

GLP-1R/GIPR Peptide Agonist ASC31 + ASC47 Shows 119.6% More Weight Loss than Tirzepatide in DIO Mice

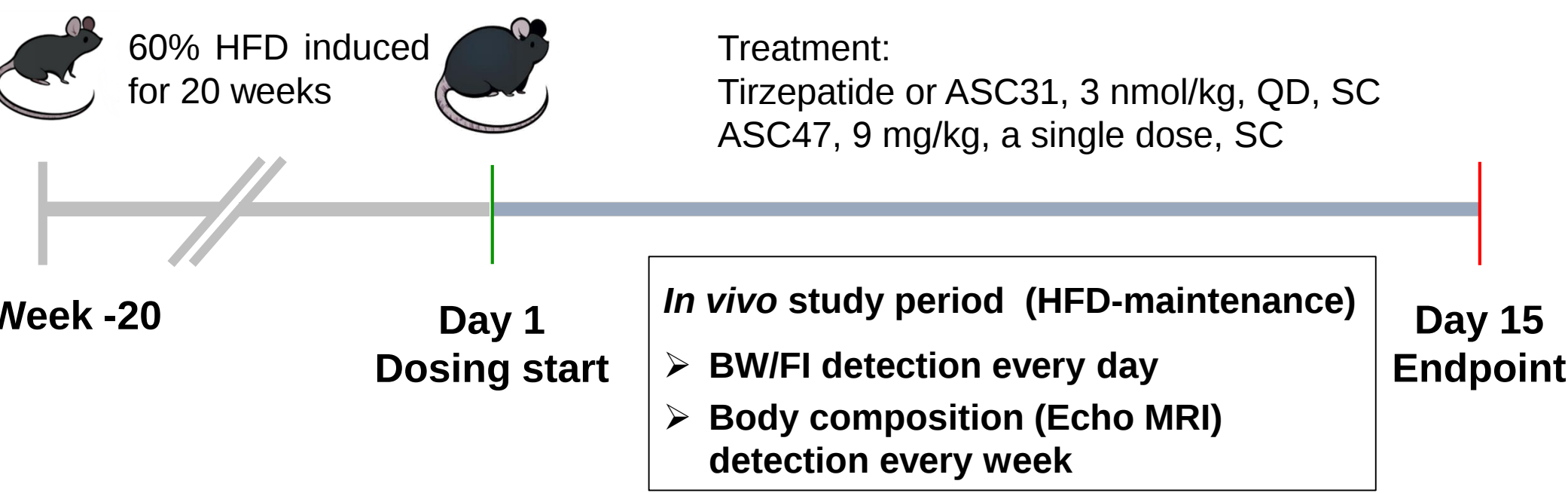
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BACKGROUND

ASC31 is a dual GLP-1R and GIPR peptide agonist, while ASC47 is an adipose-targeted small molecule THRβ selective agonist for muscle-preserving obesity treatment. ASC47 demonstrated a half-life of up to 26 days and 40 days, respectively, in Phase Ib single subcutaneous injection studies in healthy subjects with elevated low-density lipoprotein cholesterol (LDL-C) and patients with obesity, supporting once-monthly to once-bimonthly administration. This study in diet-induced obese (DIO) mice demonstrated a powerful synergy in weight loss and muscle preservation when combining ASC31 and ASC47.

METHODS

5-week-old C57BL/6J mice were fed a high-fat diet for 20 weeks. ASC47 ultra-long-acting formulation was subcutaneously (SC) injected once on Day 1. Both ASC31 and Tirzepatide were once-daily SC dose with the same formulation and the treatment regimen was maintained for 14 days. On Day 15, all the mice were sacrificed. Body weight and food intake were recorded daily. Body composition was assessed by EchoMRI weekly.

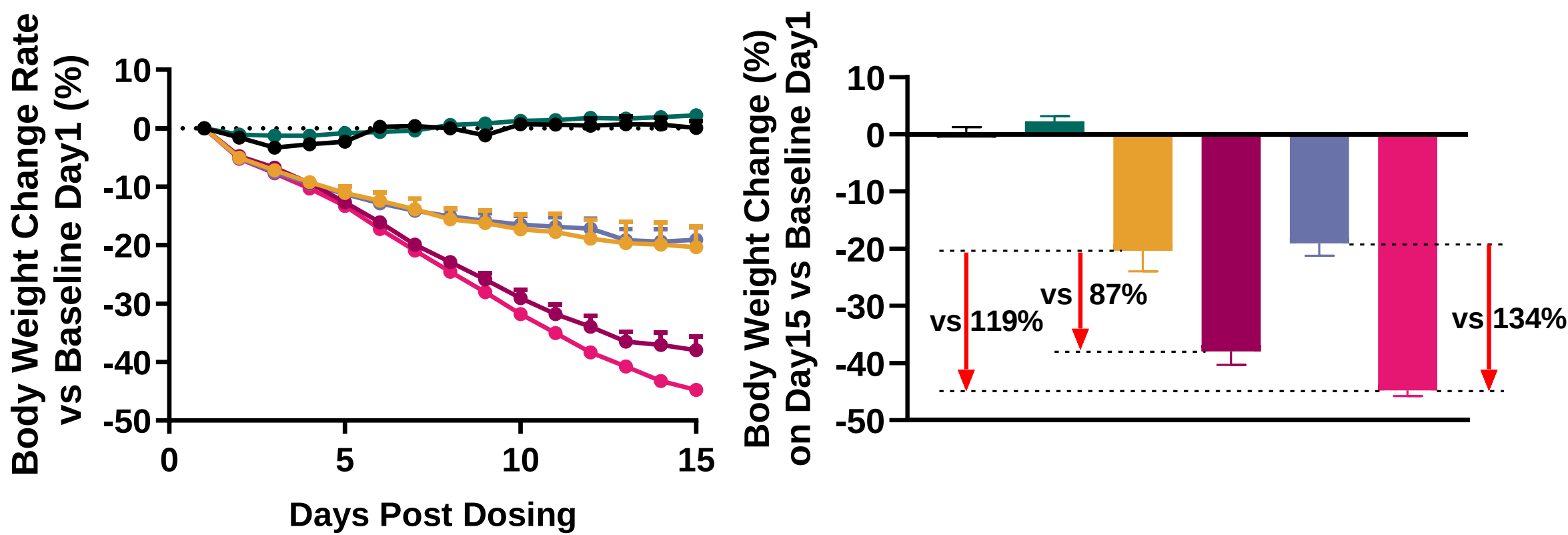


Dosing regimen

Group	Treatment	Dosing	Frequency
Healthy non-obese mice	Vehicle	—	QD*2W
DIO mice	Vehicle	—	QD*2W
Obese mice treated with Tirzepatide	Tirzepatide	3nmol/kg	QD*2W
Obese mice treated with ASC47 and Tirzepatide	Tirzepatide	3nmol/kg	QD*2W
	ASC47	9mg/kg	a single dose
Obese mice treated with ASC31	ASC31	3nmol/kg	QD*2W
Obese mice treated with ASC47 and ASC31	ASC31	3nmol/kg	QD*2W
	ASC47	9mg/kg	a single dose

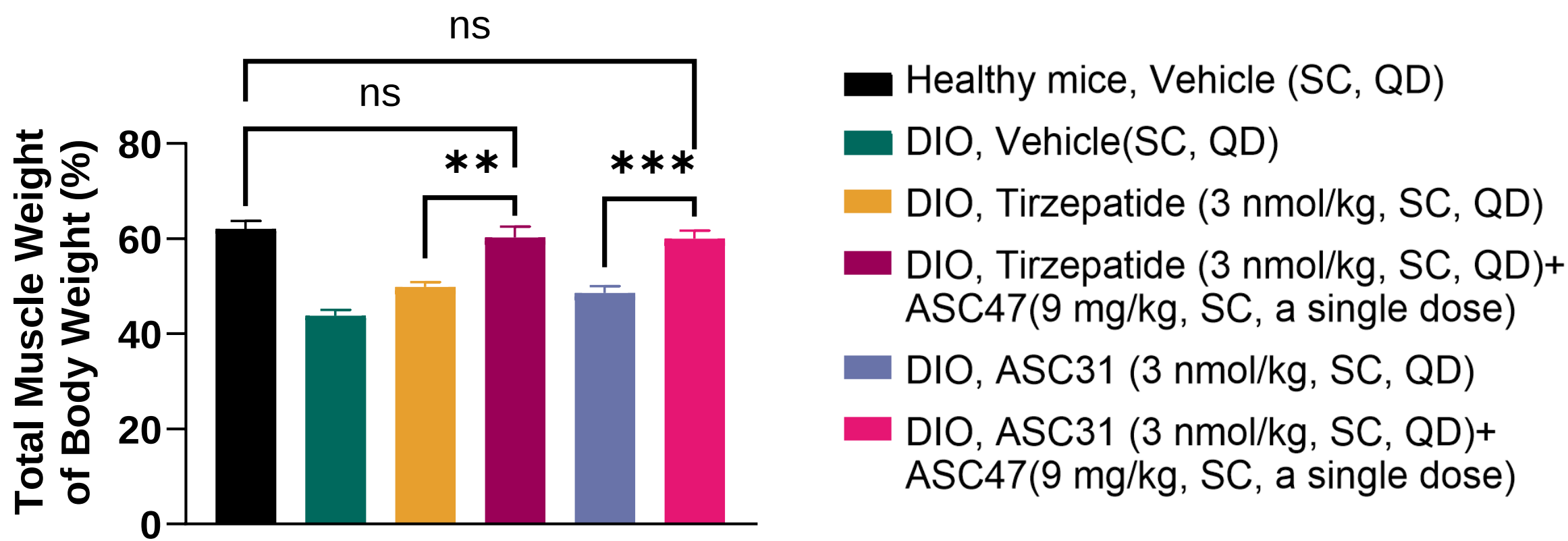
RESULTS

ASC31 + ASC47 Induces Greater Weight Loss



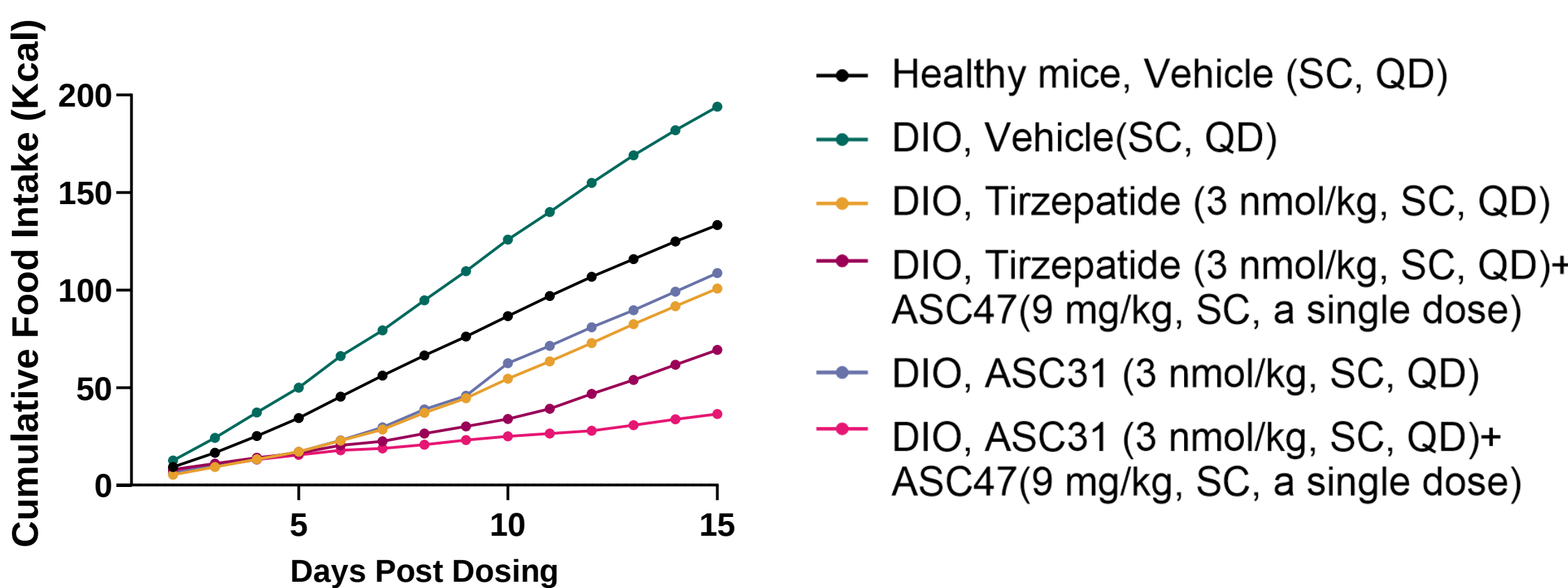
- ASC47+ASC31 (-44.8%) markedly outperformed ASC31 monotherapy (-19.1%) in weight loss, with a 134% higher reduction.
- ASC47+Tirzepatide (-38.1%) notably outperformed Tirzepatide alone (-20.4%) in weight loss (87% greater reduction).
- The average greater reduction of ASC31 (combo vs mono, 134%) is statistically significantly higher than that of Tirzepatide (87%).

ASC47 combo Therapy Promotes Muscle Preservation



- ASC47 combo therapy restores the percentage of total muscle mass over the total body weight to a normal and healthy level, through THRβ mediated activities.

ASC47 combo Therapy Suppresses More Caloric Intake



- ASC47 combo therapy achieving significantly more weight loss is partially through suppressing food intake.

Table: A Head-to-head Comparison Between Tirzepatide And ASC31 in Monotherapy And Combination Therapy

Group	Total Body Weight Change From Baseline	Total Muscle Mass/Total Body Weight Ratio	Cumulative Caloric Intake (Kcal)
Healthy non-obese mice	+0.03%	62.0%	133.3
Obese mice	+2.2%	43.8%	194.1
Obese mice treated with Tirzepatide	-20.4%	49.9%	100.8
Obese mice treated with ASC47 and Tirzepatide	-38.1% (p<0.0001 vs Tirzepatide monotherapy)	60.4% (p=0.0015 vs Tirzepatide monotherapy)	69.4 (p=0.0091 vs Tirzepatide monotherapy)
Obese mice treated with ASC31	-19.1%	48.6%	108.7
Obese mice treated with ASC47 and ASC31	-44.8% (p<0.0001 vs ASC31 monotherapy; p<0.0001 vs Tirzepatide monotherapy)	60.0% (p=0.0005 vs ASC31 monotherapy; p=0.0021 vs Tirzepatide monotherapy)	36.5 (p<0.0001 vs ASC31 monotherapy; p<0.0001 vs Tirzepatide monotherapy)

SUMMARY

- ASC31 is a dual GLP-1R and GIPR peptide agonist, while ASC47 is a small molecule THRβ-selective agonist and was designed with unique and differentiated properties to enable targeted delivery to adipose tissue.
- The combination of ASC47 and ASC31 significantly outperformed either Tirzepatide or ASC31 monotherapy in promoting weight loss, body fat loss and muscle preservation.
- The combination of ASC47 with either ASC31 or Tirzepatide restored the body composition of obese mice to the level of healthy non-obese mice.