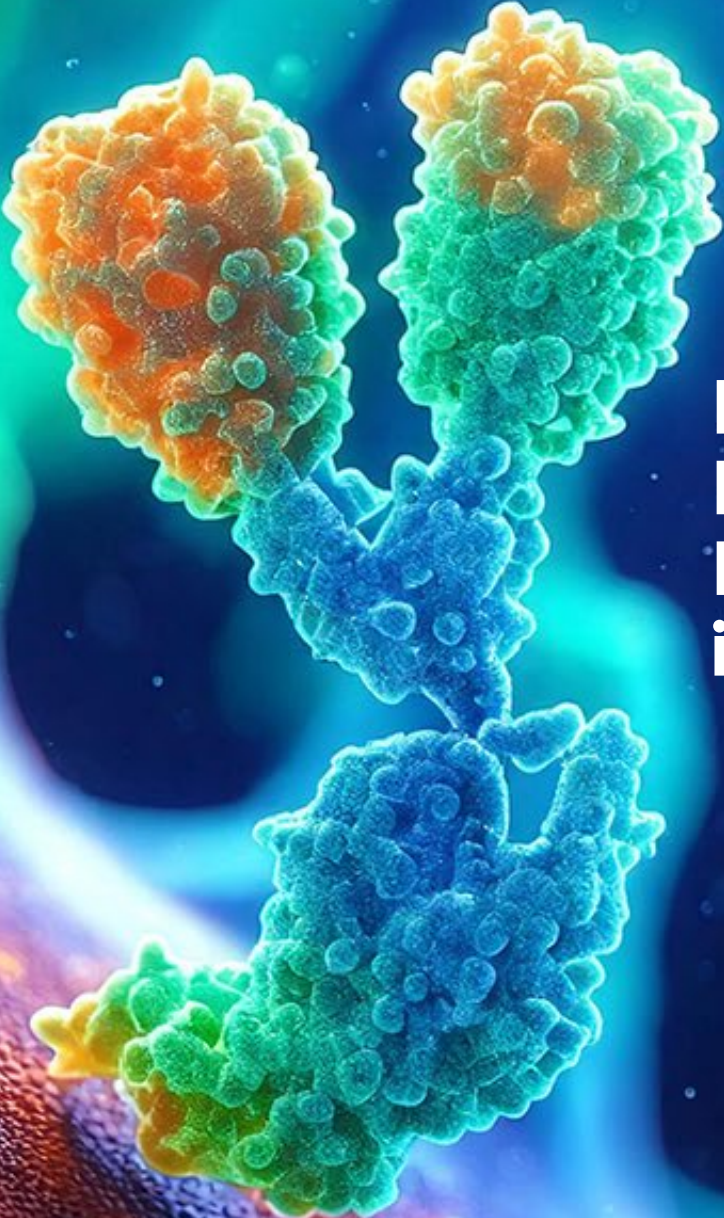


A large, detailed 3D molecular model of a protein complex is positioned on the left side of the slide. The model is composed of several subunits, each represented by a different color: orange, green, blue, and yellow. The subunits are interconnected, forming a complex, multi-lobed structure. The background is a dark blue gradient with a bokeh effect of light spots and a large, out-of-focus, colorful shape on the left side, possibly representing a cell or tissue.

Neutralization of Activin E Promotes Fat-Selective Weight Loss and Prevents Weight Regain in Preclinical Models of Obesity

Keystone Symposia

Obesity Therapeutics: Unlocking Benefits
and Minimizing Side Effect

January 29th, 2026

Disclosures

- Employed at iBio Inc.
- Shareholder in iBio Inc.

GLP-1 Revolution Sparked a New Era in Obesity Treatment

Driving Towards Next Generation Medicines



Incretin Class Agonists Have Revolutionized Obesity Treatment

>10% of American adults have taken a GLP-1¹

Interventional weight loss previously only achievable via surgery



Moving Towards Therapies That Build on That Foundation

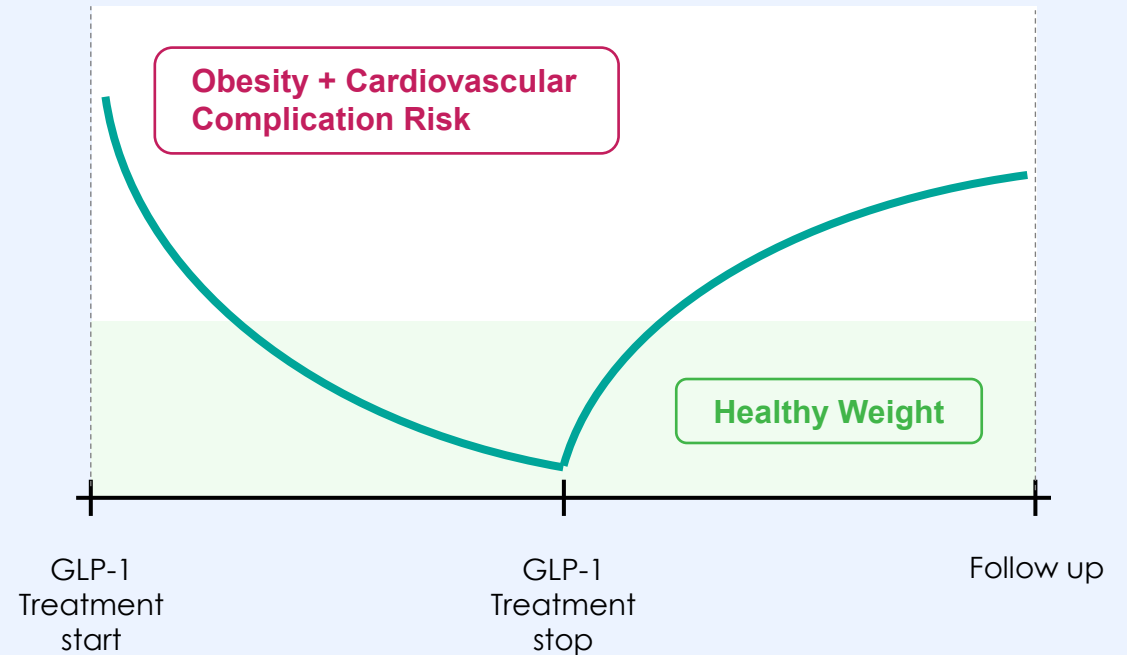
Lean mass preservation and fat-specific weight loss

Improved convenience and tolerability

GLP-1s Lead to Robust Weight Loss – But Muscle is Lost Too

“For every 1 kg weight lost... 0.32 kg lean tissue was lost and for every 1 kg weight regained..., only 0.08 kg lean tissue was regained”¹

“Compared to (control) group, the [weight loss/regain] group had a statistically significant 39% increased risk of a frailty fracture”²



Patient Preference in Chronic Disease?



Daily
Oral



Weekly
Injection



Monthly
Injection



Semi-annual
Injection



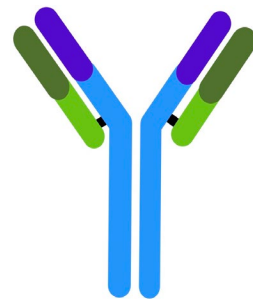
One Time
Treatment

Osteoporosis

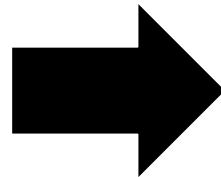
2-year randomized crossover study



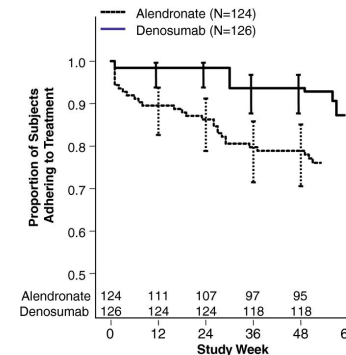
VS



Denosumab
Injection, 2x year



Better adherence?



Patient preference?

92% preferred
injection

8% preferred oral
tablet

Long acting injection is favored

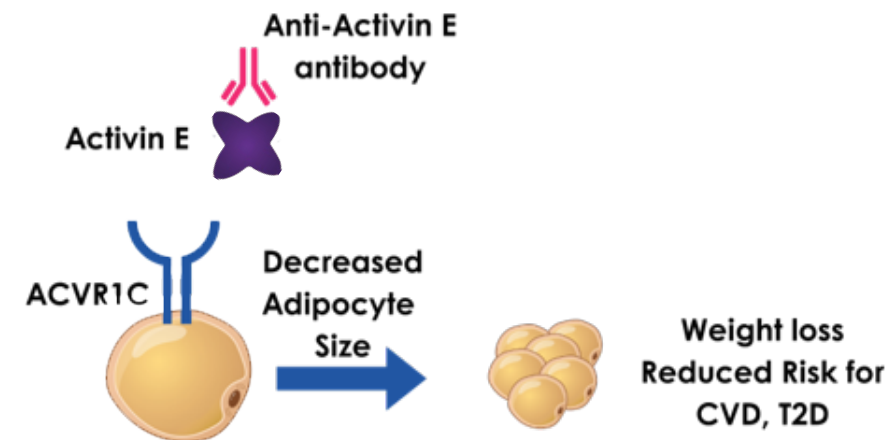
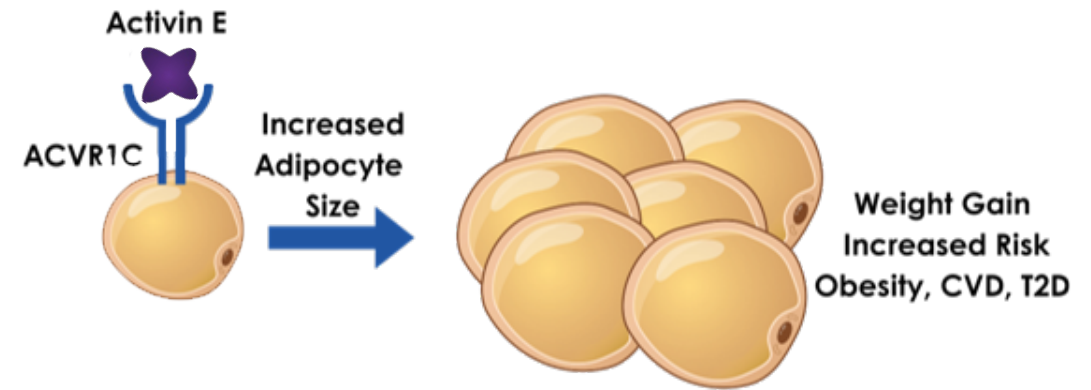
The background of the slide is a dark, textured surface. On the left side, there are several clusters of small, colorful dots in shades of blue, red, yellow, and green. These dots are arranged in a way that suggests a molecular or cellular structure. On the right side, there is a large, white, wireframe-like structure that resembles a protein or a complex molecule. The structure is composed of many small, interconnected triangles, giving it a three-dimensional, crystalline appearance. The overall aesthetic is scientific and modern.

Fat-Specific Weight Loss Activin E Antibody (IBIO-610)

High Quality Weight Loss – Targeting Fat Through Activin E

Why We Target Activin E

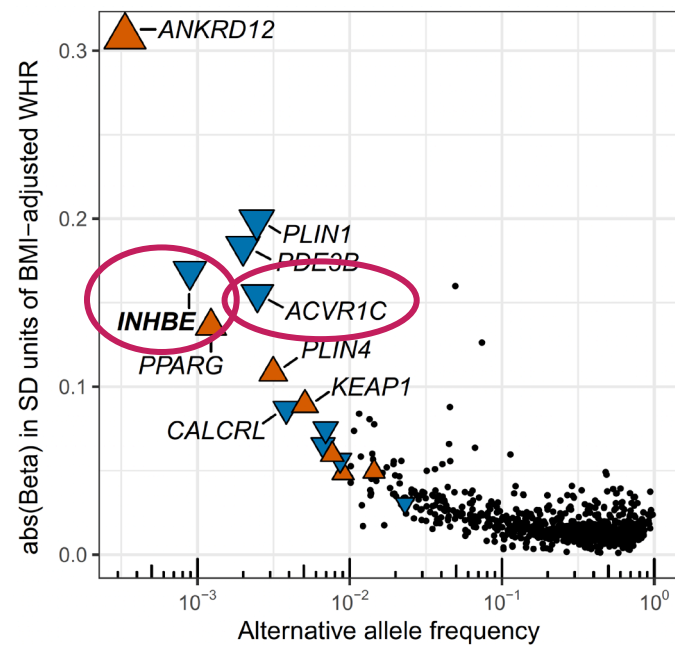
- Activin E is a Hepatokine, produced in the liver and a member of the TGF β family
- Activin E and its receptor are highly genetically validated^{1,2}
- Genetic loss of function decreases adiposity and risk for Diabetes / Cardiovascular Disease (CVD)^{1,2}
- **Multiple RNA targeting molecules provide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



Human Genetic Loss-of-Function mutations in INHBE (gene encoding Activin E) are Associated With Improved Metabolic Health

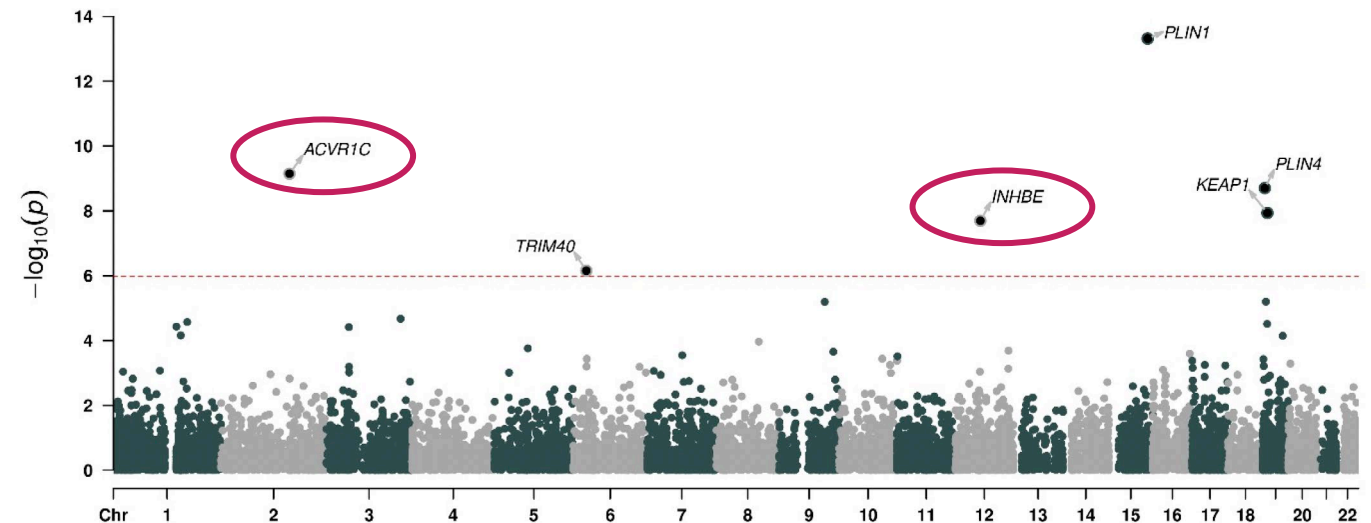


Associations with BMI-adjusted waist-to-hip (WHR) for common and rare alleles



Akbari, P. et al. Nat Commun (2022)

Waist-to-hip ratio adjusted for BMI: Loss of function and missense variants

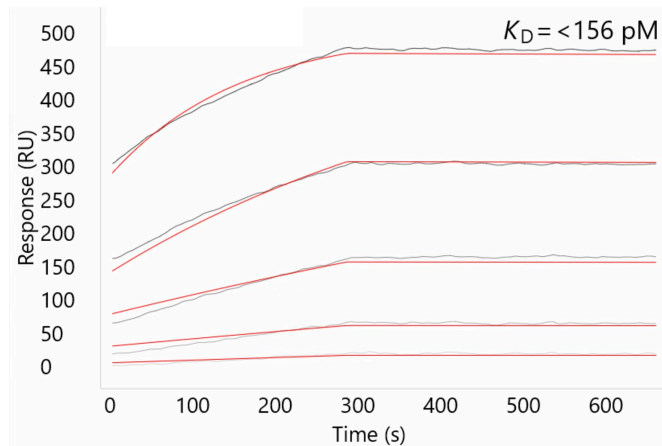


Deaton, A. M. et al. Nat Commun (2022)

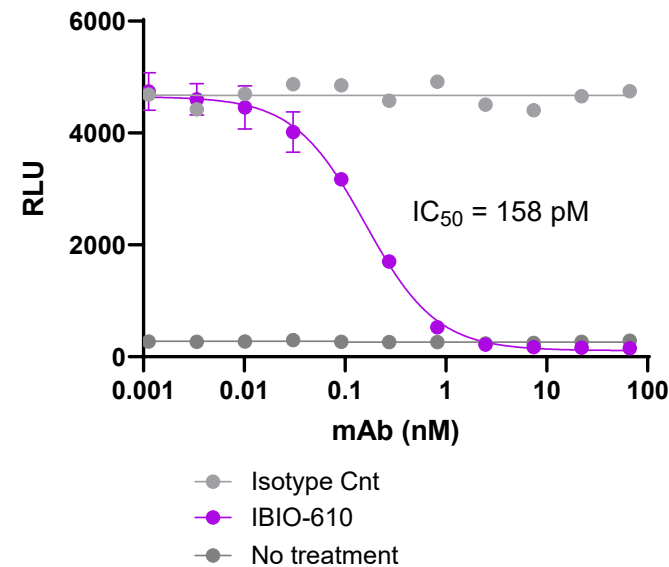
IBIO-610 Exhibits High-Affinity Binding and Potent Inhibition of Activin E Signaling in Engineered and Primary Human Fat Cells



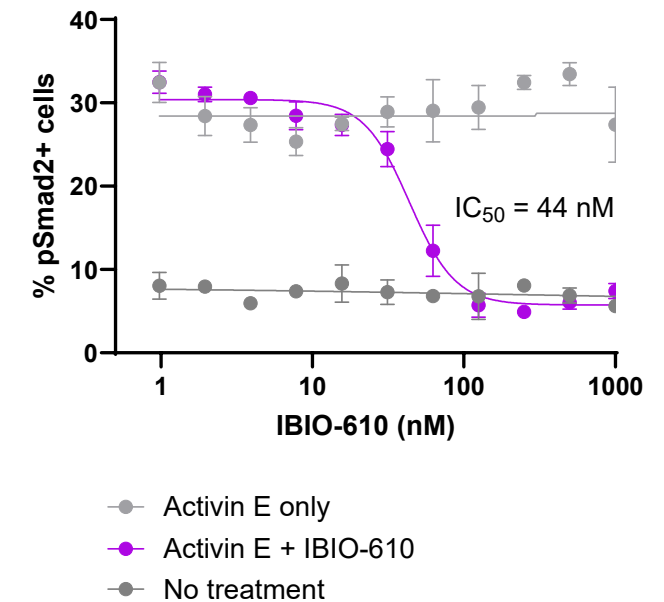
Target Protein Binding Assay



Reporter Cell Line Functional Assay



Primary Human Adipocyte Assay



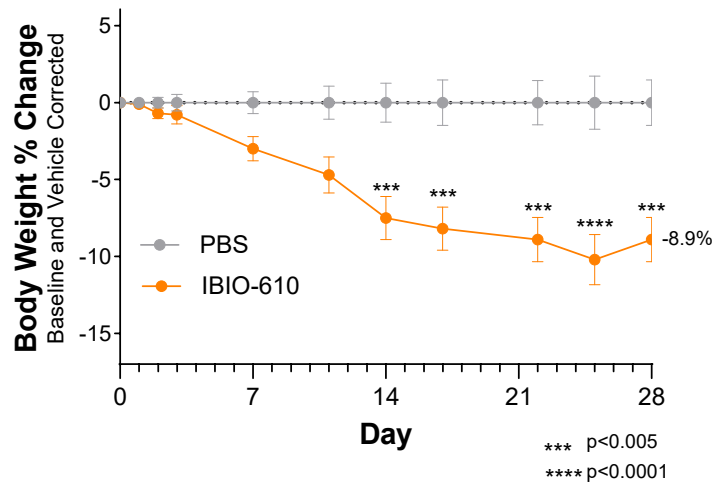
IBIO-610 Induces Fat-Selective Weight Loss in Diet-Induced Obese Mice



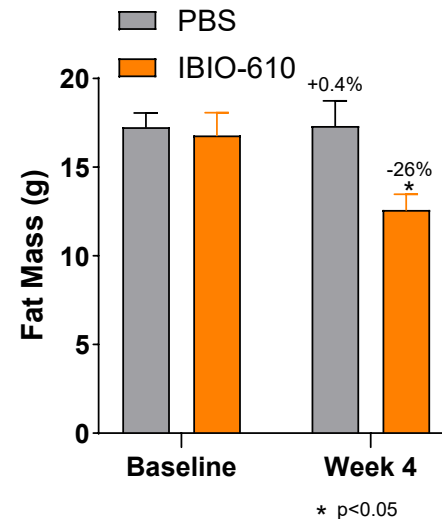
Study Design



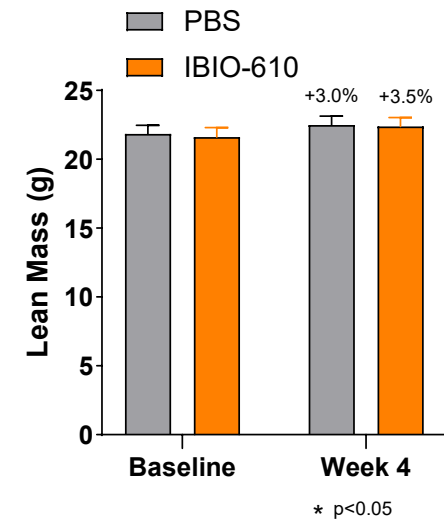
Weight Loss = 8.9%



Fat Loss = 26%



No Lean Mass Loss



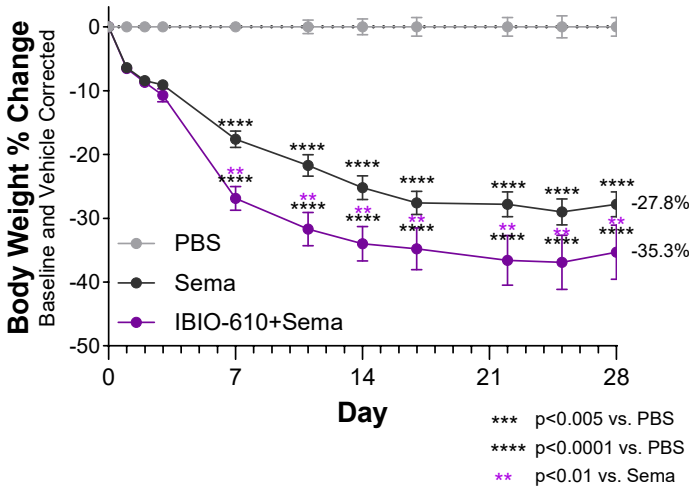
IBIO-610 Synergizes with GLP-1 Through a Distinct, Non-Appetite-Based Mechanism



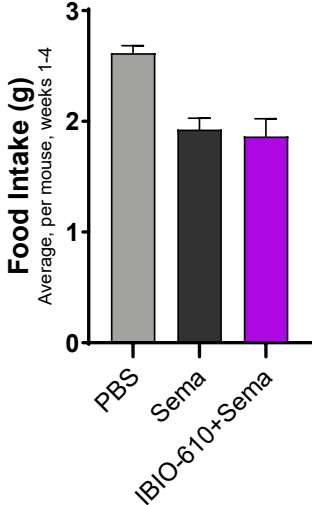
Study Design



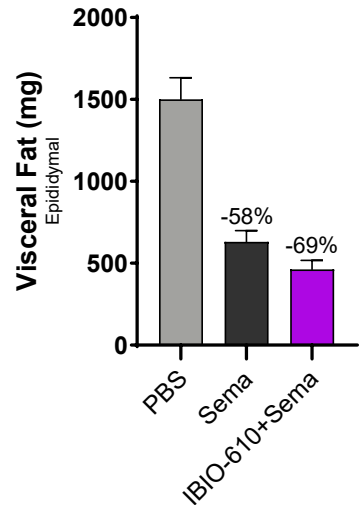
Synergistic Weight Loss



No Additional Appetite Suppression

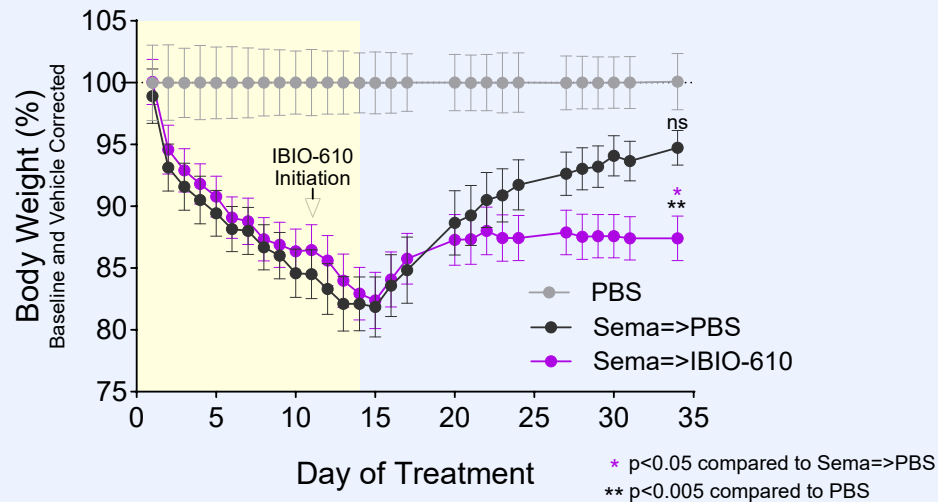


Visceral Fat Reduction

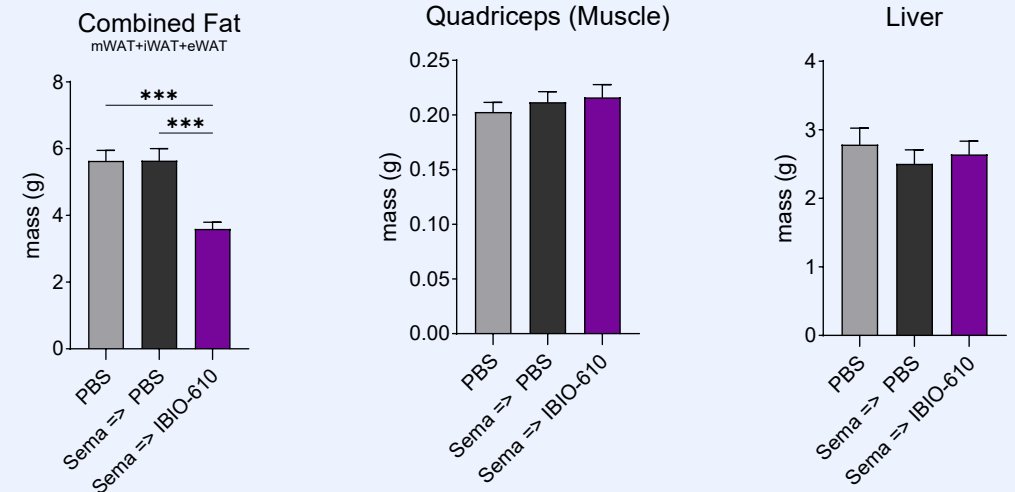


IBIO-610 Observed to Prevent Weight Regain Following GLP-1 Treatment in Obese Mice

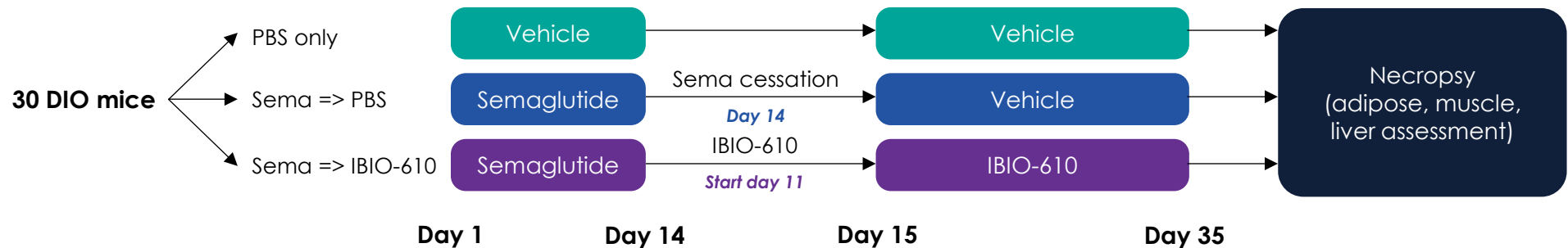
Significant Prevention of Weight Regain



Fat-Specific Effect



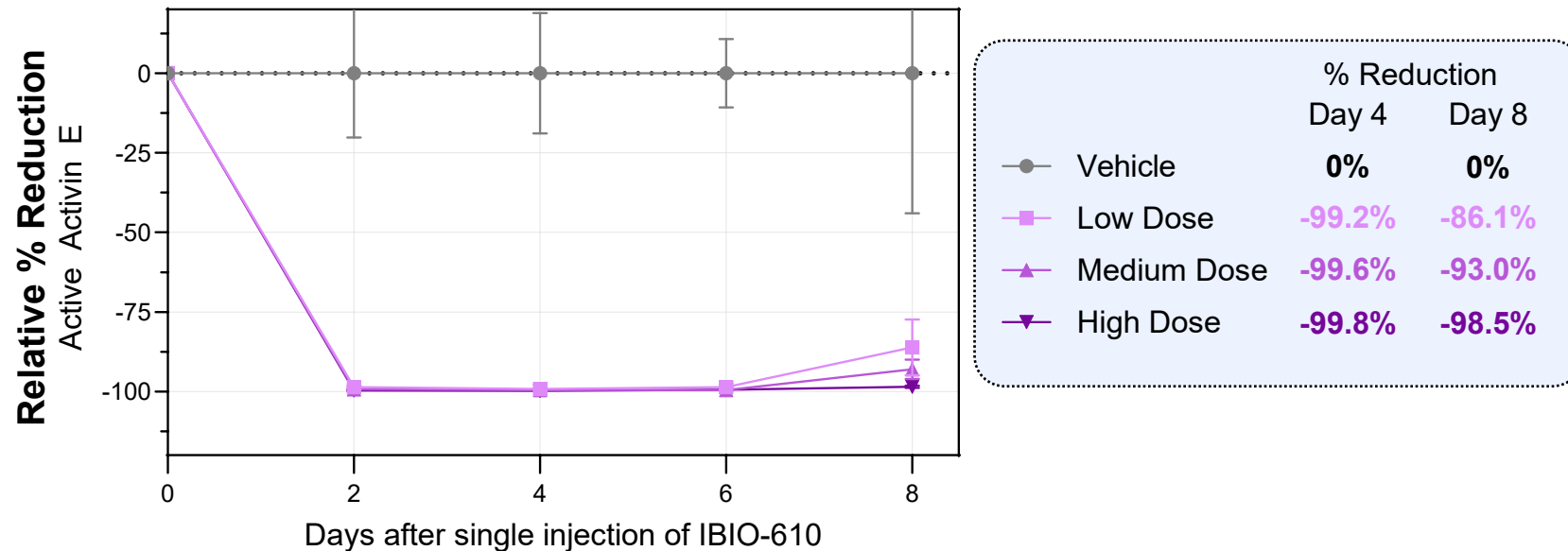
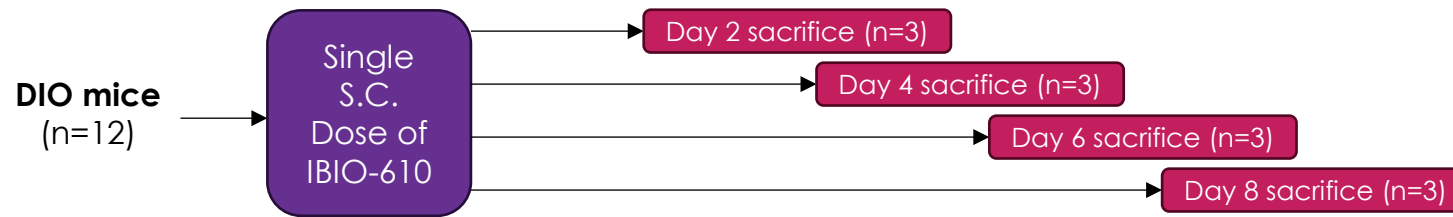
Study Design



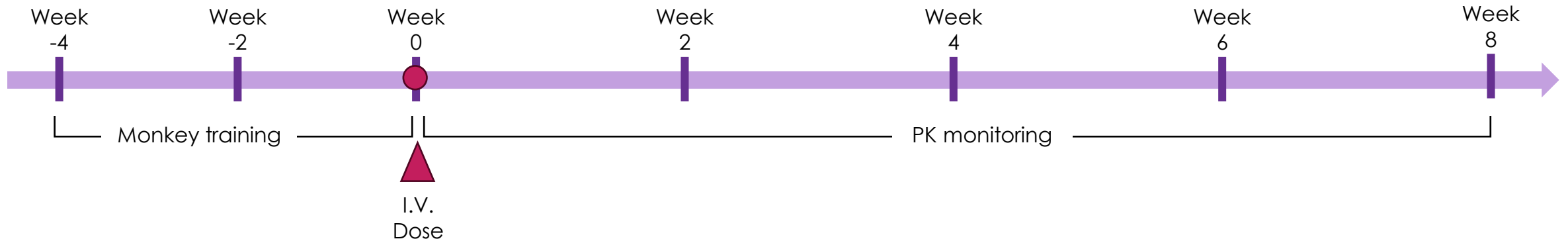
IBIO-610 Reduces Serum Levels of Activin E in Mice

Active Activin E % Reduction – Study Design

Repeated for each dose level, including vehicle



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



NHP Characteristics

- Obese, aged NHPs
- Age 8-15 years
- ~ 18%-51% body fat

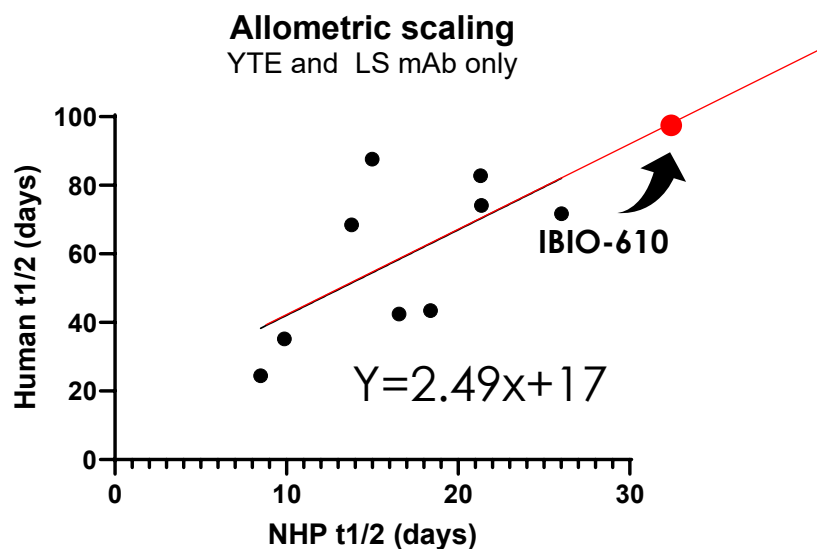
Study design

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

Pharmacokinetics in Non-Human Primates Shows Potential for Extended Half-life in Humans



Allometric Scaling Model for Half-Life Extended Antibodies¹

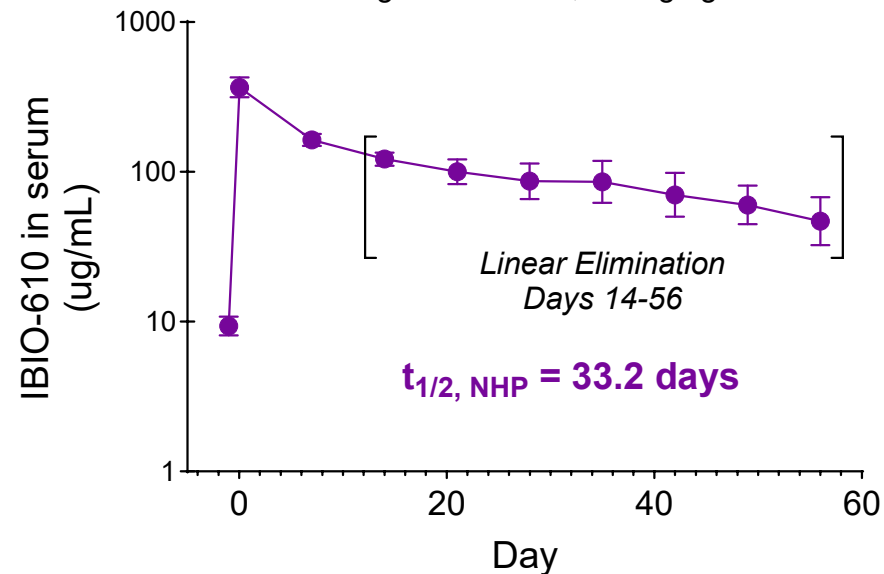


Generic allometric scaling model for antibodies²

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

Obese NHP Pharmacokinetics

Single I.V. Dose, 10 mg/kg



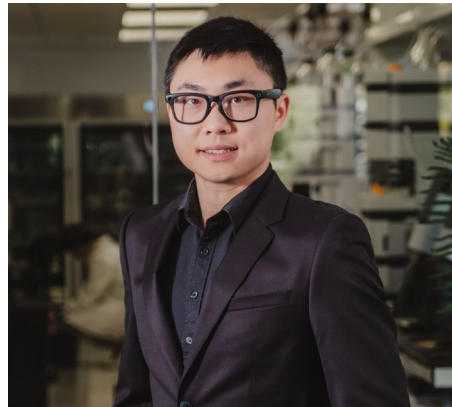
Species	$t_{1/2}$ (days)
NHPs	33.2 days
Humans (predicted)	47-100 days

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

The Team



Q&A

