Deep, Durable Activin E Suppression by Antibody Blockade Drives Fat-Selective Effects in Obese Non-Human Primates

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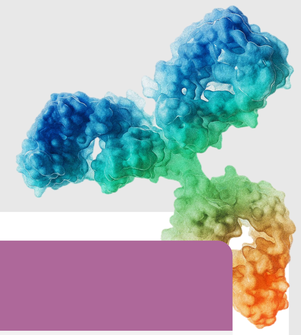


Background

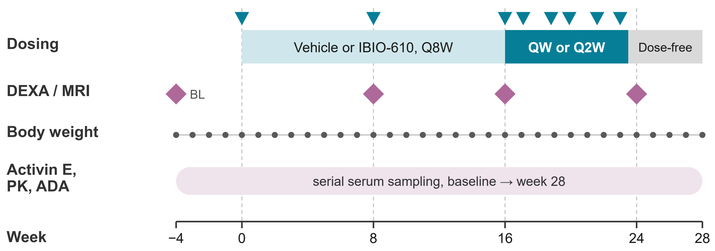
Human genetics point to Activin E–ALK7 as a fat-selective obesity target

- Activin E (INHBE) is a hepatokine that signals through ALK7 on adipocytes to suppress lipolysis and promote fat storage.[1]
- Rare INHBE loss-of-function variants are associated with lower waist-to-hip ratio and protection from type 2 diabetes.[2,3]
- IBIO-610 is a half-life–extended antibody that neutralizes circulating Activin E.



Objective: Test whether intermittent IBIO-610 dosing sustains Activin E blockade and shifts body composition over 28 weeks in obese NHPs

Study Design

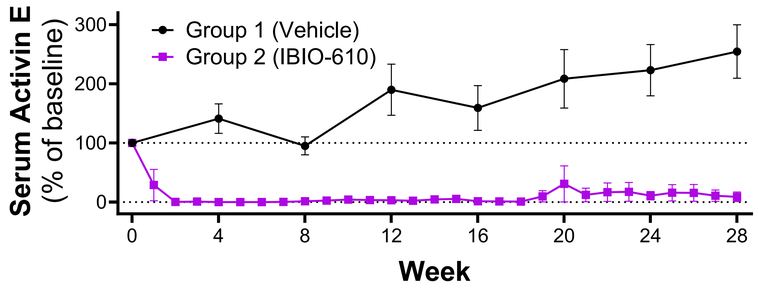


- Vehicle (**n=6**) or IBIO-610 (**n=5**)
  Obese NHPs, 8–15 years old, 18–51% body fat
- Total fat and lean mass by DEXA; visceral fat by abdominal MRI; body weight weekly
- Circulating active Activin E by serum bioassay; IBIO-610 exposure and anti-drug antibodies (ADA) monitored
- Body weight and composition expressed as change from baseline, corrected for vehicle
- Exploratory: subcutaneous (SC) adipose biopsies, H&E

Target Engagement

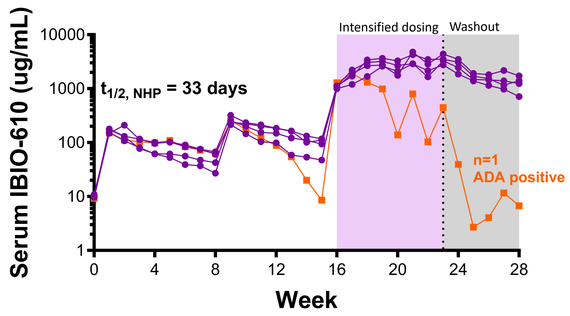
Intermittent dosing sustained near-complete Activin E suppression through week 28

Serum active Activin E



- **Greater than 97% suppression** at all time points from 3 of 4 NHPs
- One NHPs developed a detectable ADA response and was excluded from target engagement analysis

IBIO-610 Exposure



Adipose Histology

Directionally lower crown-like structure and neutrophil scores in SC adipose with IBIO-610 treatment

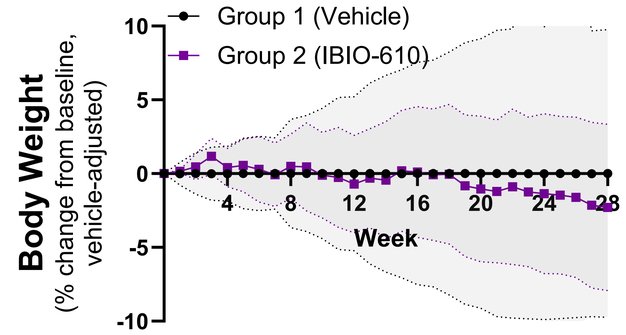
Score per animal	Vehicle (n=6)						IBIO-610 (n=5)				
Mononuclear cells	3	2	2	2	2	1	2	2	2	2	2
Crown-like structures	2	2	1	1	1	0	1	1	1	0	0
Neutrophils	3	3	3	2	2	2	2	2	2	2	2

Exploratory; quantitative immune-cell phenotyping pending.

Body Weight

Body weight was 2.3% lower vs vehicle at week 28

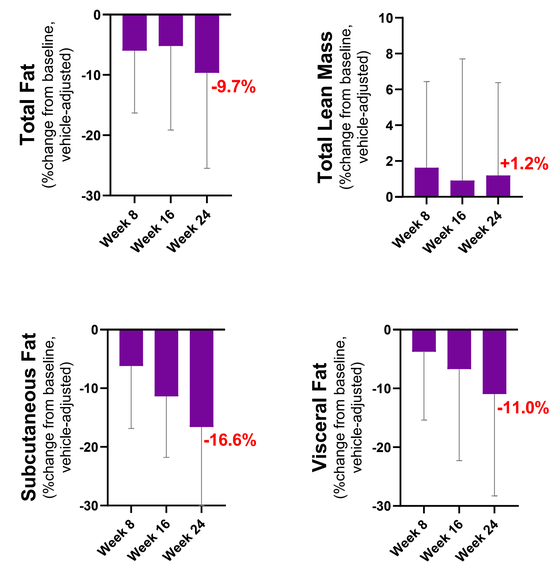
Change in body weight from baseline



Body Composition

Fat reduced relative to vehicle in IBIO-610 group at all timepoints

Change in body composition from baseline



1. Adam et al. PNAS 32;120 (2023)
2. Akbari, P. et al. Nat Commun 13, 4844 (2022).
3. Deaton, A. M. et al.. Nat Commun 13, 4319 (2022).