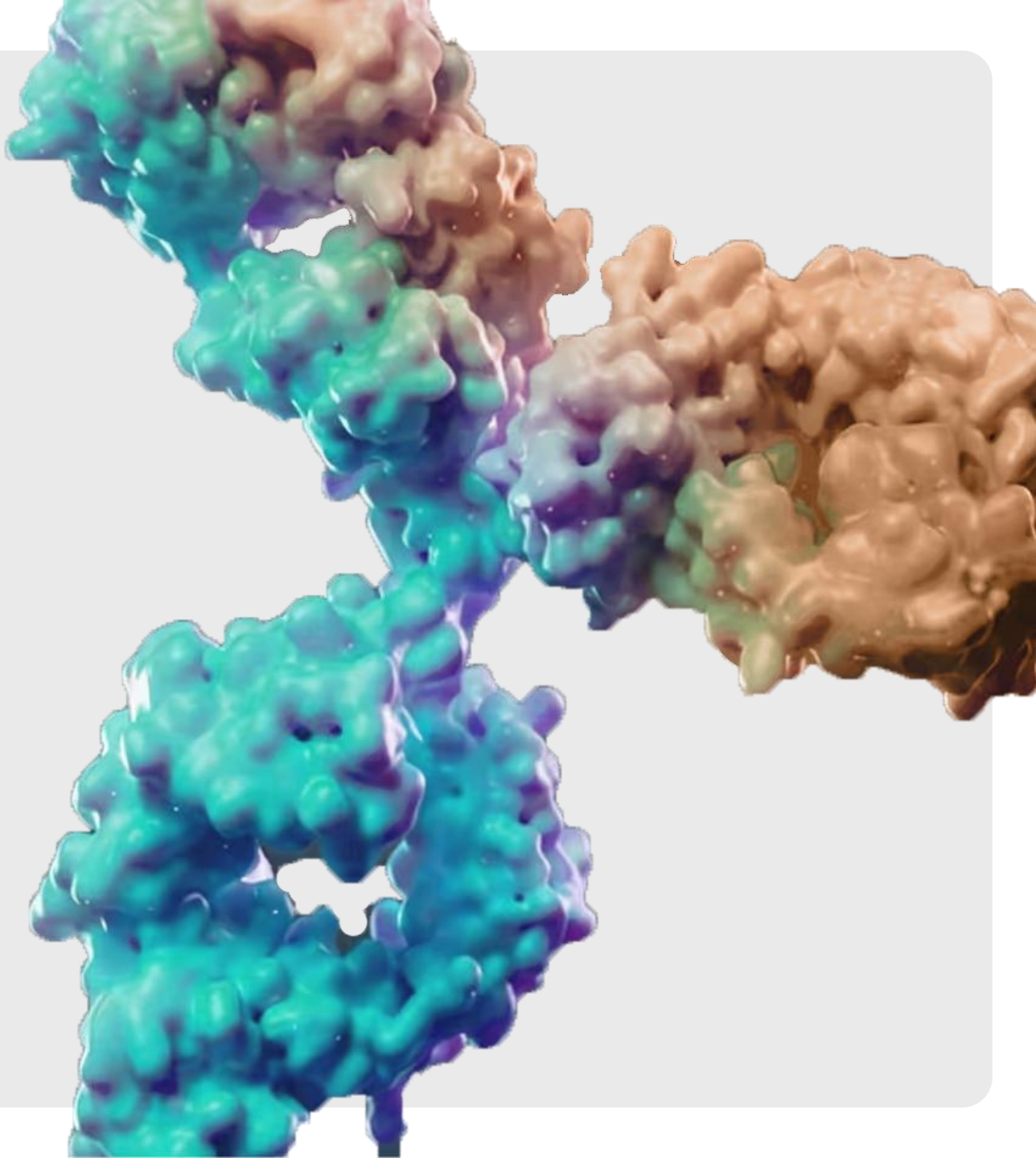
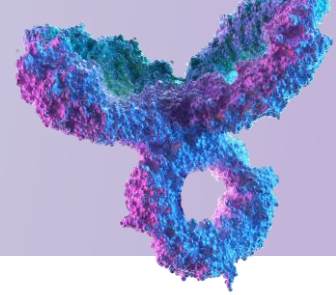
Myostatin and Activin A Bispecific



Combined Myostatin and Activin A Antagonism
Precision Bispecific Approach to Address Root Drivers of PH-HFpEF*



Targeting the Core Biology of Disease Across Multiple Organs

- Our bispecific antibody is designed to selectively neutralize what are believed to be key pathological ligands:
  - **Activin A** → cardiac fibrosis and vascular remodeling[1]
  - **Myostatin/GDF11** → skeletal muscle dysfunction and exercise intolerance[2,3]
- Together, these pathways address two major biological drivers of PH-HFpEF.

Selective Modulation Rather Than Broad Pathway Blockade[4]

- Our bispecific antibody is constructed from first principles to achieve intentional selectivity
- Intentionally spares related signaling molecules maintaining physiologic balance
- Focused on disease-driving biology

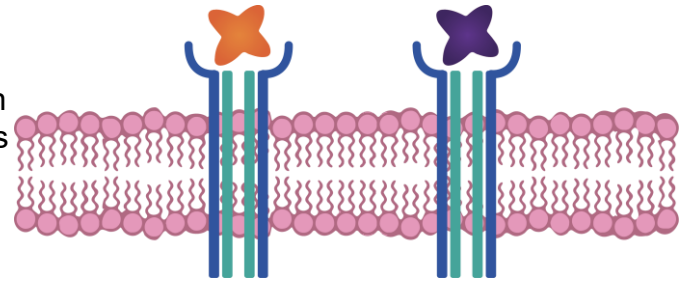
Platform-Enabled Precision Engineering

- Mammalian display platform allows rapid generation of highly selective multispecific antibodies
- Design strategy enabled by iBio's experience in the TGF-β superfamily

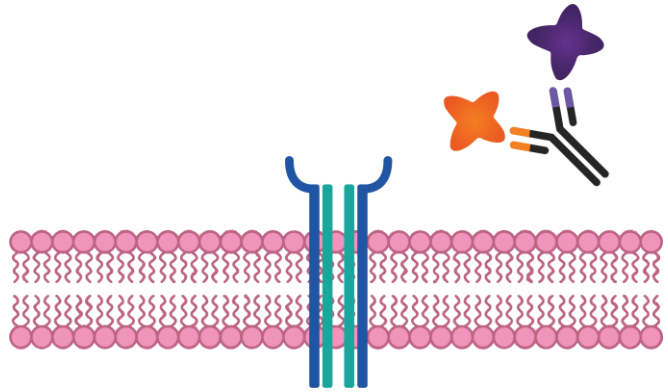
Strategic Value

- A differentiated, multi-organ therapeutic approach in a clinically validated pathway with strong partnering potential.

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



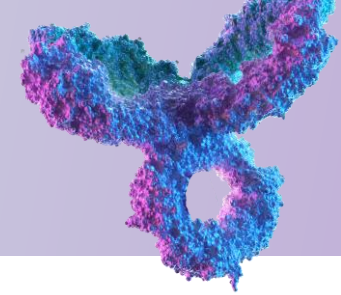
Simultaneous blocking of Myostatin and Activin A leads to **muscle growth**

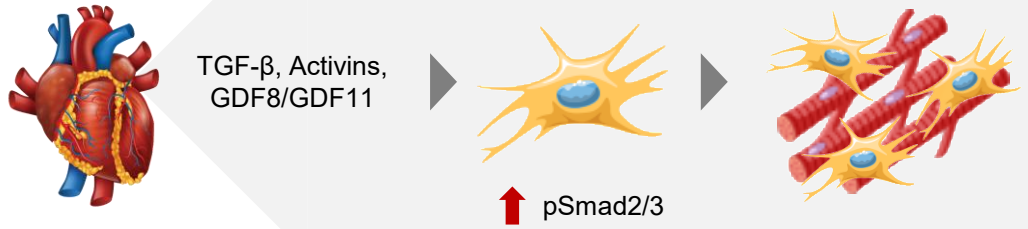


* Pulmonary Hypertension (PH) in Heart Failure With Preserved Ejection Fraction (HFpEF)

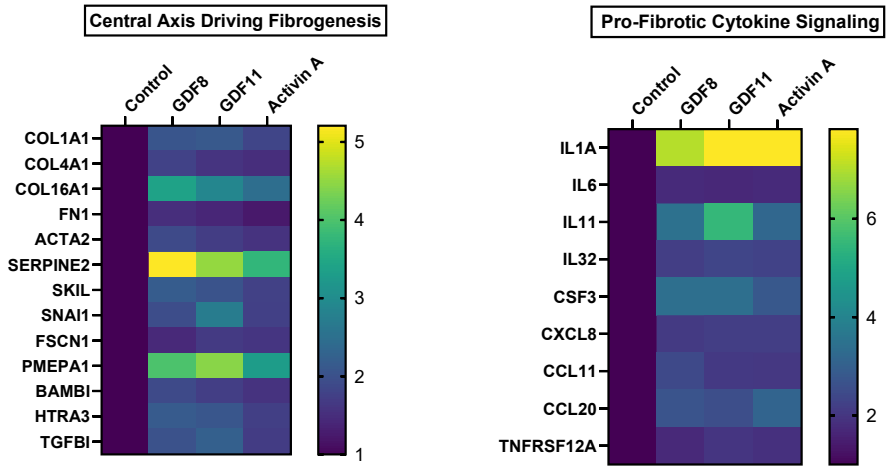
1. Roh, J., et al. Sci Transl Med (2020)
2. Abati, E., et al. Cell Mol Life Sci (2022)
3. Zimmers, T.. et al. Basic Res Cardiol (2017)
4. Lan, Z., Lv, Z., Zuo, W. & Xiao, Y. From bench to bedside: The promise of sotatercept in hematologic disorders. Biomedicine & Pharmacotherapy 165, 115239 (2023)

GDF8, GDF11, and Activin A Promote Fibrotic Activation of Cardiac Fibroblasts

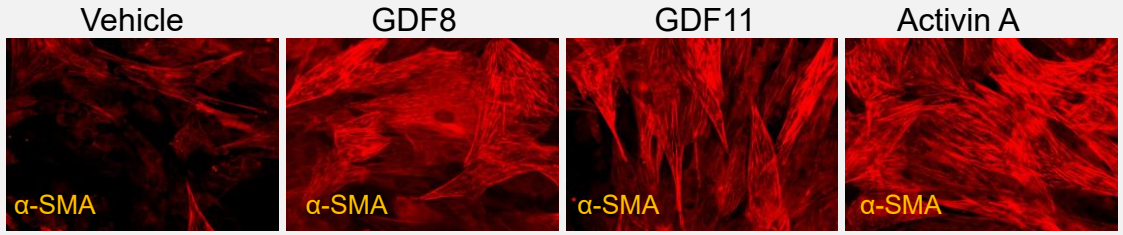


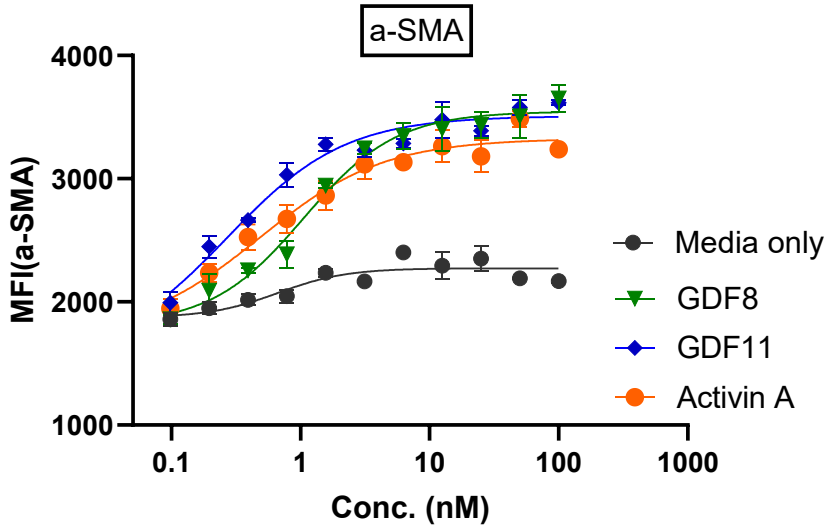


Induction of Fibrotic and Pro-Inflammatory Gene Expression in Human Cardiac Fibroblasts



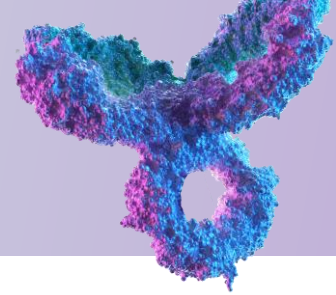
INDUCE KEY FIBROTIC PROTEIN EXPRESSION- α-SMA*



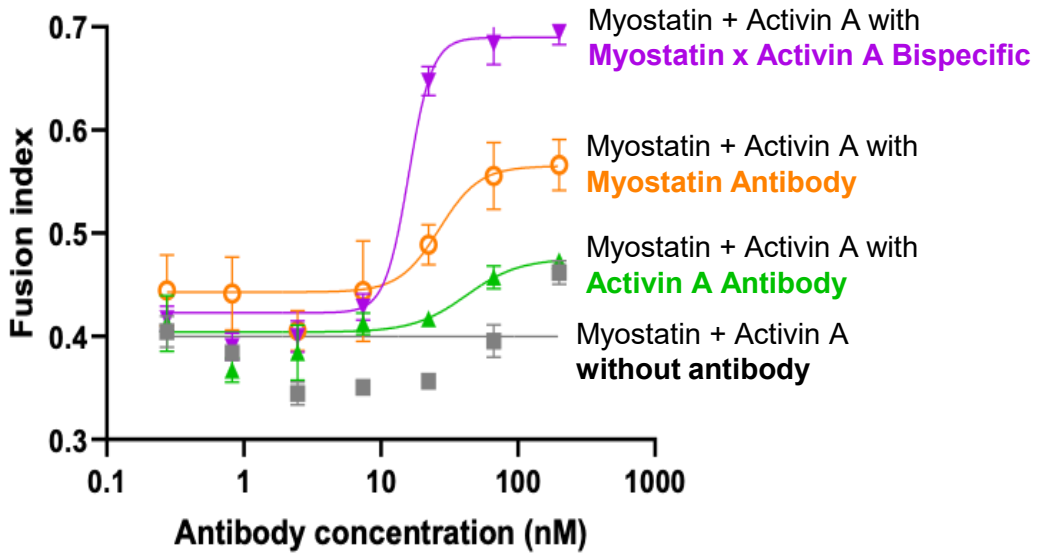


*Alpha-Smooth Muscle Actin (α-SMA); marker for fibroblast activation
Data on file

iBio's Myostatin and Activin A Bispecific: Combined, Antibody-Mediated Blockade of GDF8/GDF11/Activin A



INCREASED MUSCLE FUSION INDEX IN HUMAN MUSCLE STEM CELLS IS A SURROGATE OF MUSCLE GROWTH



IMPROVEMENT IN STRESS-INDUCED RIGHT VENTRICULAR REMODELING

Mouse Model of HFpEF

- Diet-induced obesity
- Induced hemodynamic stress