IBIO-600

Long-Acting Anti-Myostatin Antibody

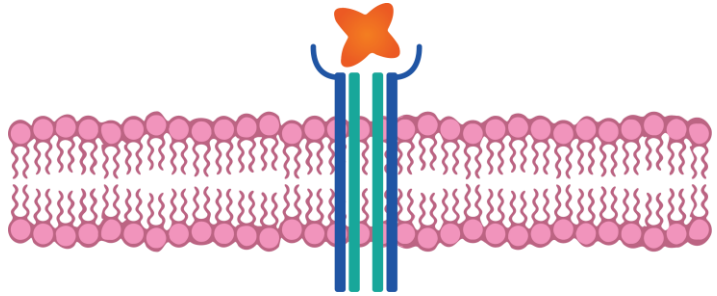
Strengthening the Weight Loss Journey: Myostatin Inhibition to Preserve Muscle Mass

We are developing Myostatin inhibitors to potentially **preserve and increase muscle mass**, **complementary to** current treatments

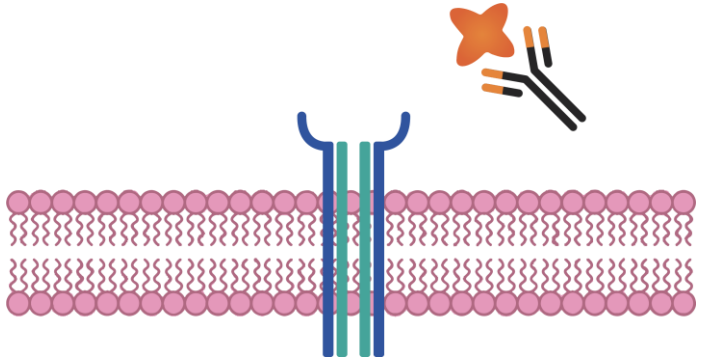
Why We Target Myostatin

- **Incretin drugs** reduce caloric intake, causing **weight loss in both fat and muscle**
- Myostatin is a **highly validated key negative regulator** of muscle mass[1]
- Inhibition of Myostatin function observed to drive significant **muscle growth** with a generally positive safety profile in some third-party studies
- Beyond its effects on muscle, Myostatin plays a role in the **regulation of total body fat mass**[2]

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



Blocking of Myostatin leads to **muscle growth**



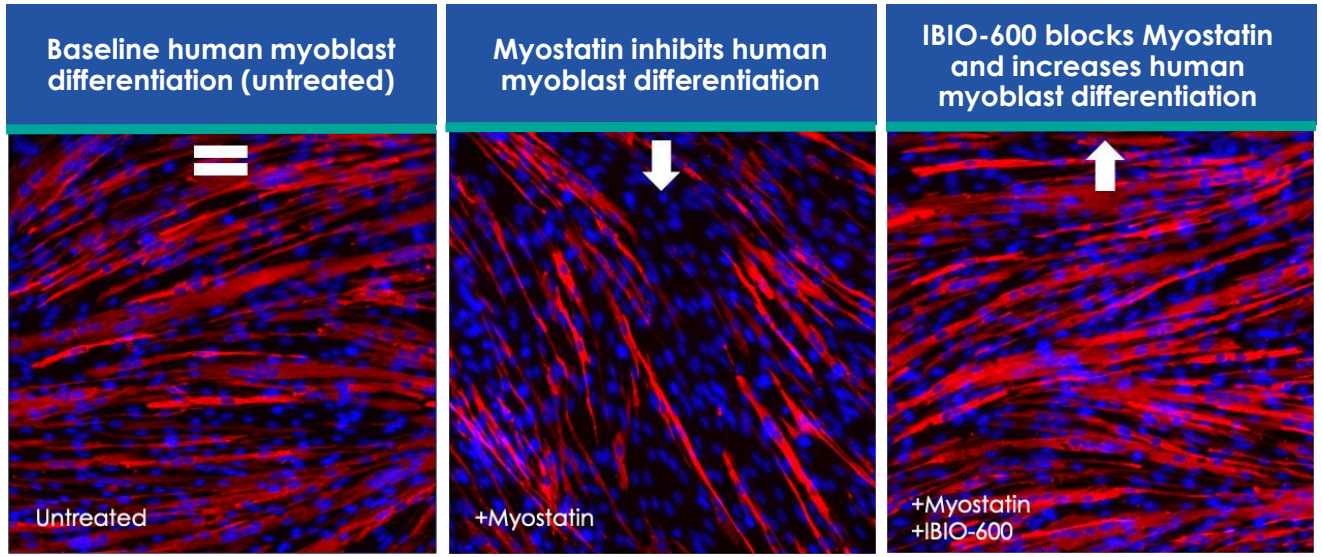
1. Schuelke M. (2004). New England Journal of Medicine 350(2682–2688).
2. Deng, B. (2017). Nutrition and Metabolism, 14(29).

IBIO-600: A Differentiated Long Acting Anti-Myostatin Program

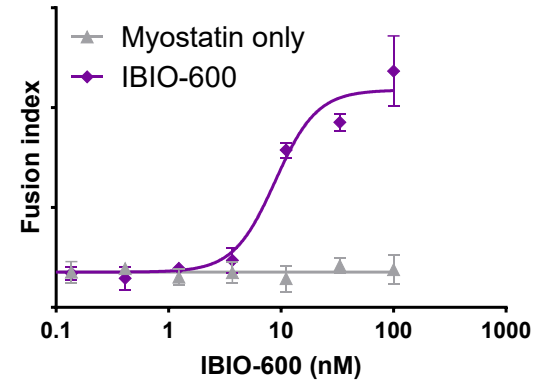
Improved Pharmacokinetics	Potential best-in-class PK based on allometric scaling and dosing regimen suggests **2-4x improved PK** over competitors
Dual Mechanism	Dual myostatin and GDF11 blockade has potential for **improved lean mass preservation** and **fat mass reduction**
Enhanced Manufacturability	Optimized for **high expression** and **stability** to enable efficient manufacturing process
Coformulation Optionality	**High formulation** concentration to **lower injection** volume
Convenience	Potential administration potentially as infrequent as **twice a year**

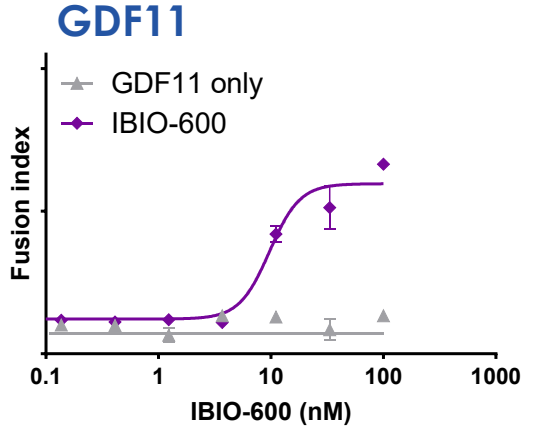
IBIO-600 Enhances Muscle Differentiation in Human Myoblasts by Targeting the Two Growth Suppressors Myostatin and GDF11

The **human Myoblast differentiation** model is **highly predictive** of **muscle growth** in humans[1]



IBIO-600 Increases Myoblast Differentiation

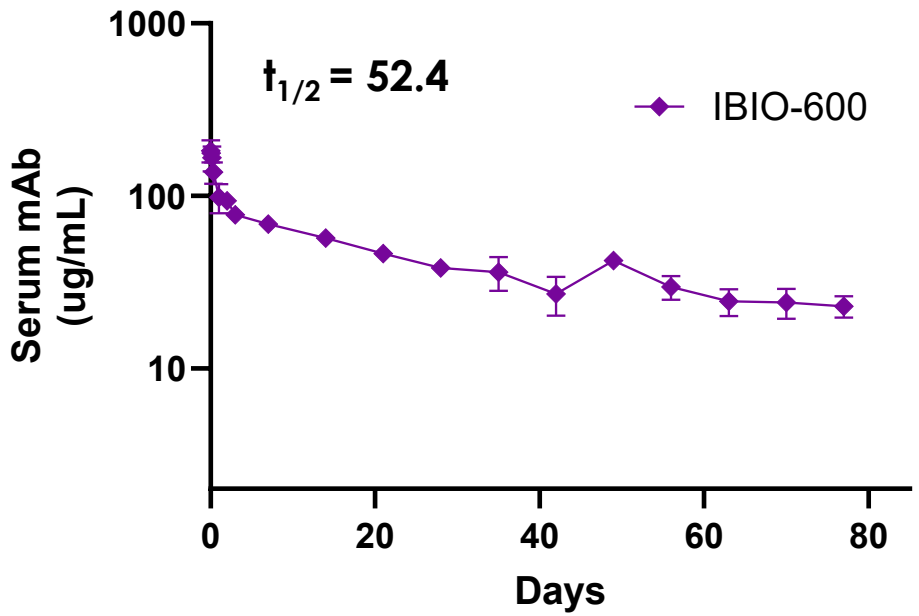




1. Francis, T., Soendenbroe, C., Lazarus, N. R., Mackey, A. L. & Harridge, S. D. R. Insights into human muscle biology from human primary skeletal muscle cell culture. J Muscle Res Cell Motil (2025) doi:10.1007/s10974-025-09696-w.
- Data on file

IBIO-600 Fc Engineering Drives Extended Half-Life in Obese NHPs

12 Week Pharmacokinetics Data[1]



Study Details:

- *Obese, aged NHPs*
- *Monthly DEXA scan for body composition*
- *Periodic PK sampling*

IBIO-600 Fc Engineering Results in Enhanced FcRn Binding

Clone	Fc	Fold increase over standard IgG
IBIO-600 FAB	Standard IgG4	**1.0**
IBIO-600	Engineered IgG4	**16.5**

IBIO-600 Observed to Have Extended Half-Life in NHPs

Dose	$t_{1/2}$ (days)
5 mg/kg, I.V.	**52.4**

Study Design:

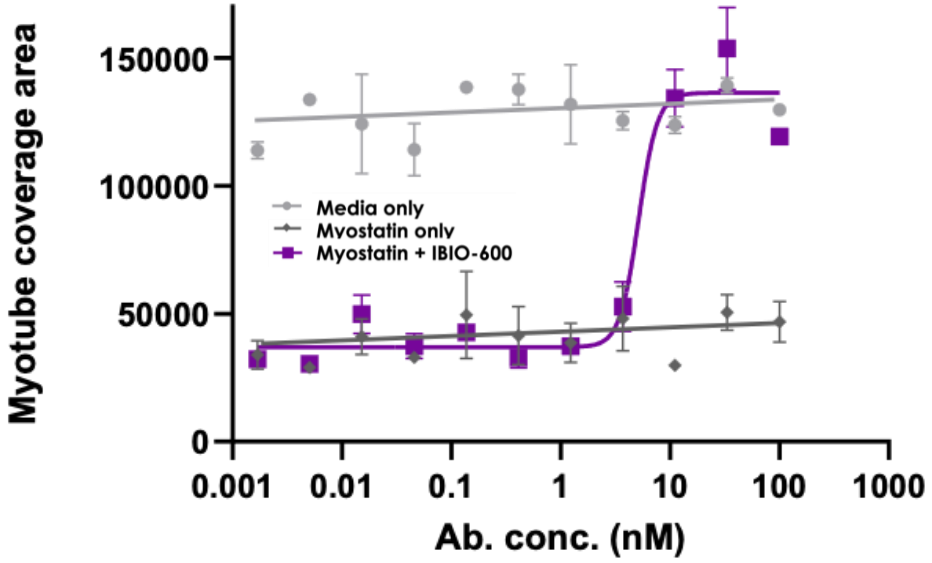
- *N=3 per group*
- *5mg/kg single I.V. dose*

1. *Linear elimination phase used to estimate half-life with simple linear model Data on file*

IBIO-600 Dose Modeling From Human Muscle Cells and Monkey PK Suggests Low Dose Requirements to Block Myostatin for Extended Durations

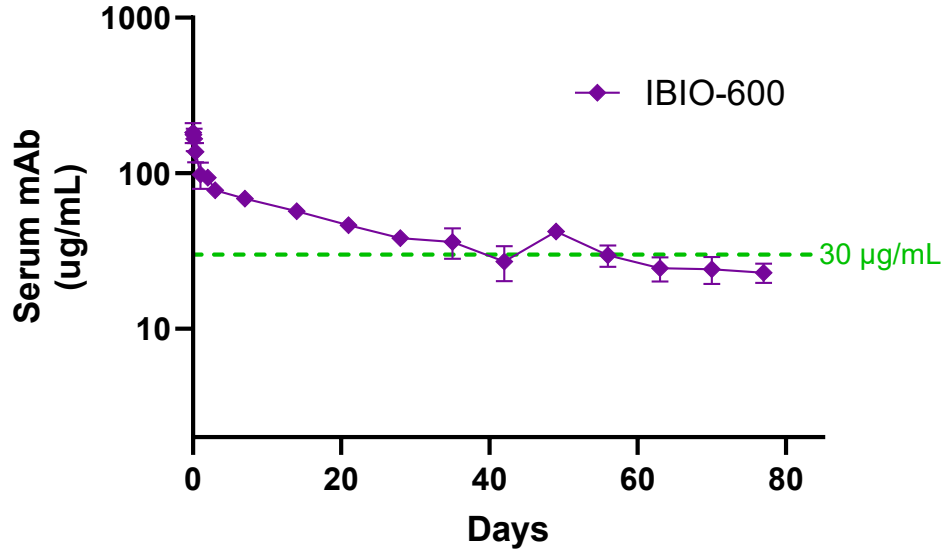
IBIO-600 Blocked the Effect of Myostatin on Human Muscle Cells

IC_{90} (90% inhibition level) = 1.2 ug/mL (7.97 nM)



At 5 mg/kg Dose, IBIO-600 Achieved >90% Myostatin Inhibition for 8 Weeks

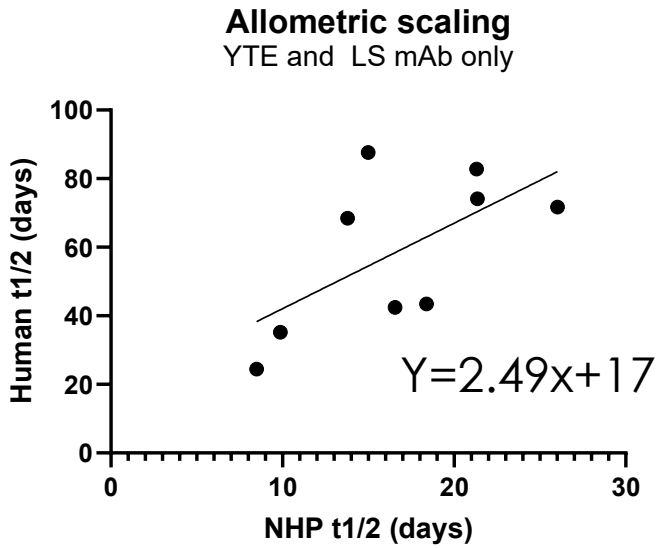
IC_{90} in muscle (1.2 ug/mL) translates to 30 ug/ml plasma levels assuming mAb Muscle/Plasma Ratio ~4%



Allometric Scaling Predicts Potentially Extended Half-Life for IBIO-600, Enabling Infrequent Dosing and Prolonged Myostatin Inhibition

Allometric Scaling Model for Half-Life Extended Antibodies[1]

Generic allometric scaling model for antibodies[2]



$$T_{1/2Human} = T_{1/2NHP} \times \left[\frac{\text{Human Body Weight}}{\text{NHP Body Weight}}\right]^{0.15}$$

Measured NHP and Expected Human Half-Life of IBIO-600

Dose	NHP $t_{1/2}$ (actual)	Human $t_{1/2}$ (predicted)[1,2]
5 mg/kg, I.V.	52.4	**74-147 days**

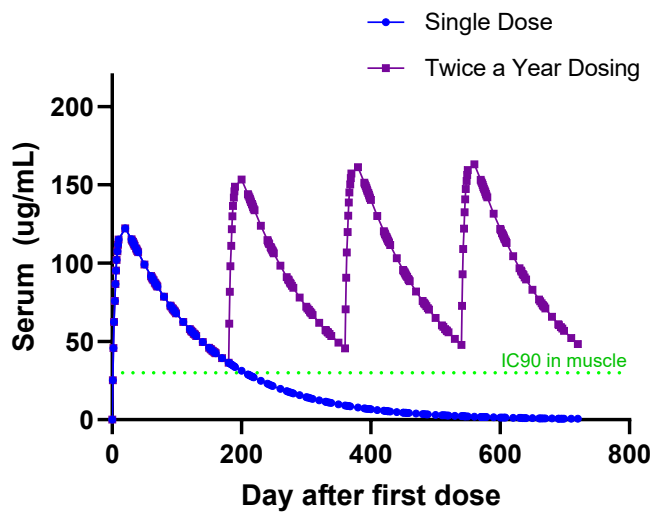
1. *Haraya, K. & Tachibana, T. Translational Approach for Predicting Human Pharmacokinetics of Engineered Therapeutic Monoclonal Antibodies with Increased FcRn-Binding Mutations. BioDrugs* ***37****, 99–108 (2023).*
2. Nakamura, G. *et al.* Predicting Method for the Human Plasma Concentration–Time Profile of a Monoclonal Antibody from the Half-life of Non-human Primates. *Biological and Pharmaceutical Bulletin* **43**, 823–830 (2020).

Data on File

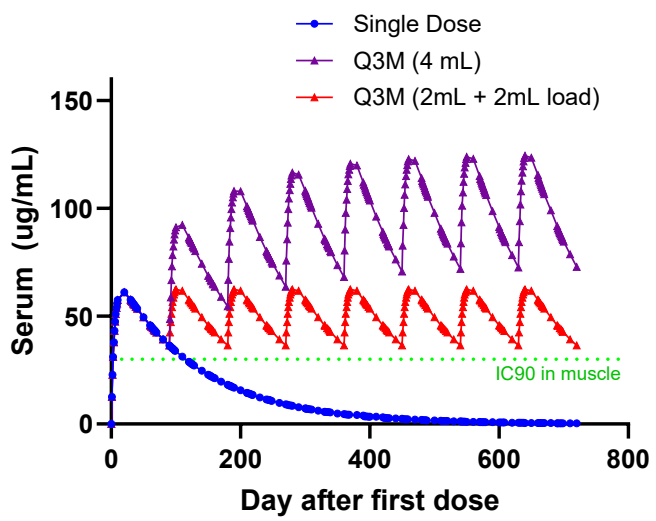
PK Modeling Suggests IBIO-600 Can Be Dosed Twice-Yearly, Quarterly, or Co-Formulated With Weekly GLP-1s

Modeling Assumptions:	150 mg/mL formulation	$T_{1/2}$ = 90 days	Bioavailability = 70%

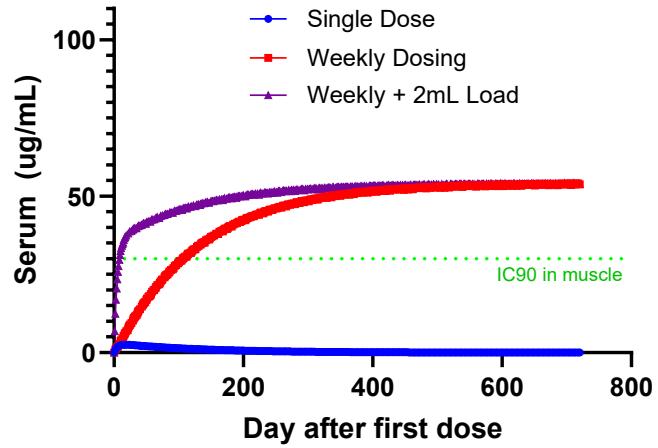
Twice Per Year Dosing
(4 x 2 mL s.c.)



Quarterly Dosing
(2 x 2 mL s.c. or 1 x 2 mL s.c. + 2 mL loading dose)



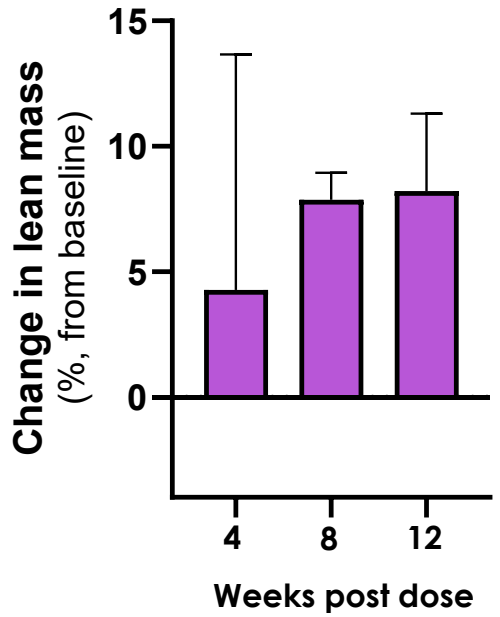
Co-Dosing With Weekly GLP-1
(1 x 0.167 mL s.c. injections)



Single Clinically Relevant Low Dose of IBIO-600 Observed to Drive Sustained Muscle Gain and Fat Loss in Aged, Obese Non-Human Primates

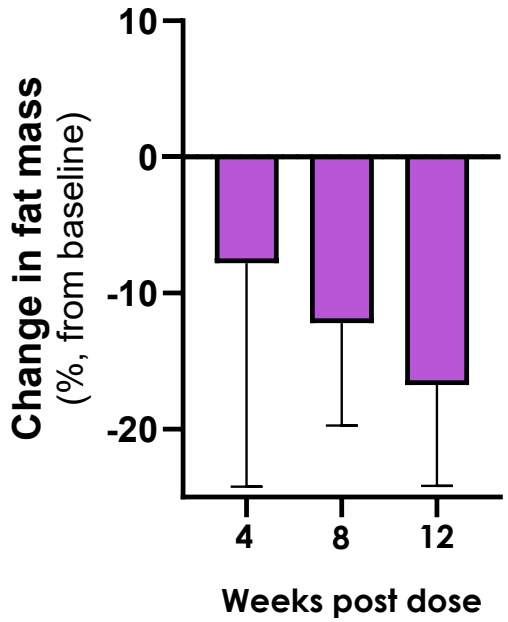
Percent Increase in Lean Mass

Single 5 mg/kg Dose



Percent Decrease in Fat Mass

Single 5 mg/kg Dose



ROI (gluteal and thigh region) DEXA
Data on file