

ASC47, a Muscle-Preserving Weight Loss Drug Candidate for Obesity, in Combination with Semaglutide, Demonstrated Superior Weight Loss to Semaglutide Monotherapy in a Preclinical Model

Jinzi Jason Wu and Chengfei Wu. Ascletis Pharma (China) Co., Limited, Hong Kong

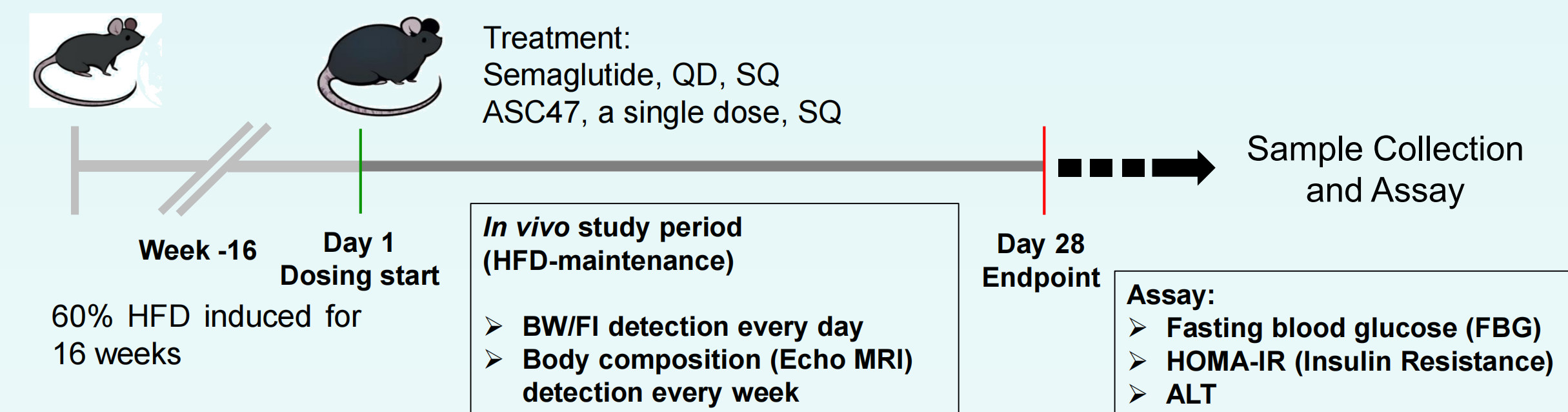


① INTRODUCTION

ASC47 is a small molecule $\text{THR}\beta$ selective agonist and was designed with unique and differentiated properties to enable targeted delivery to adipose tissue. ASC47 is a muscle-preserving weight loss drug candidate to treat obesity. ASC47 demonstrated a half-life of up to 26 days and 40 days, respectively, in Phase Ib single subcutaneous injection studies in healthy subjects and patients with obesity, supporting once-monthly to once-bimonthly administration. This study demonstrated a powerful synergy in weight loss and muscle preservation when combining ASC47 and semaglutide in diet-induced obese (DIO) mice.

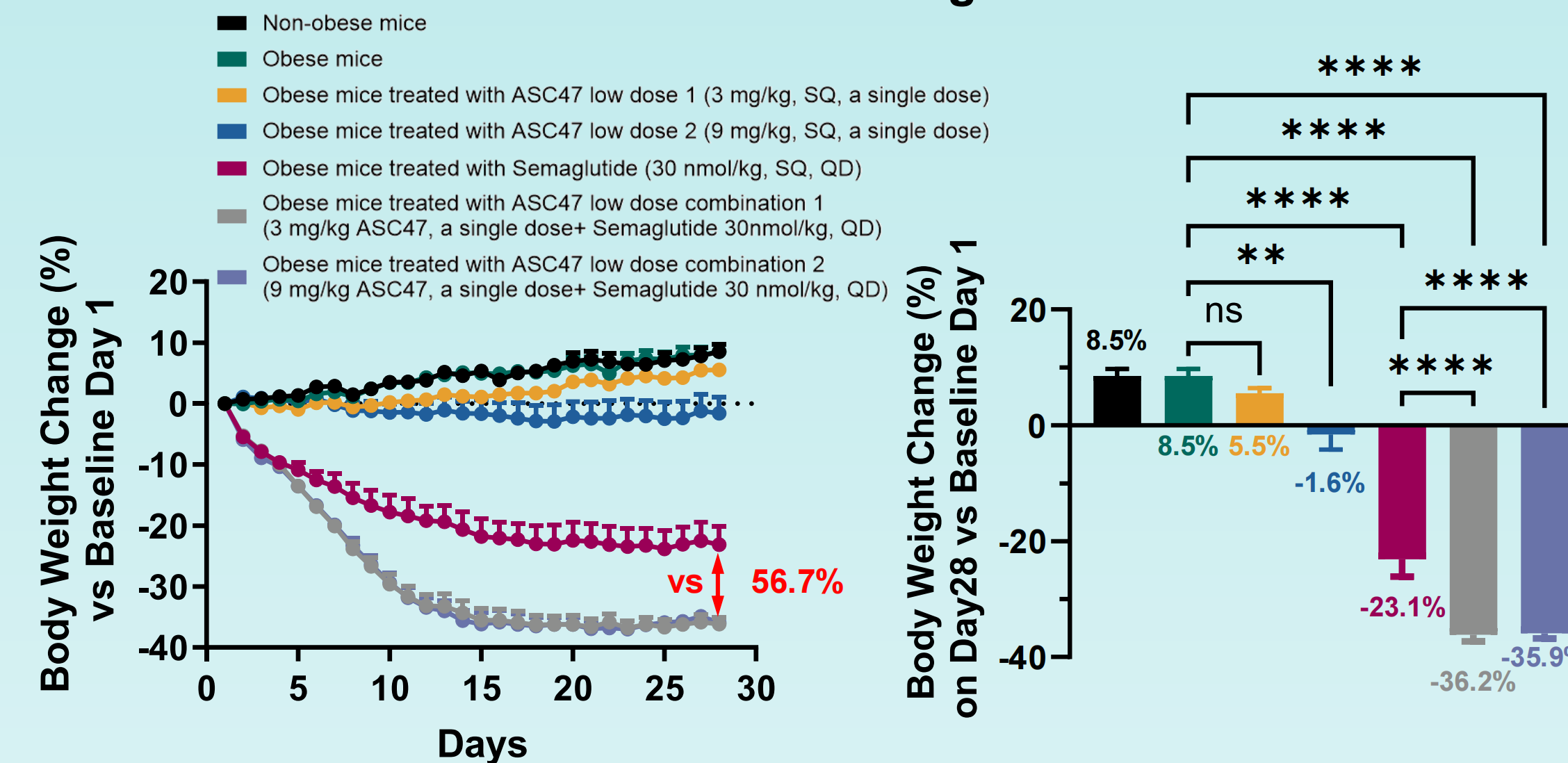
② METHODS

Male C57BL/6J mice were fed a high-fat diet (60% HFD) for 16 weeks prior to start. Mice were treated once-monthly and once daily with vehicle in healthy non-obese mice group and obese mice group. ASC47 low dose 1 and low dose 2 group were subcutaneously injected with ASC47 once at the dose of 3 mg/kg and 9 mg/kg, respectively. 30 nmol/kg of semaglutide were subcutaneously injected daily in semaglutide monotherapy group. ASC47 low dose combination 1 and low dose combination 2 were treated with 3 mg/kg or 9 mg/kg of ASC47 once and 30 nmol/kg semaglutide daily. The total efficacy duration was 28 days. Body weight and food intake were recorded daily. Body composition was assessed by Echo MRI weekly.



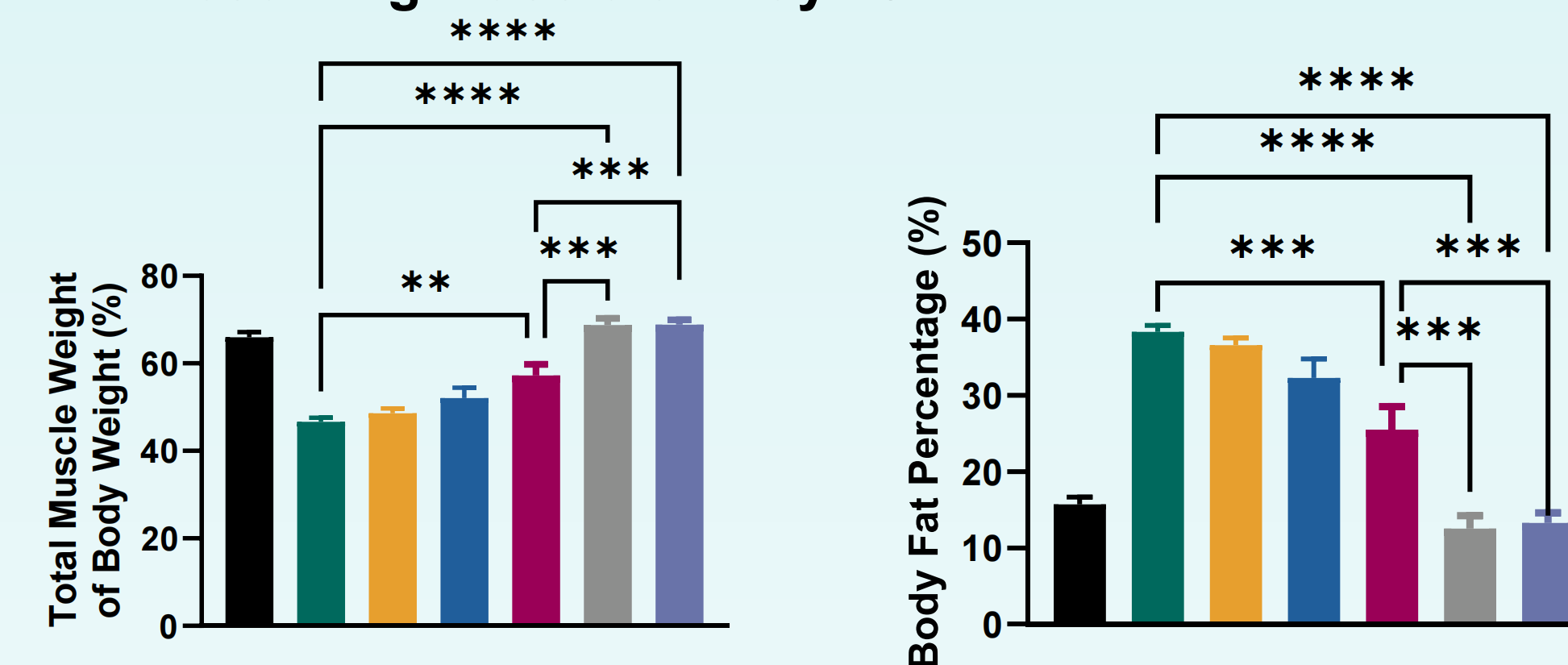
③ RESULTS

ASC47 + Sema Induces Greater Weight Loss vs Sema Alone



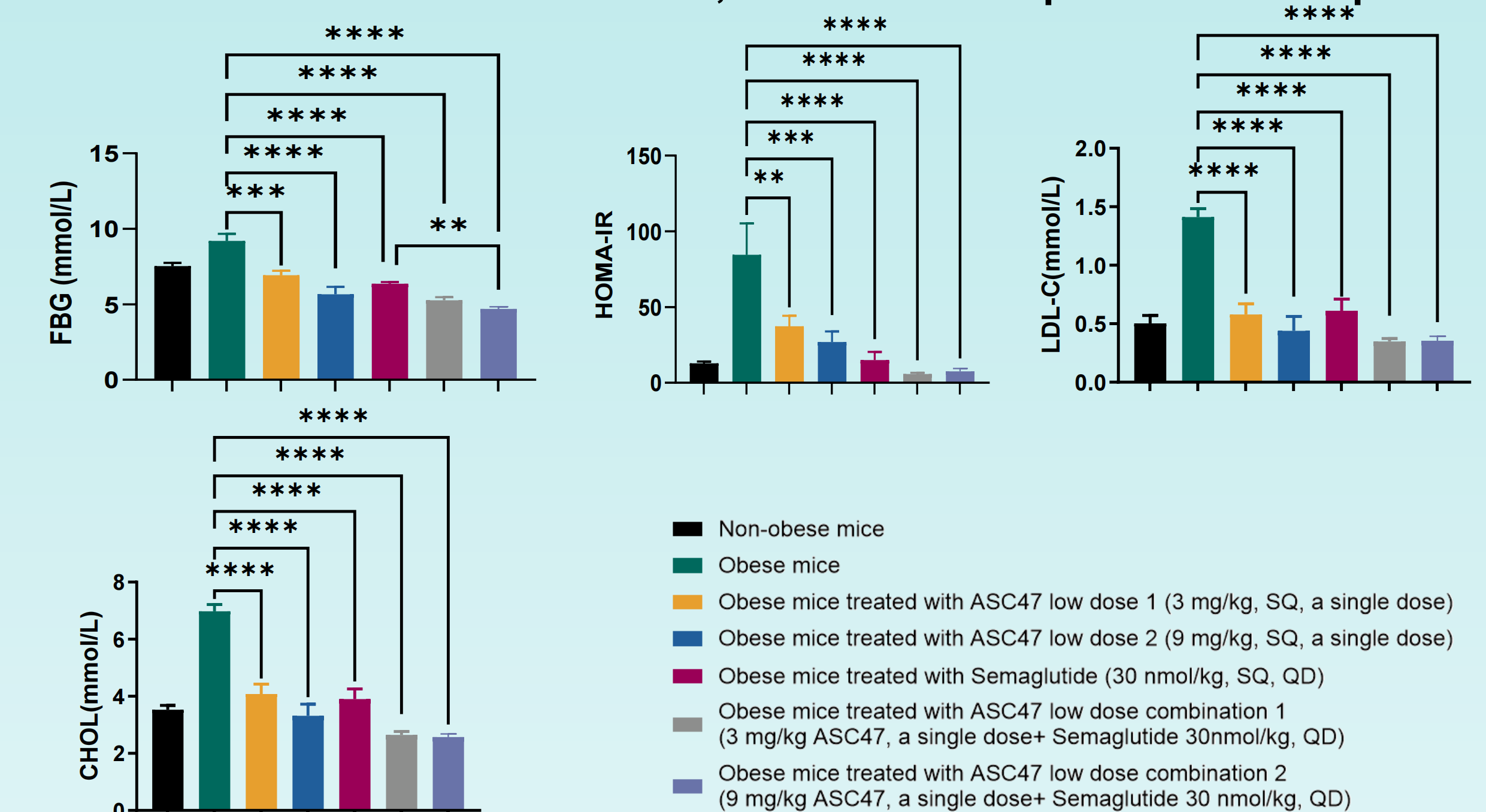
- ASC47 low dose combination 1 showed an average total body weight reduction of 36.2%, a 56.7% greater reduction in body weight compared to semaglutide monotherapy (23.1%).

ASC47 + Sema Induces Greater Fat Loss vs Sema Alone while Preserving Muscle on Day 28



- ASC47 low dose combination treatments restored muscle percentage to healthy levels and induced a 51% greater fat loss than semaglutide monotherapy.

ASC47 + Sema Decreased FBG, IR and Blood Lipids without Hepatotoxicity



- At Day 28, ASC47 low dose combination therapies decreased FBG(fasting blood glucose), IR(insulin resistance) and blood lipids significantly than obese mice without hepatotoxicity.

④ SUMMARY

- ASC47 is a small molecule $\text{THR}\beta$ selective agonist and was designed with unique and differentiated properties to enable targeted delivery to adipose tissue.
- ASC47 is a muscle-preserving weight loss drug candidate to treat obesity. ASC47 low dose combination 1 showed more significant weight loss (-36.2%) than semaglutide monotherapy, achieving a 56.7% greater reduction in body weight compared to the latter (-23.1%).
- ASC47 low dose combination therapies led to enhanced fat reduction and brought the muscle percentage back to a healthy state, unlike semaglutide, which was unable to achieve this.
- ASC47 low dose combination therapies regulated FBG, IR and blood lipids without hepatotoxicity.

