IBIO-600

Long-Acting Anti-Myostatin Antibody

Transition slide

Myostatin Antagonism

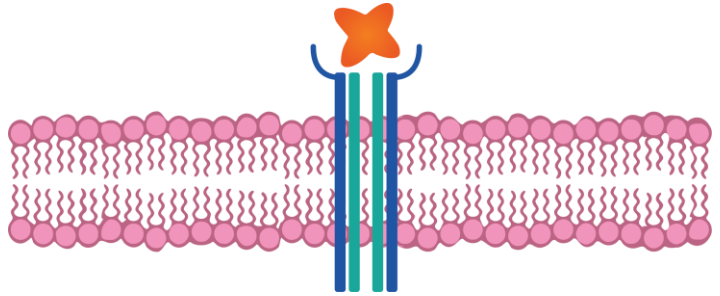
Enhancing the Quality of Weight Loss by Maintaining Muscle Mass During and After Weight Loss with GLP-1s

We are developing Myostatin inhibitors to **preserve and increase muscle mass**, **complementary to** treatment with **GLP-1 drugs**

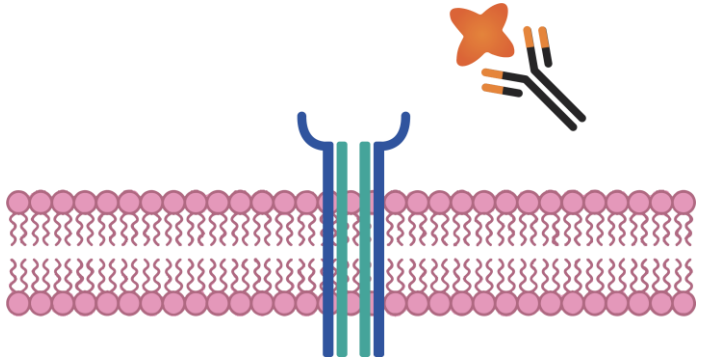
Why We Target Myostatin

- **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 drives significant **muscle growth without** apparent **adverse health effects**
- 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 Long-Acting First-in-Class Anti-Myostatin Antibody

First Anti-Myostatin Antibody With a Target Product Profile Specifically Tailored for an Obese Patient Population

IBIO-600
Long-Acting Anti-Myostatin Antibody

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[1]

Target product profile characteristics for obese patients

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

AI-enabled CDR design

- Rapidly generates novel IP
- Large library of novel lead molecules

Single-shot multi-dimensional lead optimization

- Optimized for affinity, half-life and manufacturability

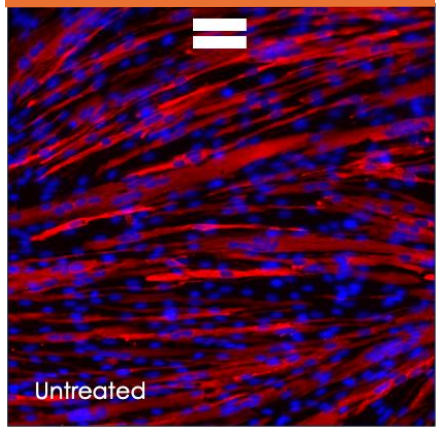
1. Data on file

IBIO-600 Increases Muscle Differentiation in Primary Human Myoblast Cells

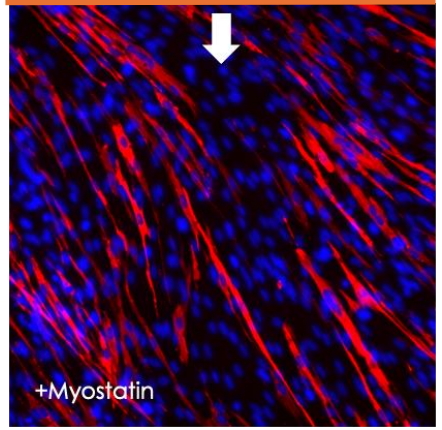
Red indicates muscle cell growth and development (as measured by myoblast differentiation)

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

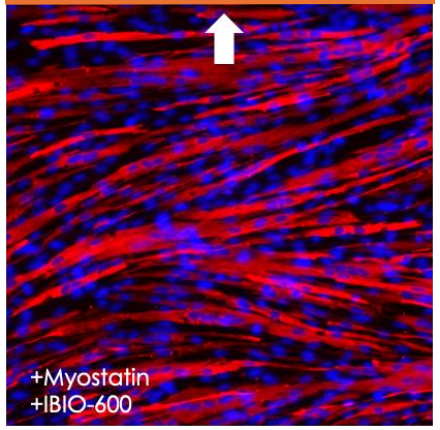
Baseline human myoblast differentiation (untreated)



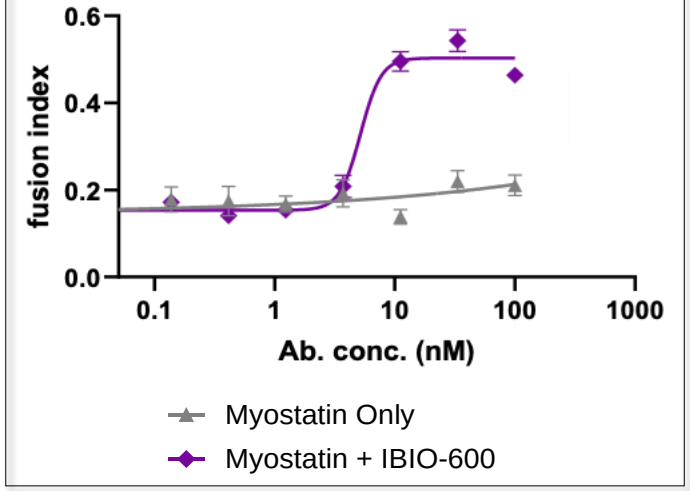
Myostatin inhibits human myoblast differentiation



IBIO-600 blocks Myostatin and increases human myoblast differentiation

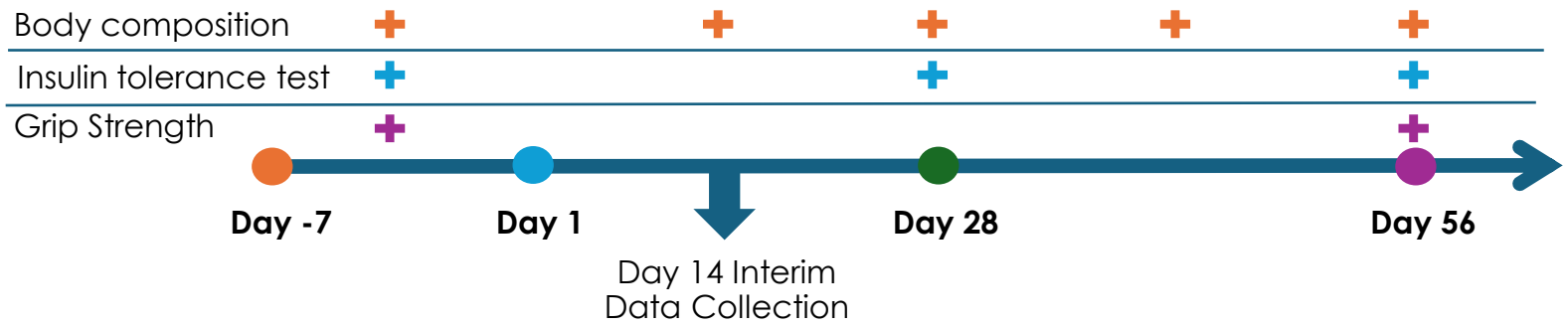


IBIO-600 potently increases myoblast differentiation



Interim Data: IBIO-600 Preserves Muscle Mass in GLP-1 Treated Diet Induced Obesity Mice

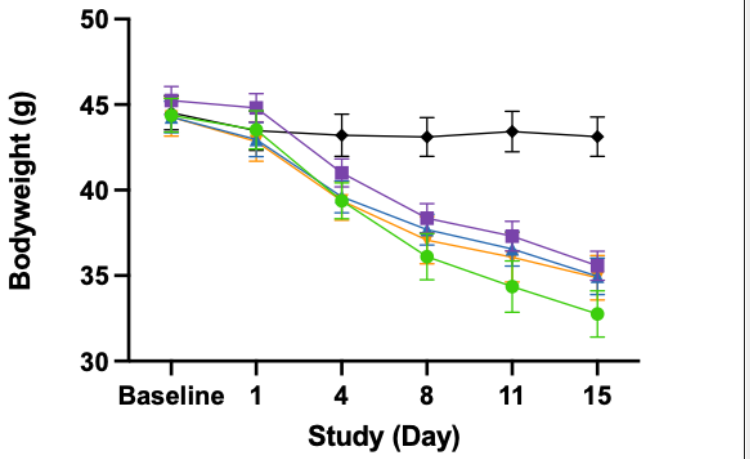
Study Design



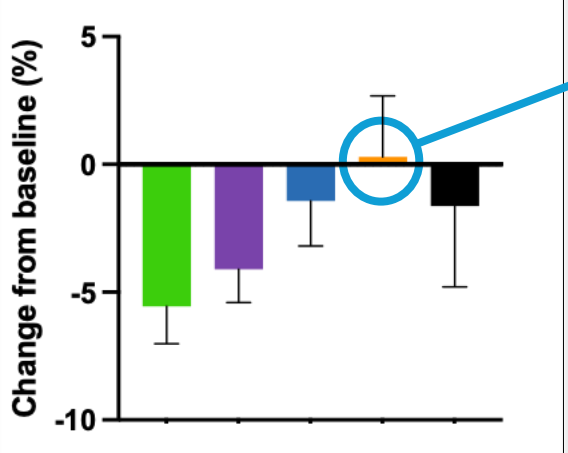
Interim Data

- Sema only
- Sema + 1mg/kg IBIO-600
- Sema + 3mg/kg IBIO-600
- Sema + 10mg/kg IBIO-600
- No treatment

Body weight loss up to day 14



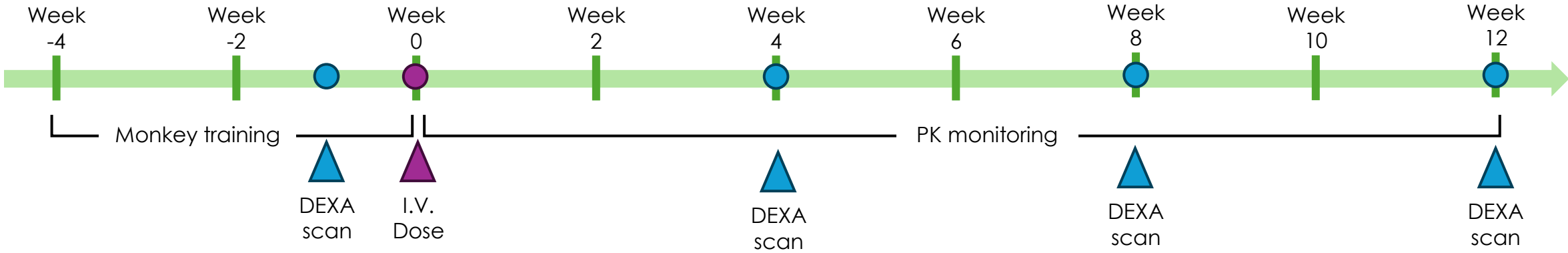
Lean mass change on Day 14



Sema + 10 mg/kg IBIO-600

In this study the murine surrogate antibody of IBIO-600 was used

IBIO-600 Pharmacokinetics (PK) Study in Non-Human Primates (NHPs)



Study details

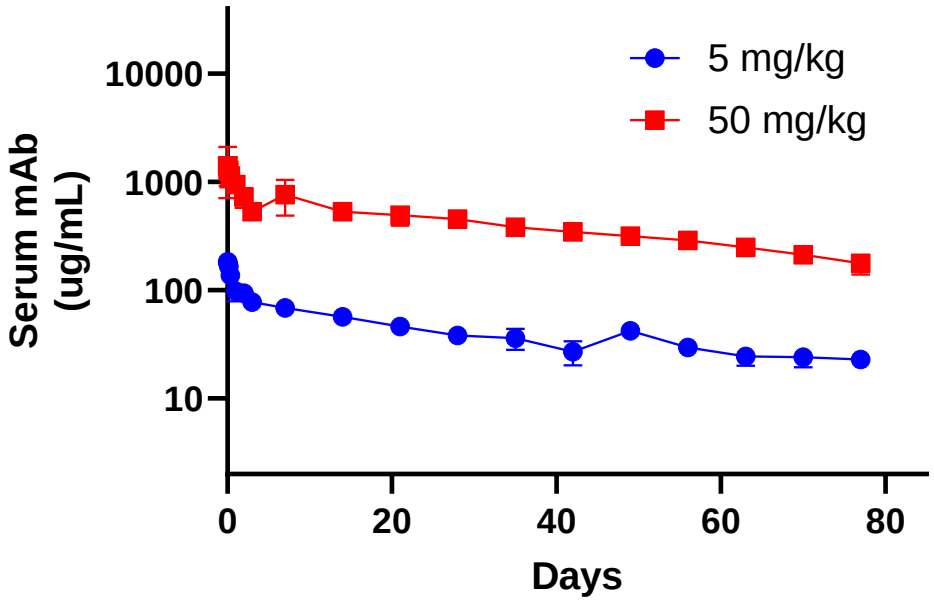
- Obese, aged NHPs
- Performed at Kunming Biomed International (KBI)
- Material produced transiently by Wuxi Biologics

Study design

- N=3 per group
- 2 arms, single I.V. dose
  - 5mg/kg
  - 50 mg/kg
- DEXA scan for body composition every 4 weeks
- Periodic PK sampling

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

12 Week Pharmacokinetics Data[1]



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**

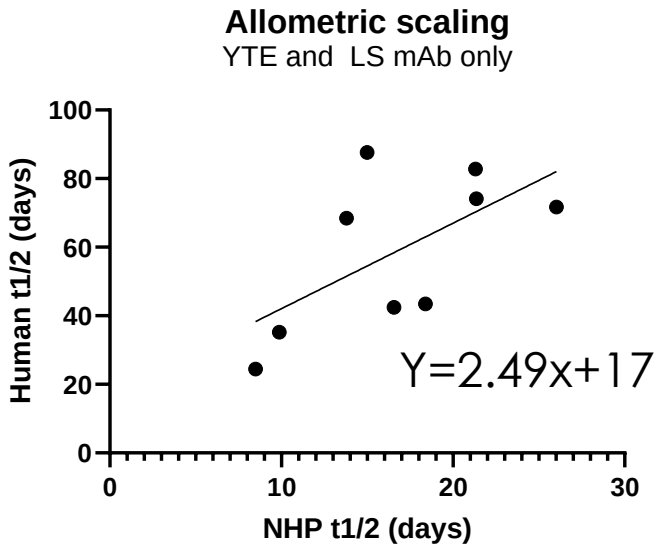
IBIO-600 demonstrates extended half-life in NHPs

Dose	$t_{1/2}$ (days)
5 mg/kg	**52.4**
50 mg/kg	**40.7**

1. Linear elimination phase used to estimate half-life with simple linear model

Allometric Scaling Suggests Meaningfully Extended Half-Life for IBIO-600 in Humans

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 predicted human half-life of IBIO-600

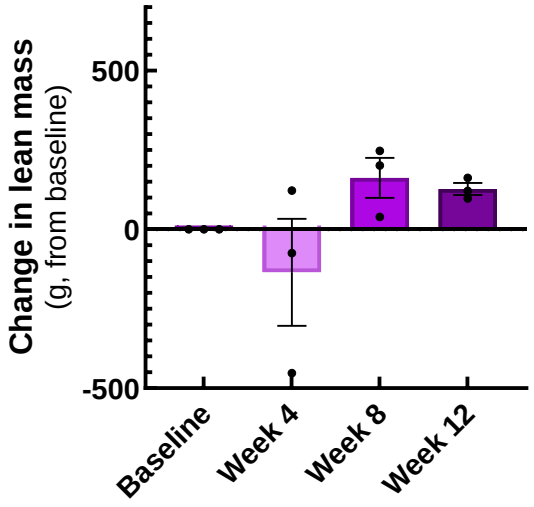
Dose	NHP $t_{1/2}$ (actual)	Human $t_{1/2}$ (predicted)[1,2]
5 mg/kg	52.4	**74-130 days**
50 mg/kg	40.7	**57-101 days**

1 https://pmc.ncbi.nlm.nih.gov/articles/PMC9709760/#CR37
2 https://www.jstage.jst.go.jp/article/bpb/43/5/43_b19-01042/_html/-char/en

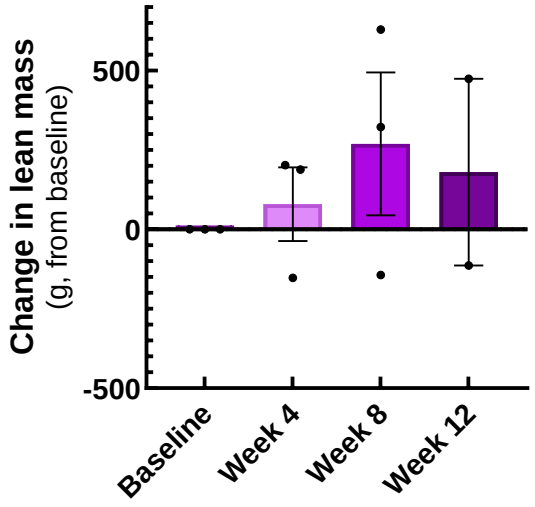
Lean Mass Peaks at 8 Weeks Remains Elevated at 12 Weeks After a Single IBIO-600 i.v. Injection

Lean Mass Increase in Grams

Single dose 5 mg/kg

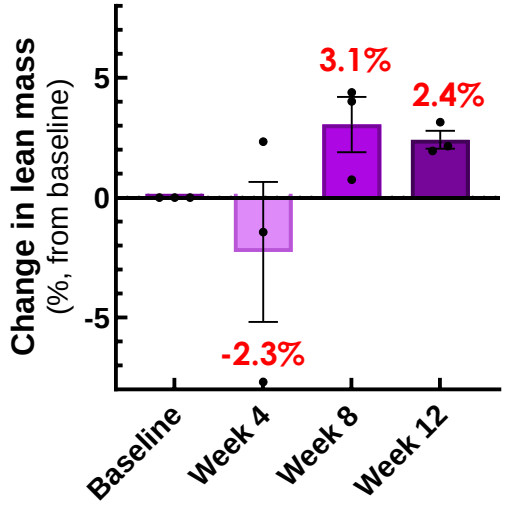


Single dose 50 mg/kg *

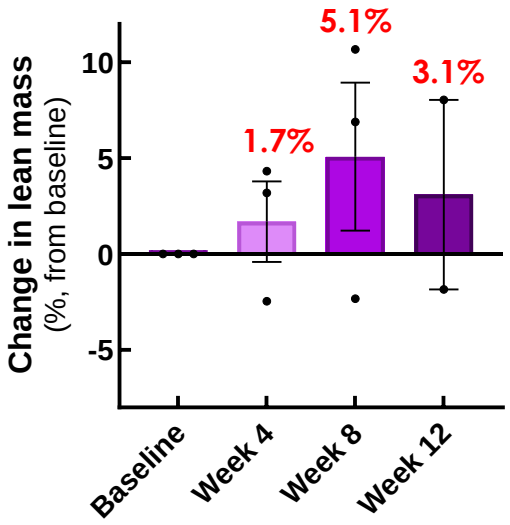


Lean Mass Increase in Percent

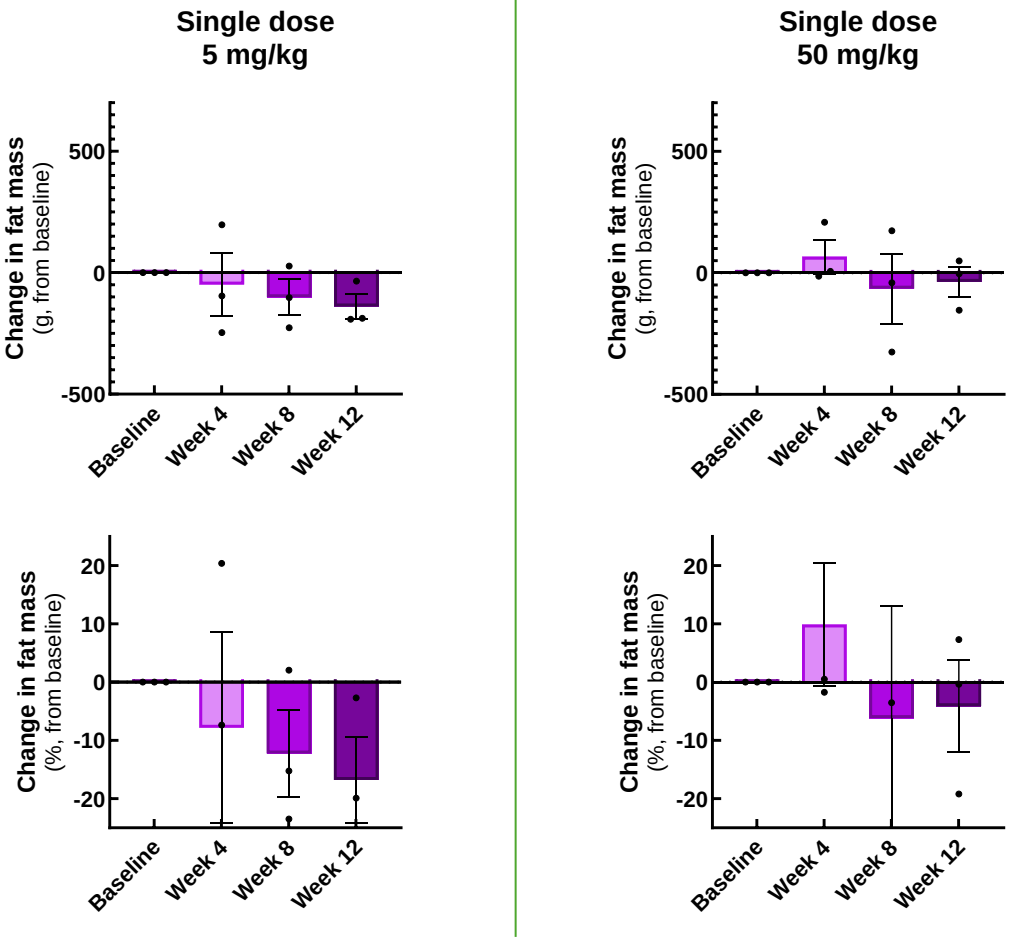
Single dose 5 mg/kg



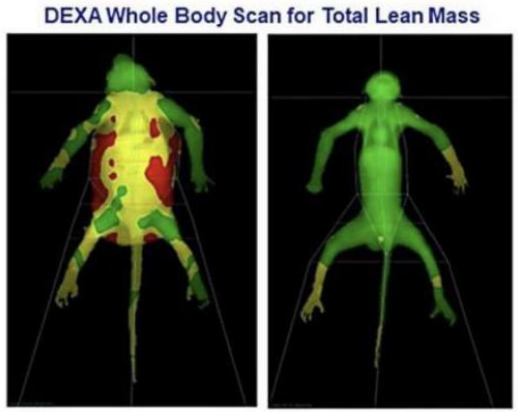
Single dose 50 mg/kg

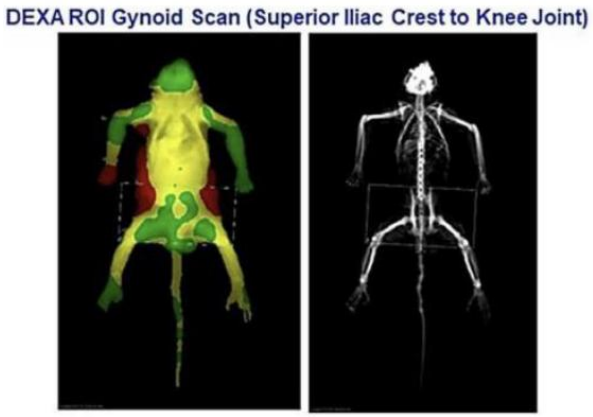


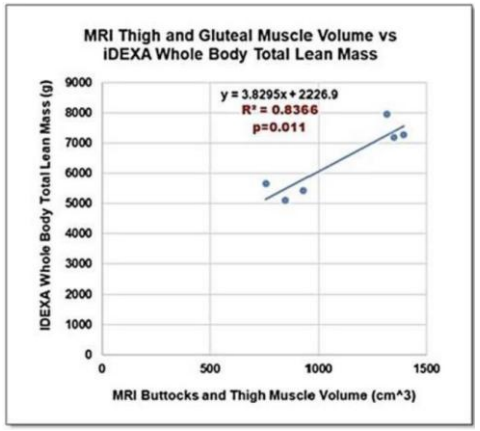
Fat Mass between Thigh and Abdomen is Reduced After a Single I.V. Dose of IBIO-600

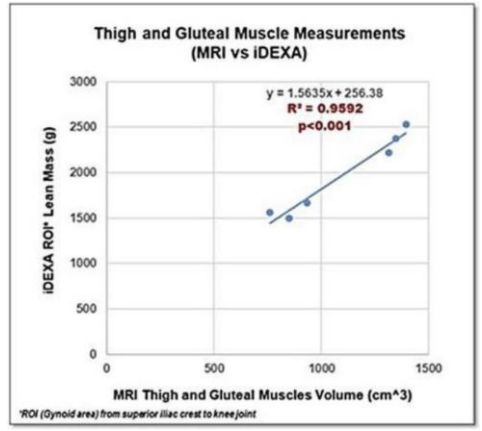


Region of Interest (ROI) DEXA Analysis of Gluteal and Thigh Regions Correlates Better with MRI Data[1]









1. Data on file