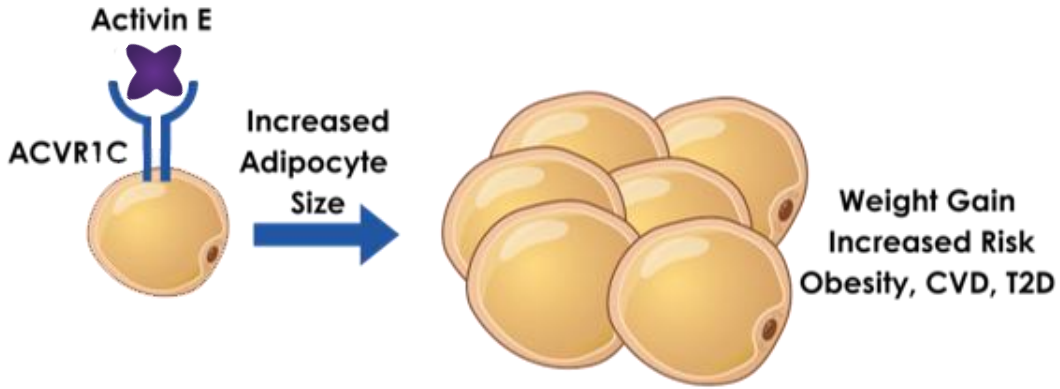
IBIO-610

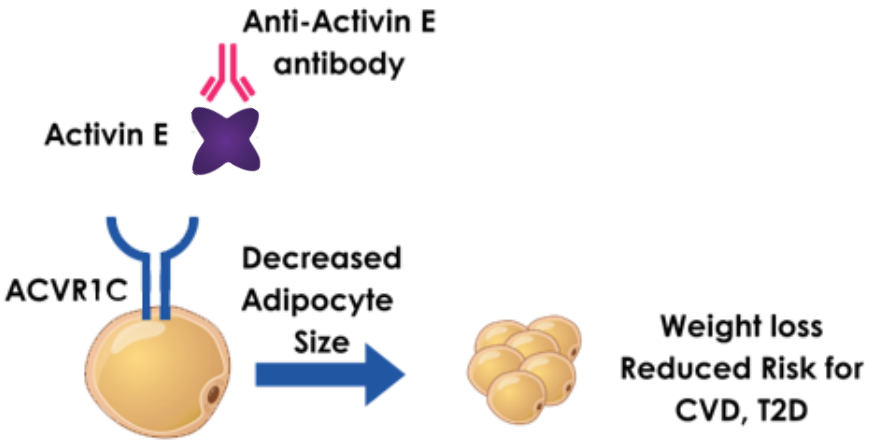
Anti-Activin E Antibody

IBIO-610 Targets Activin E to Potentially Drive Targeted Fat Loss and Maintain Weight Reduction After GLP-1 Discontinuation

Why We Target Activin E

- Activin E is a Hepatokine, produced in the liver and a member of the TGFβ family
- Activin E and its receptor are highly genetically validated[1,2]
- Genetic loss of function decreases adiposity and risk for Diabetes / Cardiovascular Disease (CVD)[1,2]
- **2 RNA targeting molecules provide preclinical pharmacological validation**
- Challenge to produce active recombinant Activin E until recently has proven to be extremely difficult for antibody discovery





1. Akbari, P. et al. Multiancestry exome sequencing reveals INHBE mutations associated with favorable fat distribution and protection from diabetes. Nat Commun **13**, 4844 (2022).
2. Deaton, A. M. et al. Rare loss of function variants in the hepatokine gene INHBE protect from abdominal obesity. Nat Commun **13**, 4319 (2022).
Type 2 Diabetes (T2D)

IBIO-610 as a Potential First-in-Class Antibody Targeting Activin E

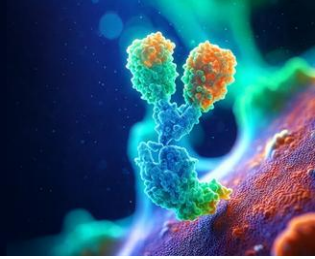
Potential Class-Leading Pathway Targeting	Antagonist antibody offers potential for **greater Activin E inhibition** than siRNA-based knockdown approaches
Dual Mechanism	Weight loss observed in pre-clinical studies with **no impact on lean mass**
Synergistic to GLP-1 Receptor Agonists	**Synergistic weight loss** with appetite reducing drugs like GLP-1 or Amylin observed in pre-clinical studies
Weight Lowering and Maintenance Therapy	**Stand-alone** weight loss intervention and weight loss maintenance post GLP-1 or Amylin treatment
Enhanced Manufacturability	Optimized for **high expression** and **stability**, enabling efficient production within a mature, globally scalable antibody manufacturing infrastructure

IBIO-610 Combines Deep Pathway Inhibition With the Accessibility and Scalability of Proven Biomanufacturing Compared to siRNA Modalities

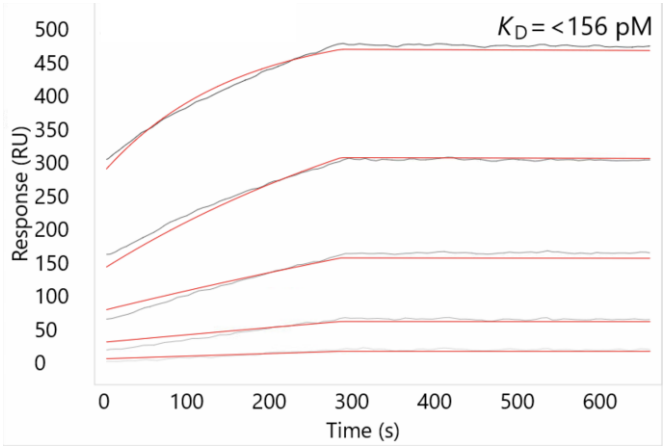
	iBio Activin E Antibody	Other Anti-Activin E Modalities siRNA
Pathway inhibition	Potentially higher inhibition (~100%)*	Partial inhibition ~60% to 85%**
Dosing Frequency	NHP PK data provides support for twice-yearly dosing	Once or twice a year**
Co-formulation with GLP-1	Attainable and synergistic	Unlikely/complex
Manufacturing and scalability	Global manufacturing infrastructure; fully scalable to serve large patient populations	Only few FDA approved siRNA molecules; limited manufacturing capabilities, peptide-like complexity for scaling

** Based on mouse data*
*** Based on NHP and initial human data*

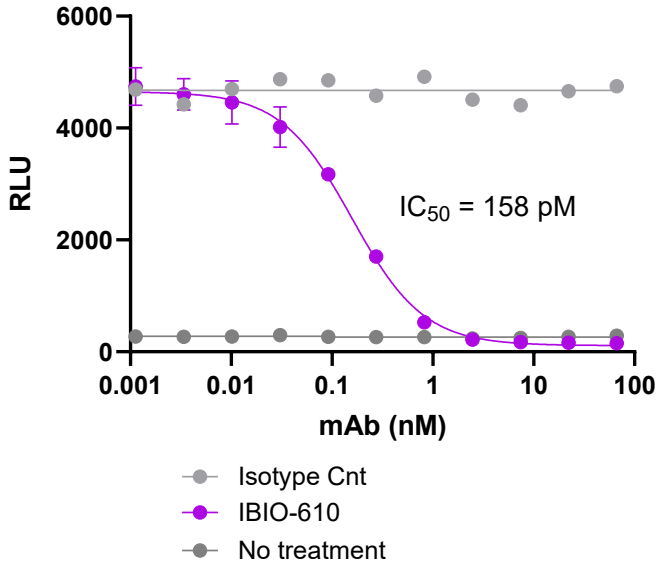
IBIO-610 Exhibited High-Affinity Binding and Potent Inhibition of Activin E Signaling in Engineered and Primary Human Fat Cells



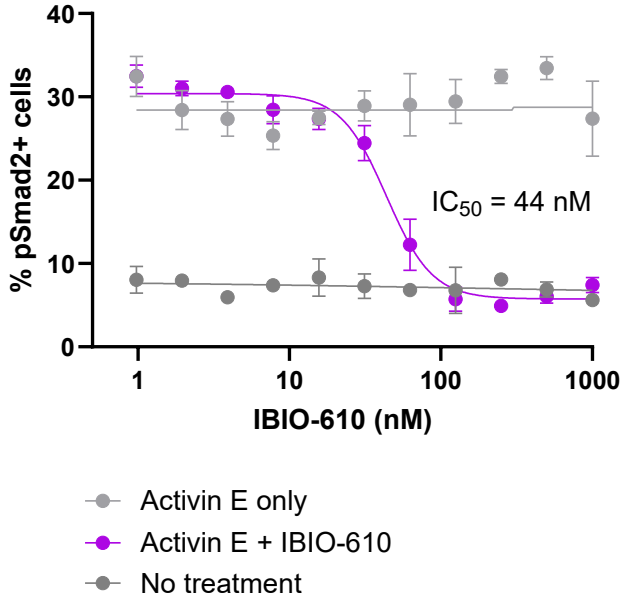
Target Protein Binding Assay



Reporter Cell Line Functional Assay



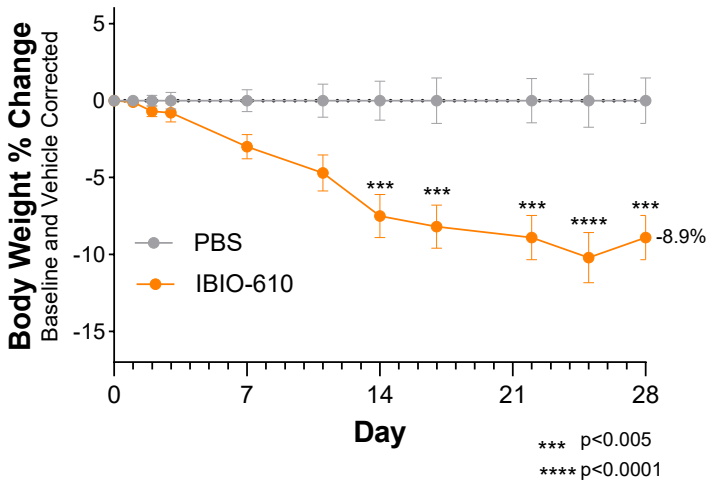
Primary Human Adipocyte Assay



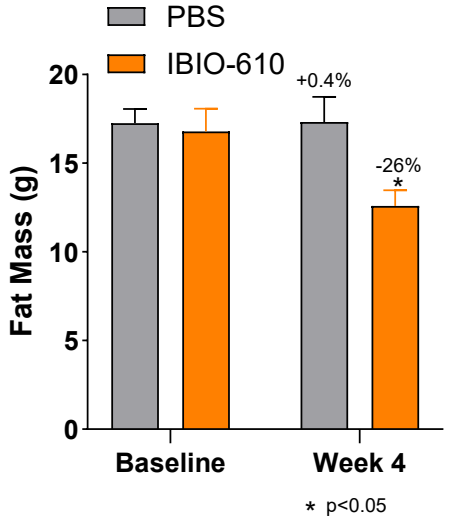
IBIO-610 Observed to Induce Fat-Selective Weight Loss in Diet-Induced Obese Mice

Study Design

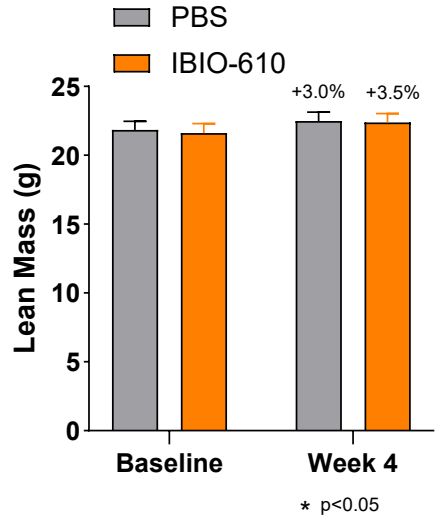
Weight Loss = 8.9%



Fat Loss = 26%



No Lean Mass Loss

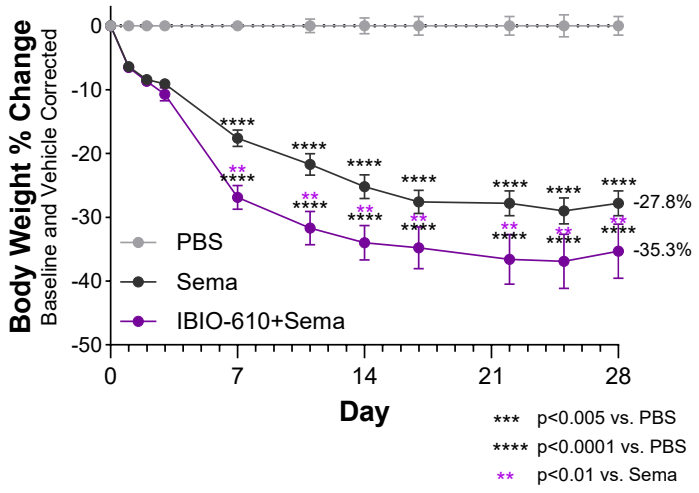


*Non-responder outlier mice removed, IBIO-610 mouse surrogate used. 10 mg/kg, BIW dosing. DIO mice Data on file

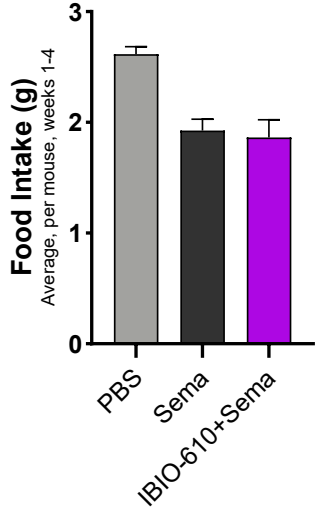
IBIO-610 Synergizes with GLP-1 Through a Distinct, Non-Appetite-Based Mechanism

Study Design

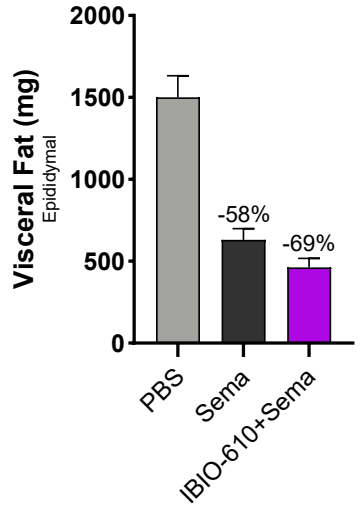
Synergistic Weight Loss



No Additional Appetite Suppression



Visceral Fat Reduction

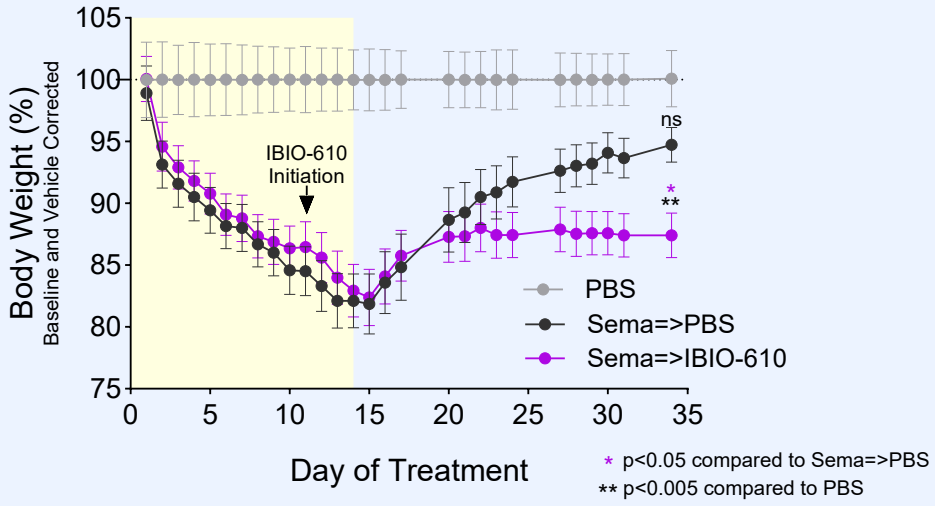


Data on file

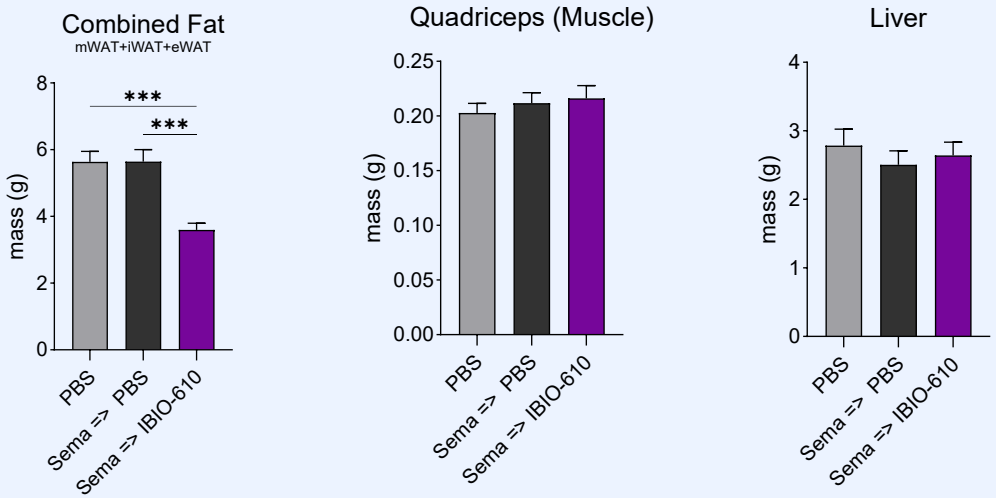
IBIO-610 mouse surrogate used, 10 mg/kg, BIW dosing. Semaglutide dosed QD at 10 nmol/kg.

IBIO-610 Observed to Prevent Weight Regain Following GLP-1 Treatment in Obese Mice

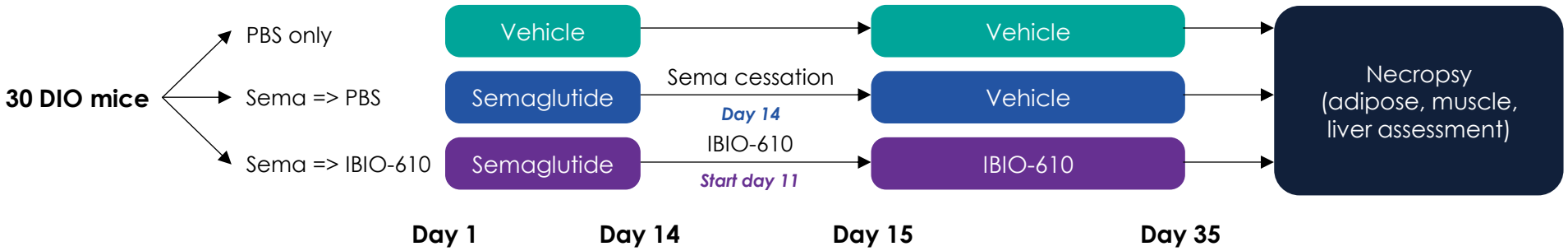
Significant Prevention of Weight Regain



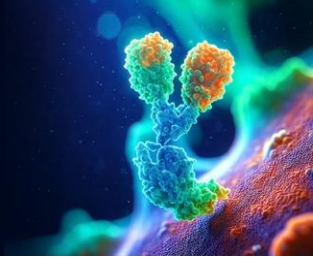
Fat-Specific Effect

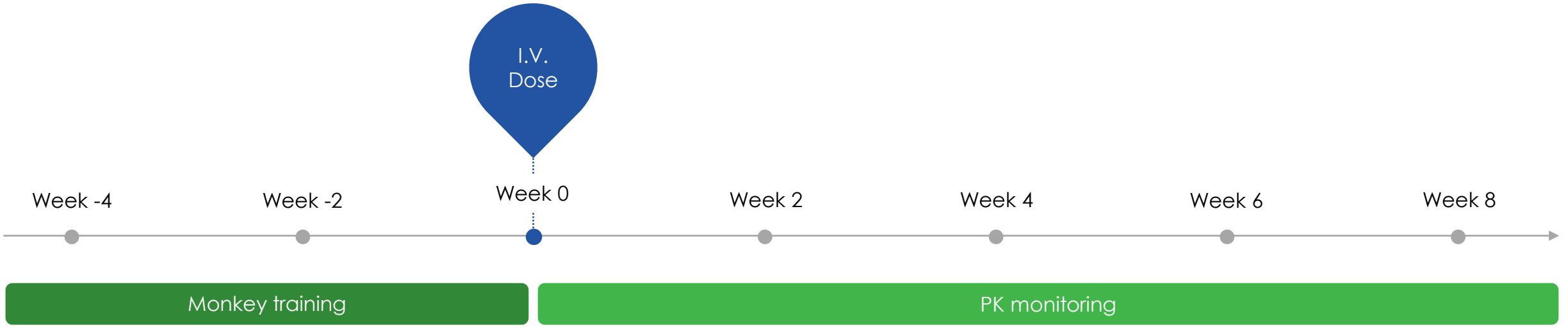


Study Design



IBIO-610 Non-Human Primate (NHP) Pharmacokinetics (PK) Study



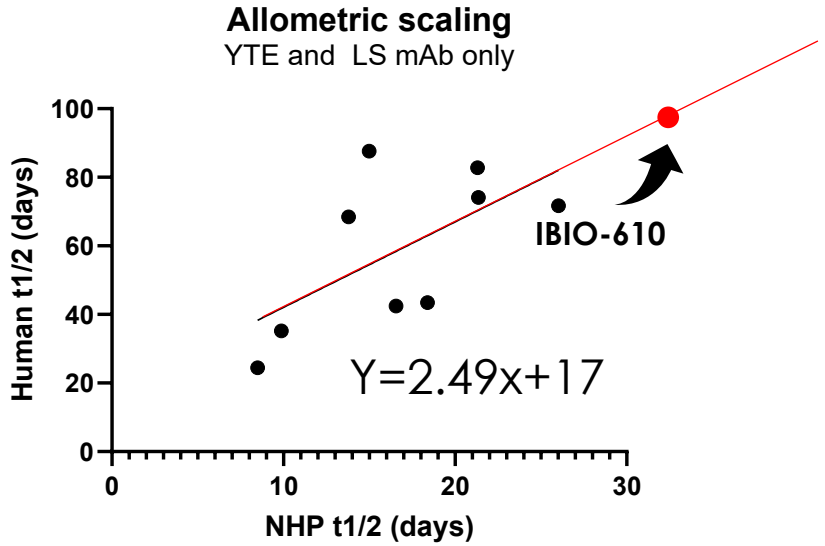


NHP Characteristics	
	Obese, mature NHPs
	Age 8-15 years
	~ 18%-51% body fat

Study Design	
	N=6 NHPs
	10mg/kg single i.v. dose
	Periodic PK sampling

Non-Human Primate Pharmacokinetics Shows Potential for Extended Half-life of IBIO-610 in Humans

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

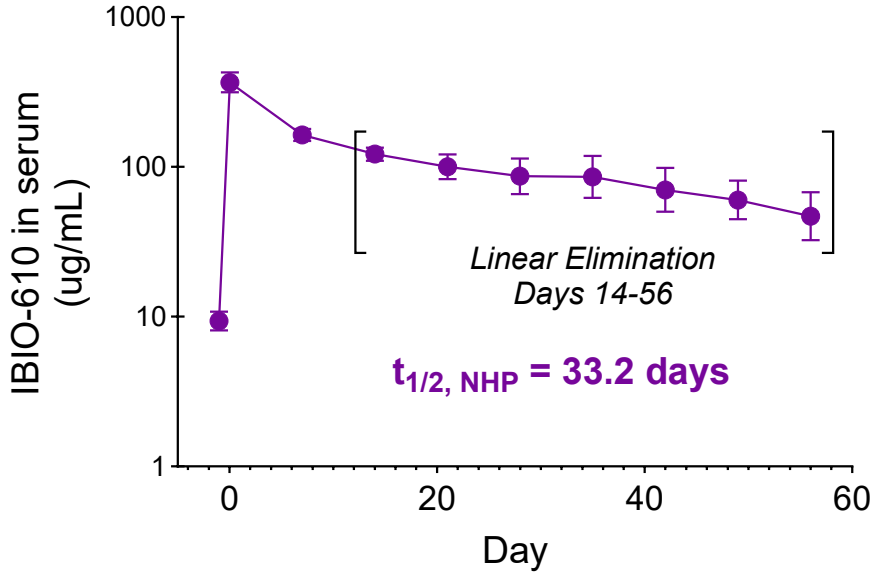


Generic allometric scaling model for antibodies[2]

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

Obese NHP Pharmacokinetics

Single I.V. Dose, 10 mg/kg



Species	$t_{1/2}$ (days)
NHPs	**33.2 days**
Humans (predicted)	**47-100 days**

1. Nakamura, G. et al. Biological and Pharmaceutical Bulletin (2020).
2. Haraya, K. & Tachibana, T. BioDrugs (2023). (Assume human BW = 100kg, NHP BW = 10kg)