Anti-Myostatin x Activin A Bispecific Antibody

Combined Myostatin and Activin A Antagonism

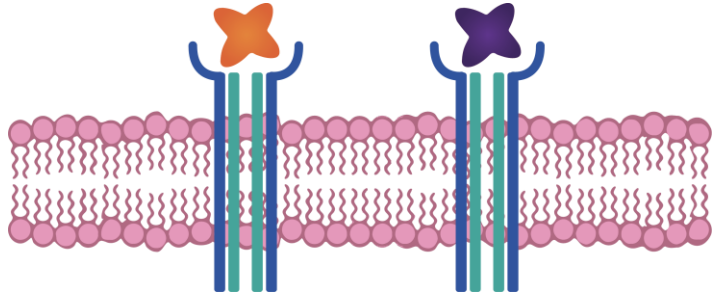
Synergistic Effect on Muscle Growth and Potential Treatment for Pulmonary Hypertension (PH) in Heart Failure With Preserved Ejection Fraction (HFpEF)

For obesity, we are developing bi-specific **co-inhibitors of Myostatin and Activin A** to **enhance muscle growth** and **improve quality of weight loss** during and after treatment with incretin drugs

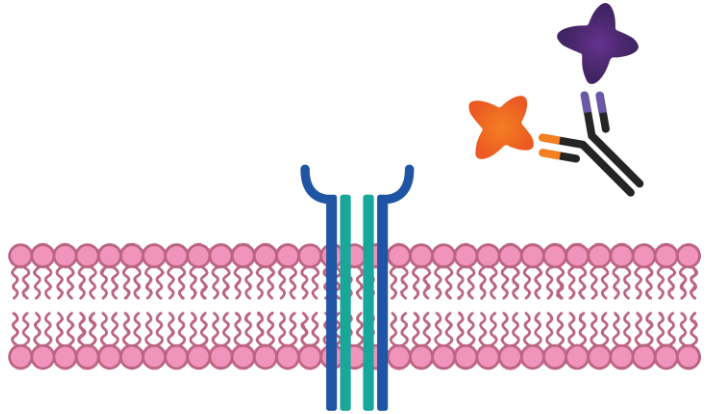
Why Myostatin & Activin A

- Myostatin and Activin A are **key negative regulators** of muscle mass
- Both are members of the TGFβ superfamily
- Activin A mechanism is **pharmacologically validated**[1, 2]
- **Combined** Activin A and Myostatin **inhibition**, **causes** more **pronounced muscle growth**[3]
- Myostatin and Activin A inhibition are **key features for treating PH-HFpEF**

Binding of Myostatin and Activin A to cells leads to **muscle atrophy**



Simultaneous blocking of Myostatin and Activin A leads to **muscle growth**



1.Villanueva, J. et al. Am J Cardiovasc Drugs (2024).
2.US20220119514A1, Regeneron corporate slides
3.Latres, E. et al. Nat Commun 8, 15153 (2017).

A Long-Acting First-in-Class Anti-Myostatin x Activin A Bispecific Antibody

Myostatin x Activin A Bi-specific

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: May avoid BMP* inhibition, minimizing bleeding risks associated with ligand traps

Target product profile for obese and potentially Ph-HFpEF patients

- Well-tolerated for long-term use
- Infrequent subcutaneous self-administration

AI-enabled CDR design

- Generates novel IP
- Large library of novel lead molecules

Single-shot multi-dimensional lead optimization

- Bi-specific optimized for affinity, half-life and manufacturability

*Bone Morphogenetic Proteins

iBio's Myostatin and Activin A Bi-Specific Targets Both Key Negative Muscle Regulators, Synergistically Increasing Muscle Mass

In Vitro Data

Only a Myostatin x Activin A bi-specific antibody fully blocks both muscle growth suppressors, enabling optimal growth, while single-target antibodies fall short

Increased muscle fusion index in human muscle stem cells is a surrogate of muscle growth