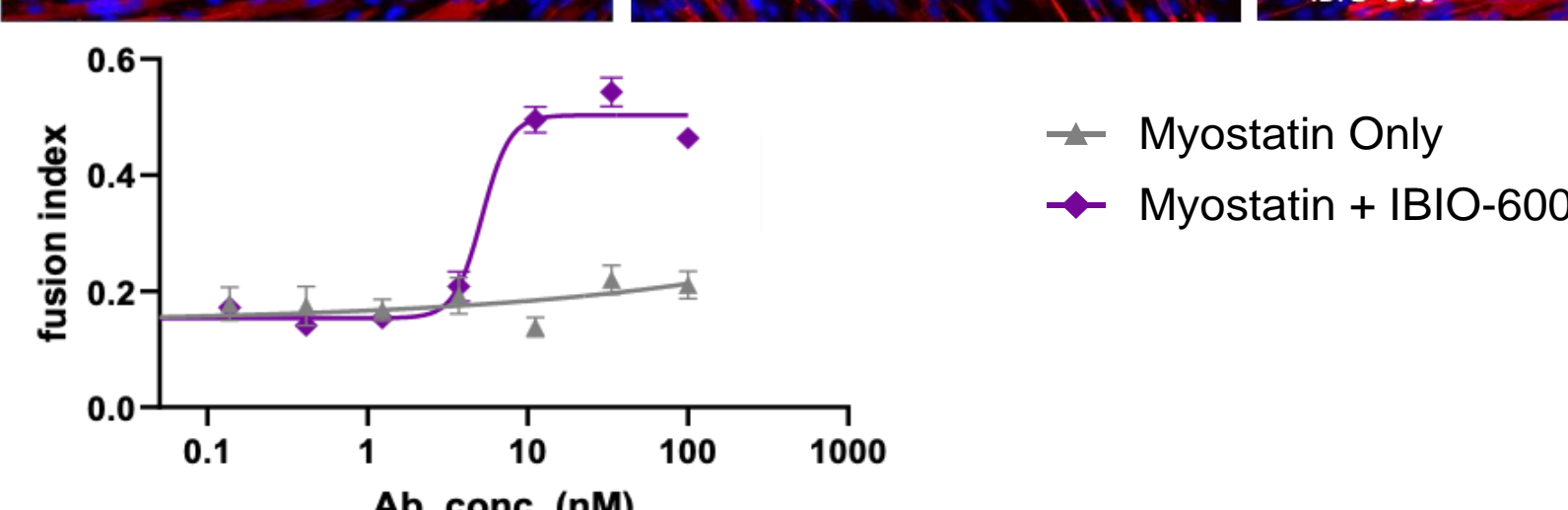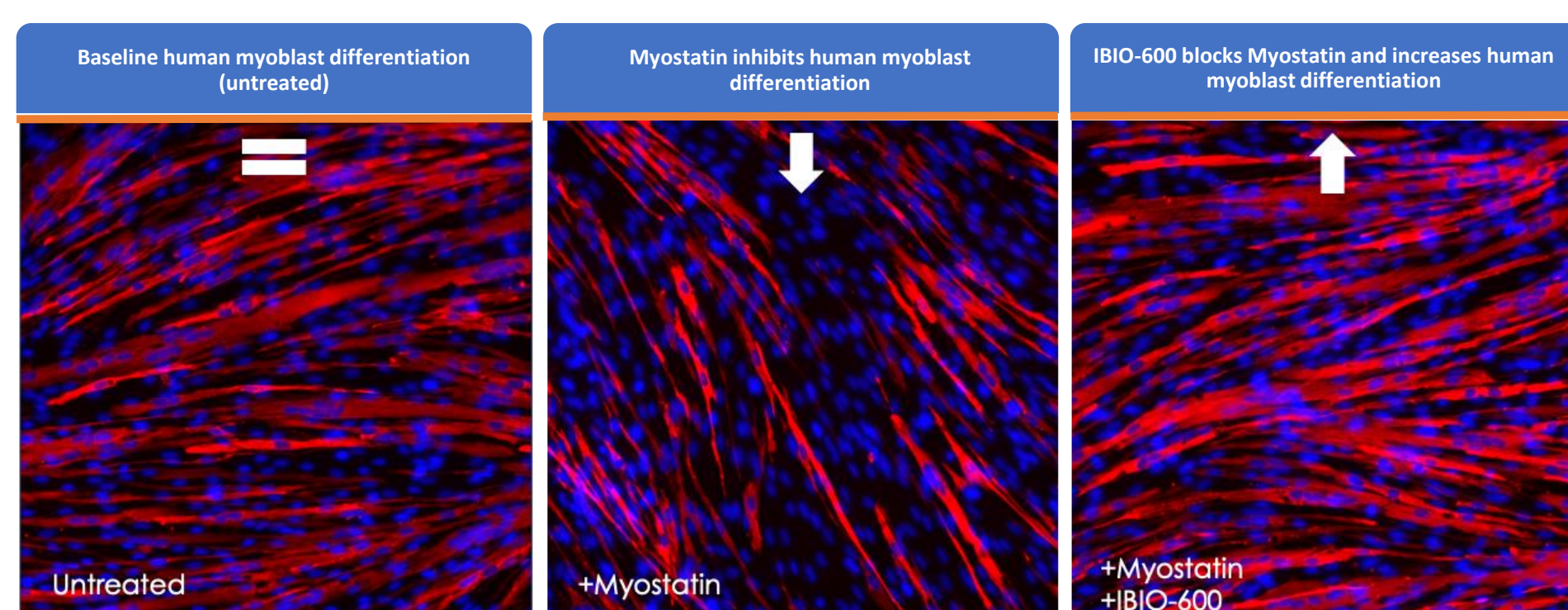### IBIO-600 differentiation

First-in-class innovation: First Myostatin therapy tailored for large, chronic disease populations

Convenient Dosing: Half-life extension anticipated to support dosing every 2-3 months
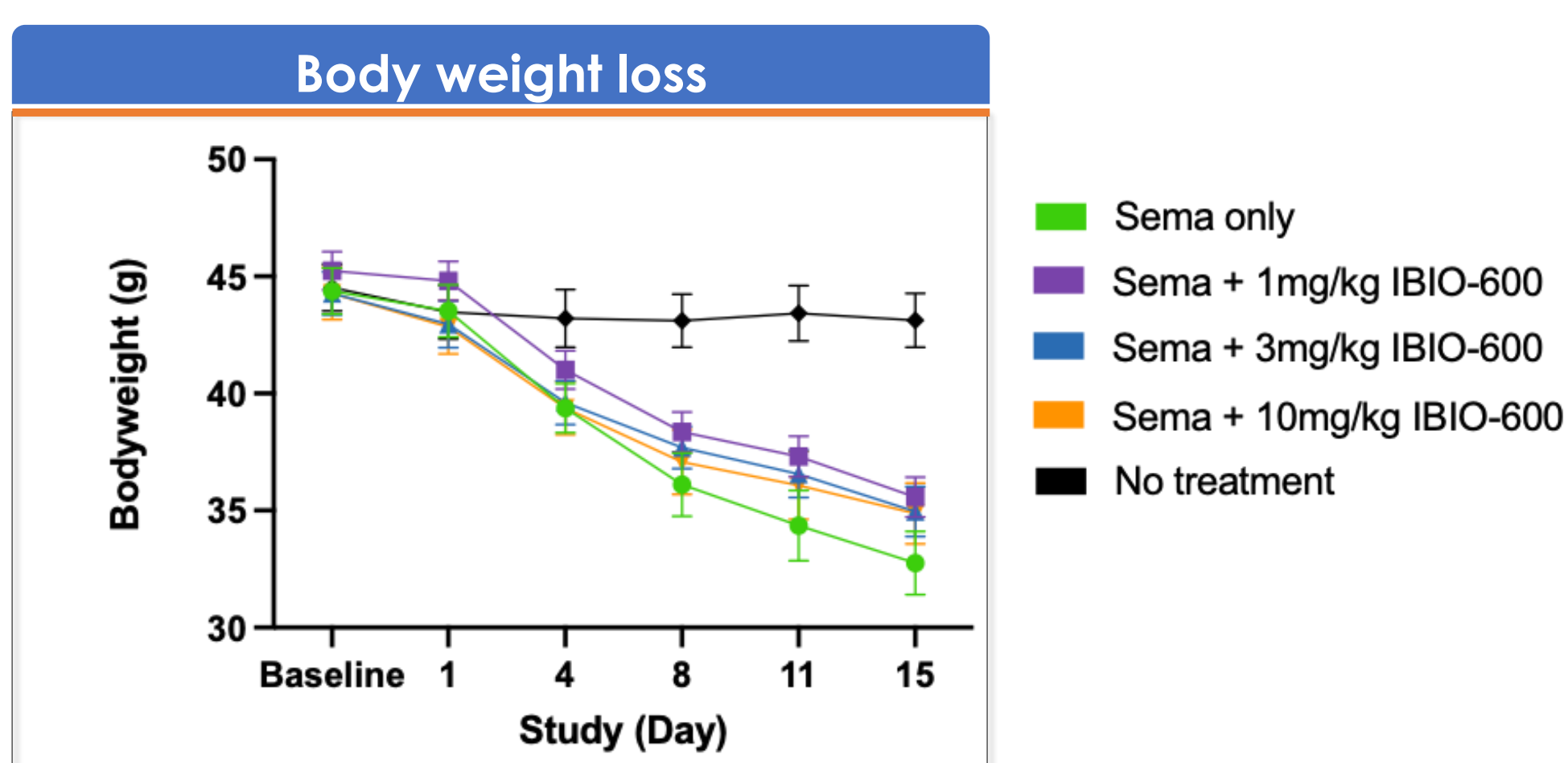
Broad Potential: Opportunities for expansion into sarcopenia, frailty, and other age-related disorders

Highly Developable: Resistant to various stress conditions, improved expression, high thermostability
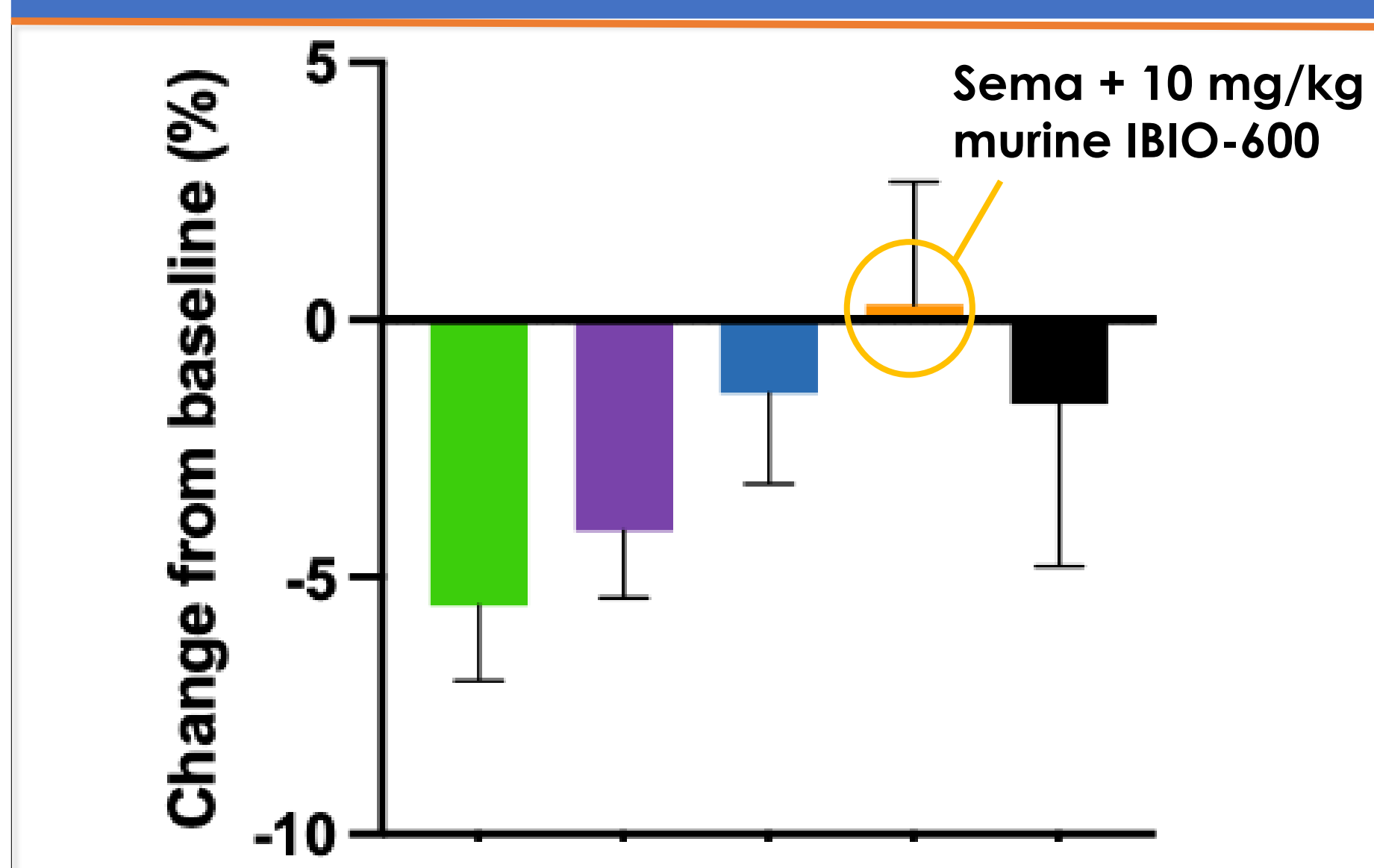
High potency in primary human myoblast cells

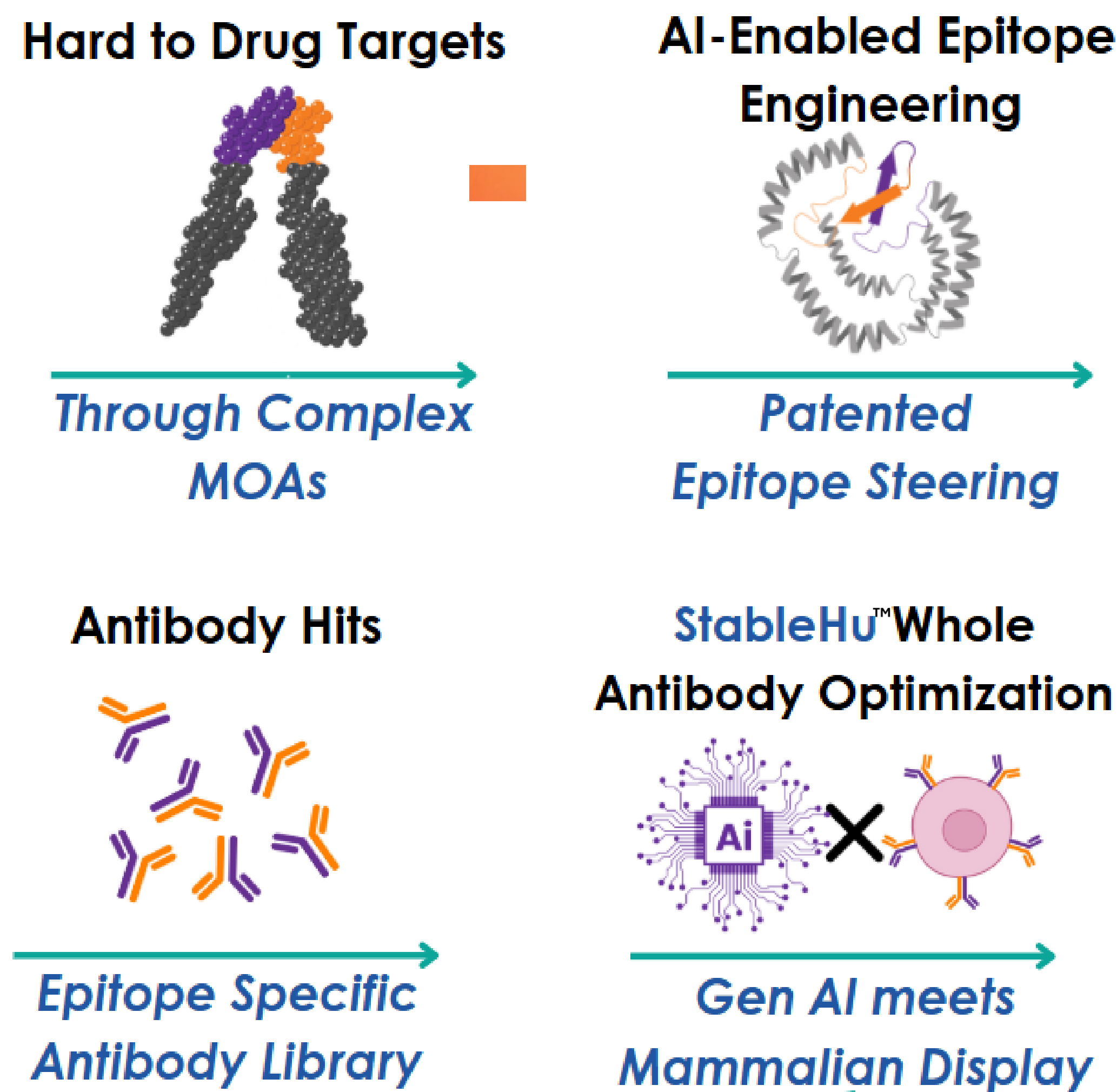Baseline human myoblast differentiation (untreated) — Untreated
Myostatin inhibits human myoblast differentiation — +Myostatin
IBIO-600 blocks Myostatin and increases human myoblast differentiation — +Myostatin +IBIO-600

fusion index vs Ab. conc. (nM)
— Myostatin Only
— Myostatin + IBIO-600

DIO mouse efficacy study

Body weight loss
Bodyweight (g) vs Study (Day): Baseline, 1, 4, 8, 11, 15
— Sema only
— Sema + 1mg/kg IBIO-600
— Sema + 3mg/kg IBIO-600
— Sema + 10mg/kg IBIO-600
— No treatment

Lean mass preservation at day 14
Change from baseline (%)
Sema + 10 mg/kg murine IBIO-600

iBio Technology Stack is a Fully Integrated Solution for Antibody Discovery

Deploy several different AI-enabled tools to discover and develop antibodies with robust drug properties

Hard to Drug Targets — *Through Complex MOAs*

AI-Enabled Epitope Engineering — *Patented Epitope Steering*

Antibody Hits — *Epitope Specific Antibody Library*

StableHu™ Whole Antibody Optimization — *Gen AI meets Mammalian Display*

Anti-Myostatin x Activin A Bispecific Antibody

Why target myostatin and activin A together?

Binding of Myostatin and/or Activin A to cells leads to **muscle atrophy**
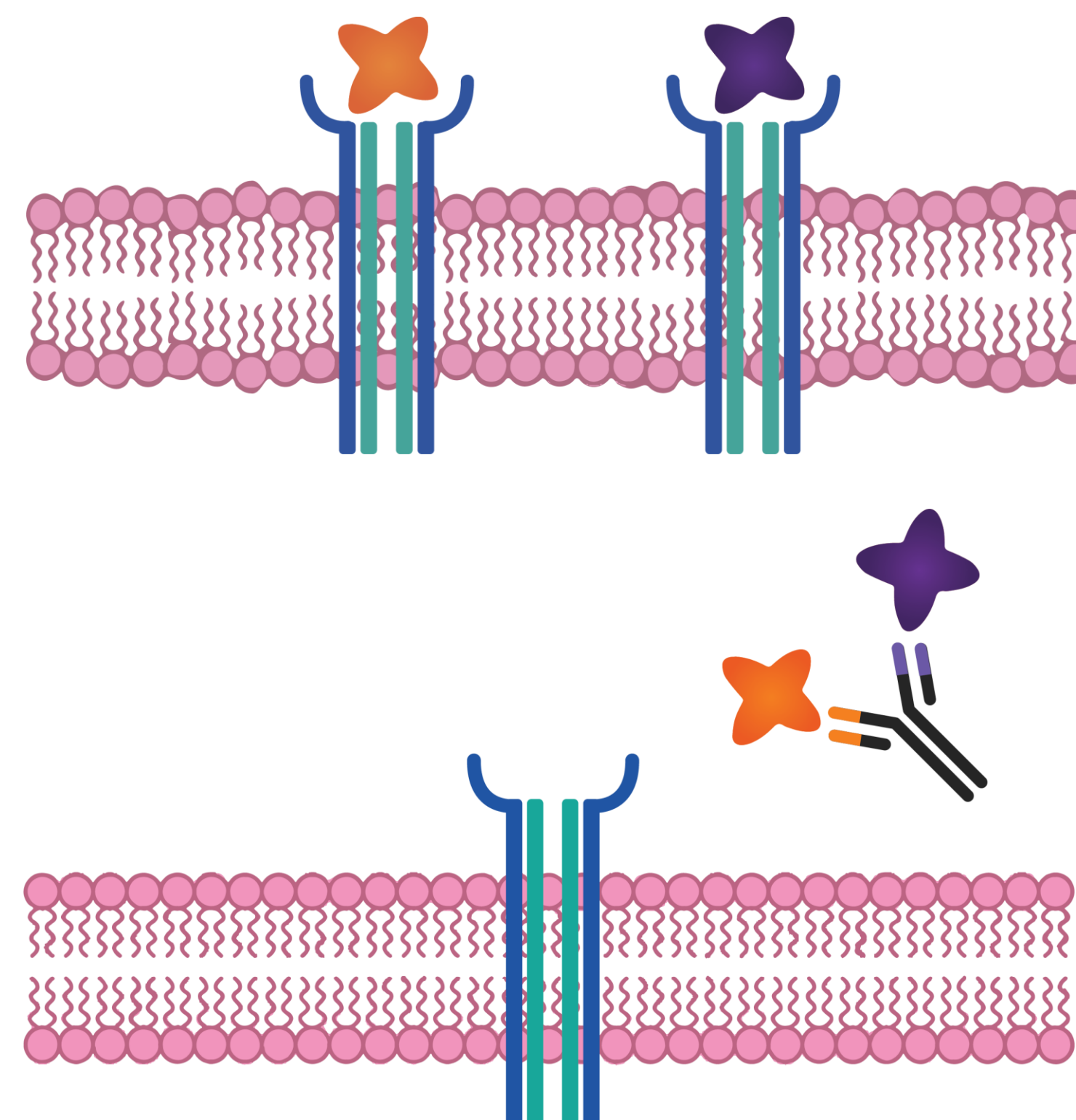
Simultaneous blocking of Myostatin and Activin A leads to **muscle growth**

iBio differentiation

First-in-class innovation: Myostatin x Activin A bispecific antibody with unique therapeutic potential
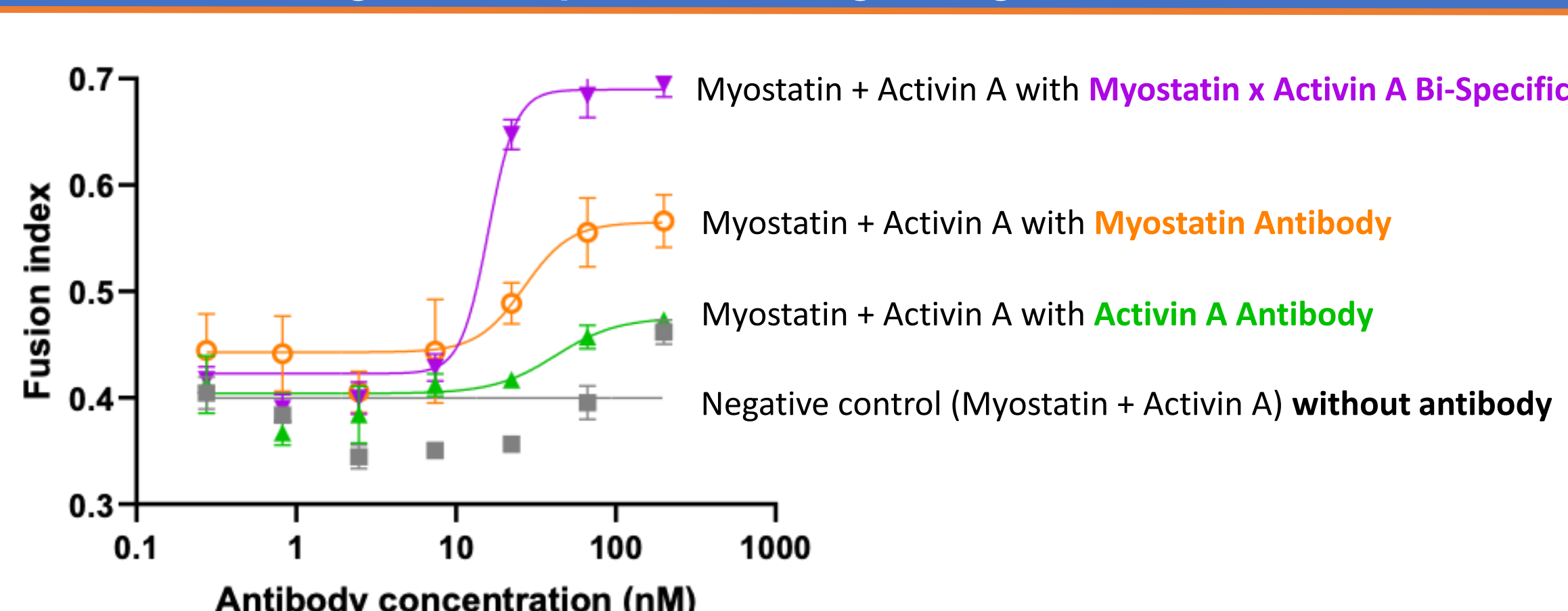
Convenient Dosing: Half-life extension potentially enables dosing every 2-3 months

Optimize Potency: Higher-valency antibody format might increase potency and reduce dose

Potential Advantage: Avoids bone morphogenic protein (BMP) inhibition, minimizing bleeding risks associated with ligand traps
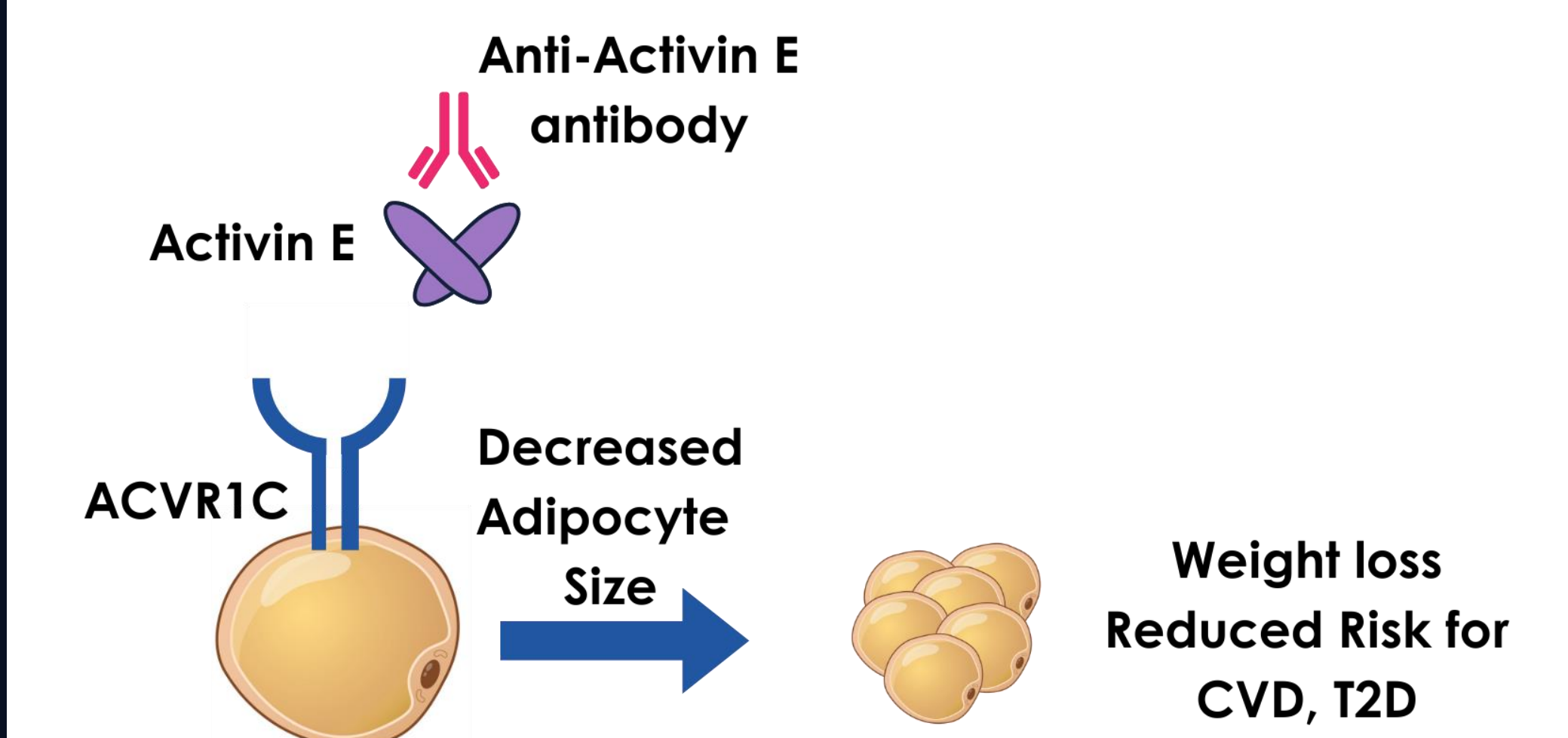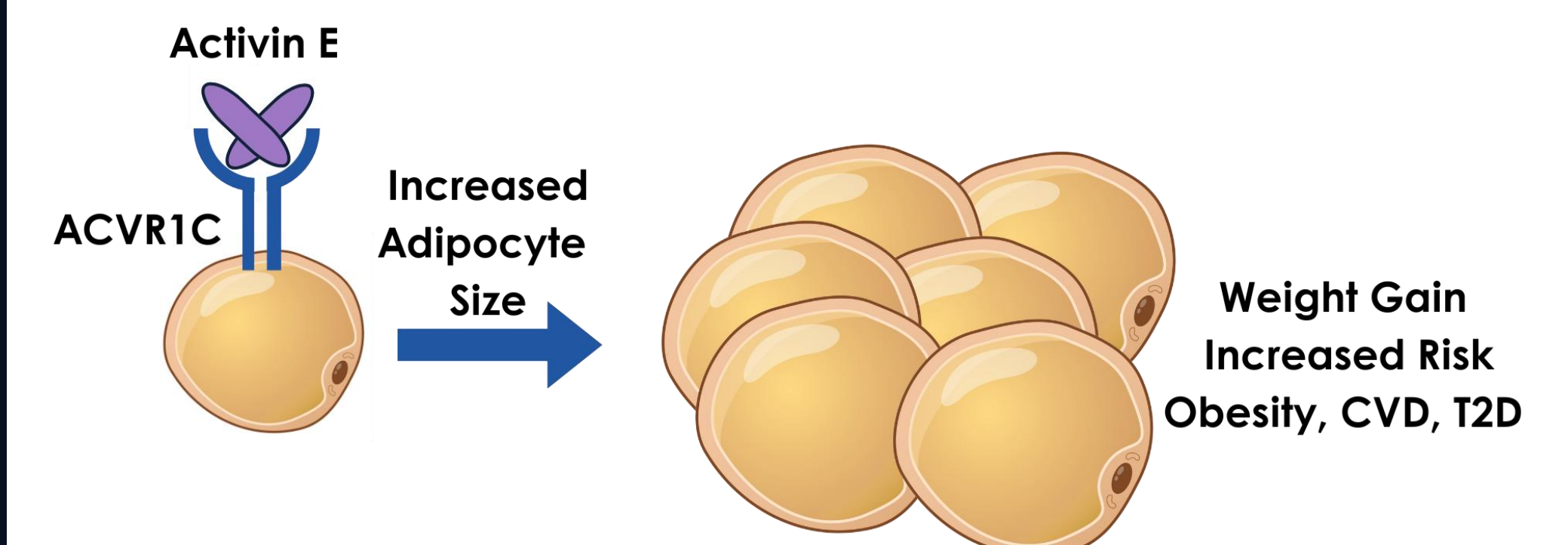
Combinatorial effects on primary human myoblast cells in cell-based assay

Robust blockade of both muscle growth suppressors, enabling increased muscle growth beyond what single-target antibodies achieve

Fusion Index vs Antibody concentration (nM)
— Myostatin + Activin A with **Myostatin x Activin A Bi-Specific**
— Myostatin + Activin A with **Myostatin Antibody**
— Myostatin + Activin A with **Activin A Antibody**
— Negative control (Myostatin + Activin A) **without antibody**

Activin E Antagonist Antibody

Why target activin E?

Activin E — ACVR1C — Increased Adipocyte Size → Weight Gain Increased Risk Obesity, CVD, T2D

Anti-Activin E antibody — Activin E — ACVR1C — Decreased Adipocyte Size → Weight loss Reduced Risk for CVD, T2D
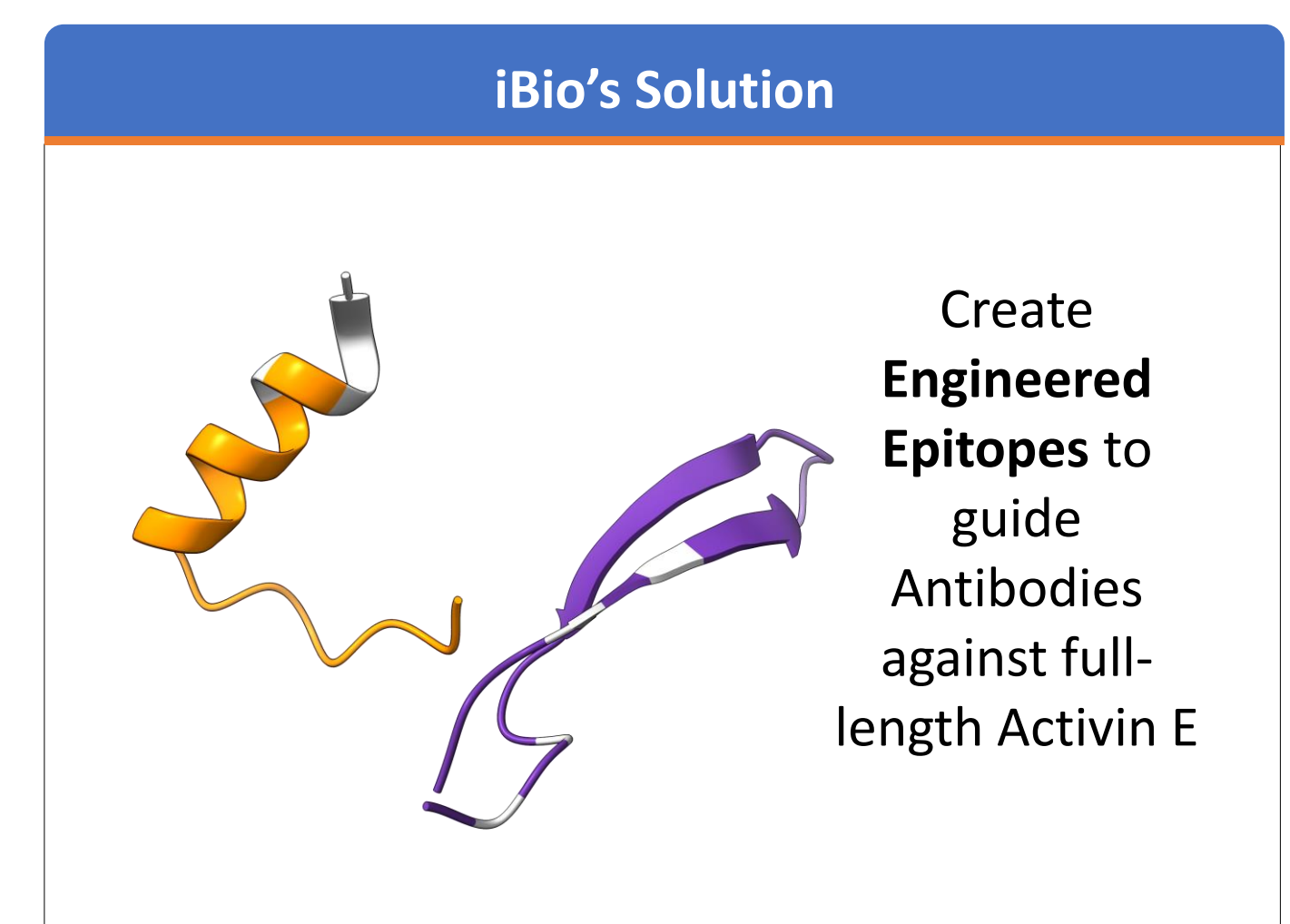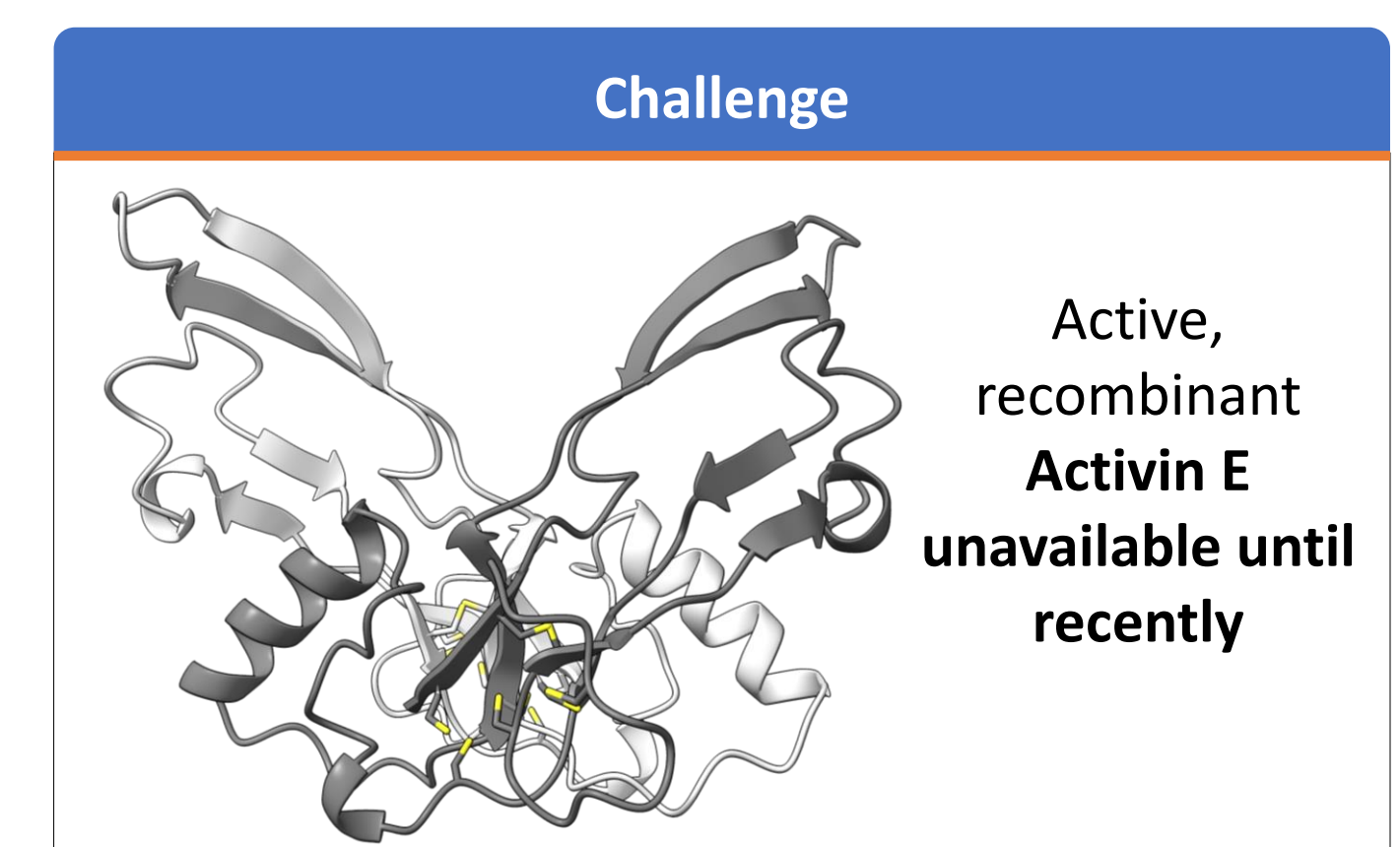
iBio Differentiation

Innovative AI solution: Epitope steering engine overcame the challenge of full-length Activin E unavailability, creating a first-in-class antibody targeting Activin E

Convenient Dosing: Half-life extension potentially enables dosing every 2-3 months

Versatile Combinability: Easily integrates with other TGFβ family targets into bispecific antibodies, offering a potential alternative to incretin drugs (fat-specific weight loss with increase in muscle mass)

Challenge
Active, recombinant **Activin E unavailable until recently**

iBio's Solution
Create **Engineered Epitopes** to guide Antibodies against full-length Activin E

First-in-class activin E antagonist mAb

Potent blockade of activin E signaling in cell-based assay

Activin E Signaling (lower is better) vs Antibody Concentration (nM)
— Activin E alone
— Activin E plus Activin E Antibody