



## Introduction & Objective

- The obesity pandemic is a major health crisis and current treatments are primarily focused on weight loss. However, health benefits from weight loss can be compromised by the weight-loss-associated loss of lean body mass.
- Petrelintide (ZP8396), a novel once-weekly amylin analog currently in phase 1 clinical testing, has shown to induce meaningful reductions in body weight in lean and overweight subjects.
- Here we investigate the effect of petrelintide on weight loss with comparison of changes of fat mass and lean mass in diet-induced obese (DIO) rats.

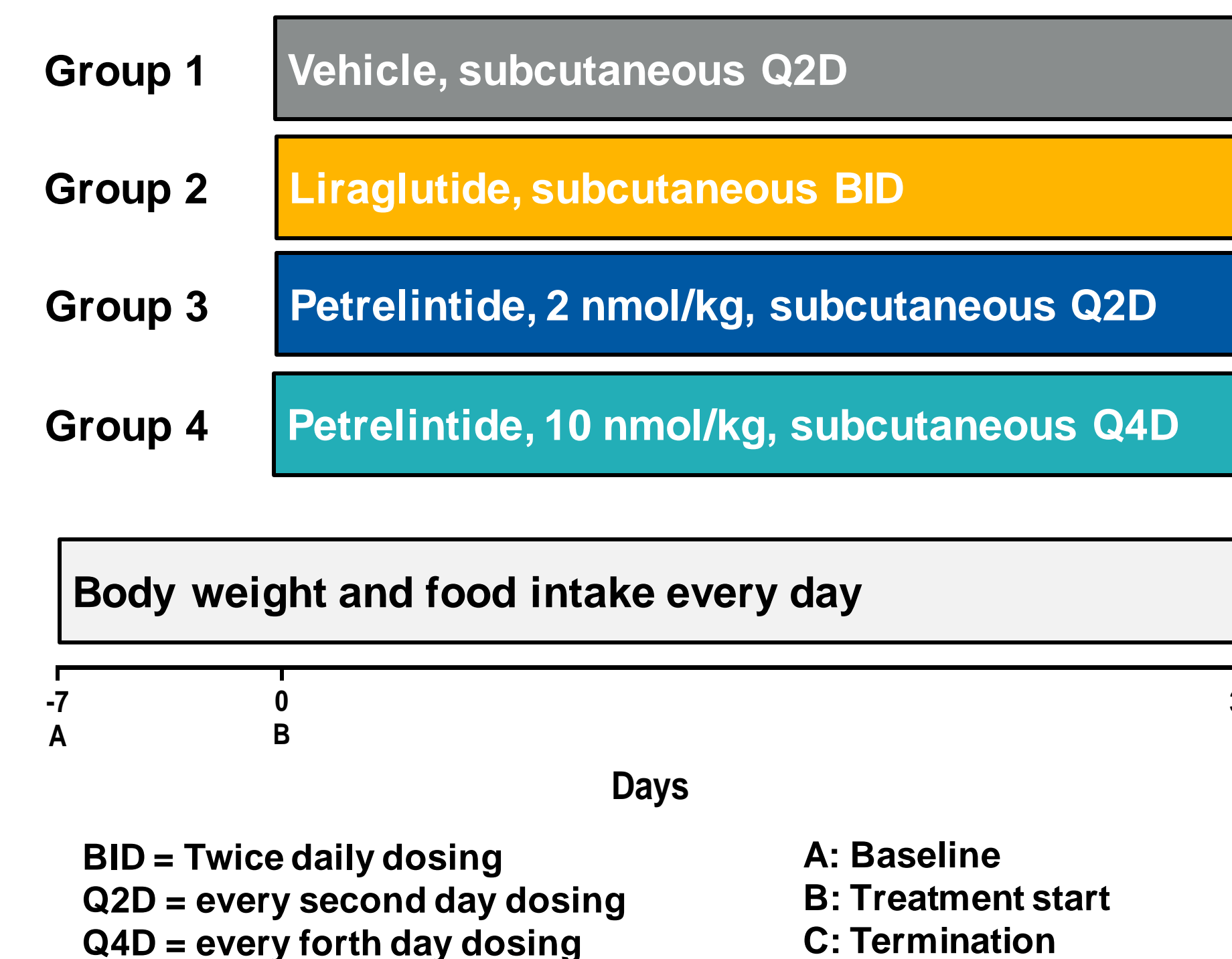
## Methods

- DIO rats (n=10 per group) were treated with either vehicle (every second day), liraglutide (5 nmol/kg twice daily) or petrelintide (2 nmol/kg every second day or 10 nmol/kg every fourth day) for a 30-day treatment period.
- Body weight was measured daily, and body composition was measured by use of EchoMRI at baseline and at day 29 of treatment (as shown below).

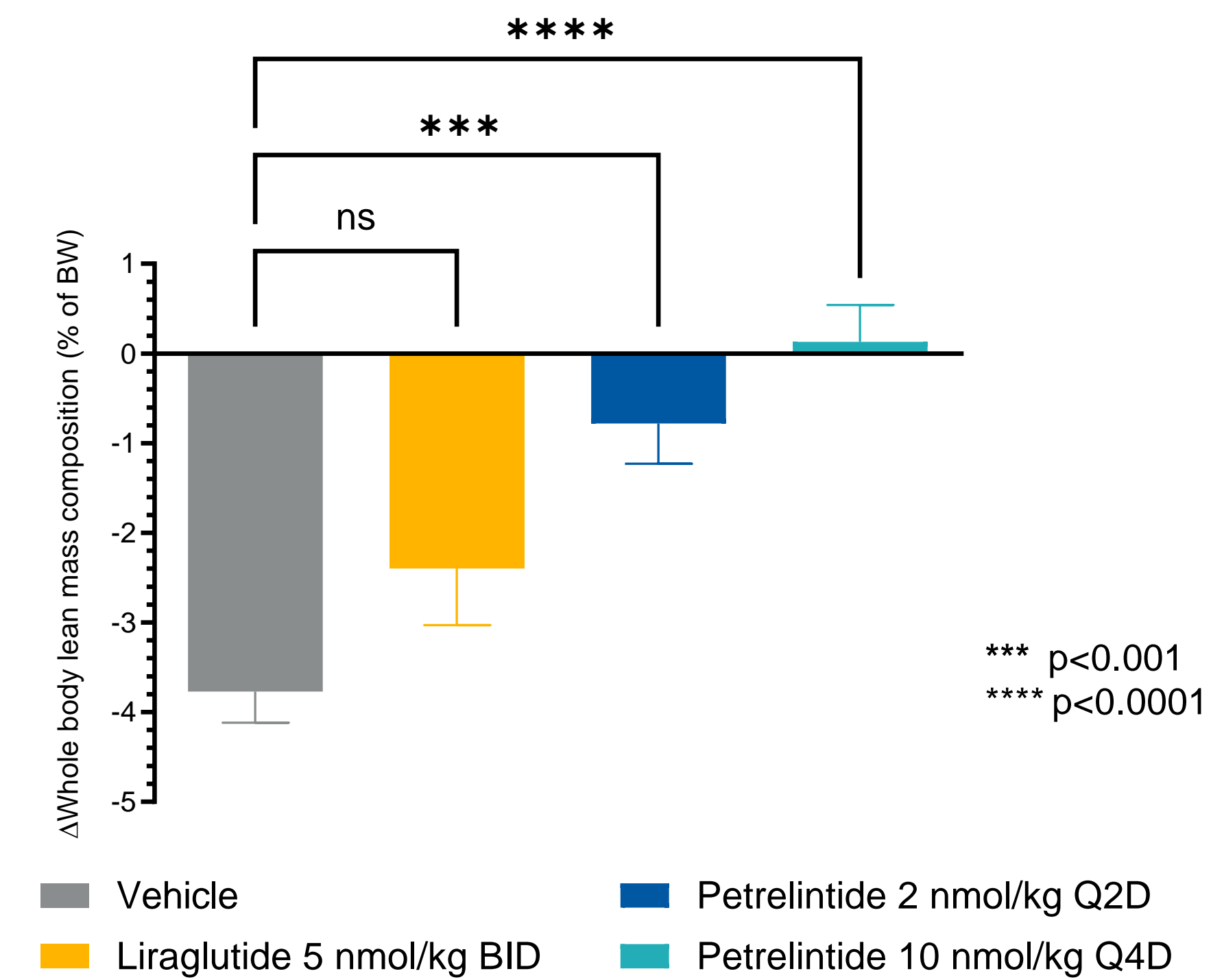
## Results

- Treatment with liraglutide and petrelintide resulted in significantly lower relative body weight compared to vehicle (3.3 % ± 0.7 vehicle, -0.1 % ± 1.1 liraglutide, -4.1 % ± 0.6 petrelintide 2 nmol/kg, -7.8 % ± 0.7 petrelintide 10 nmol/kg; relative to initial body weights ± SEM).
- Treatment with petrelintide resulted in significant preservation of relative lean mass in comparison to vehicle, which liraglutide did not (-3.8 % ± 0.3 vehicle, -2.4 % ± 0.6 liraglutide, -0.8 % ± 0.4 petrelintide 2 nmol/kg, 0.1 % ± 0.4 petrelintide 10 nmol/kg; mean change in lean mass as % of body weight ± SEM).
- Furthermore, treatment with petrelintide resulted in significant reduction of fat mass in comparison to vehicle, which liraglutide did not (3.2 % ± 0.4 vehicle, 2.0% ± 0.5 liraglutide, -0.3 % ± 0.5 petrelintide 2 nmol/kg, -1.6 % ± 0.5 petrelintide 10 nmol/kg; mean change in fat mass as % of body weight ± SEM).

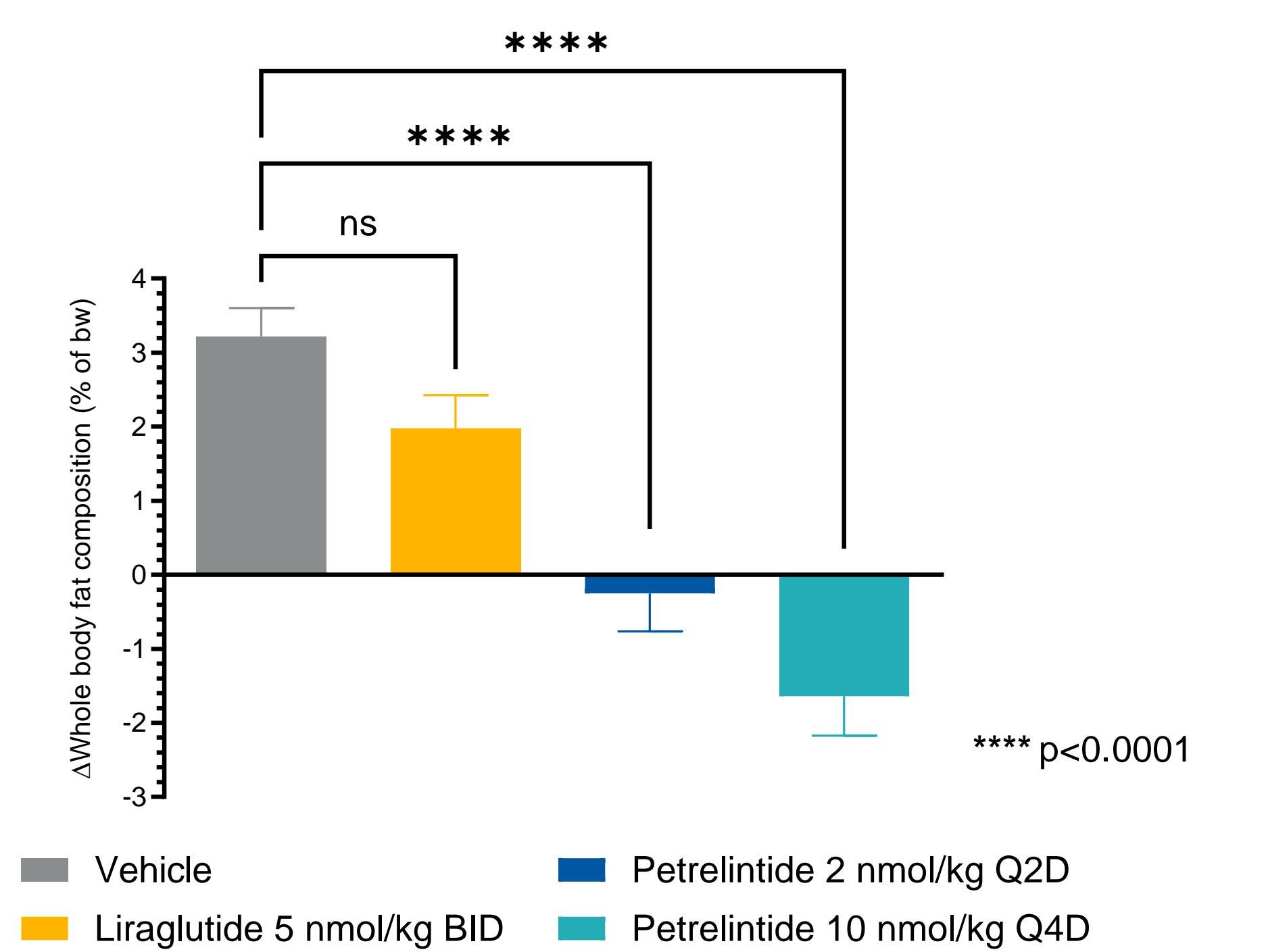
## Study design



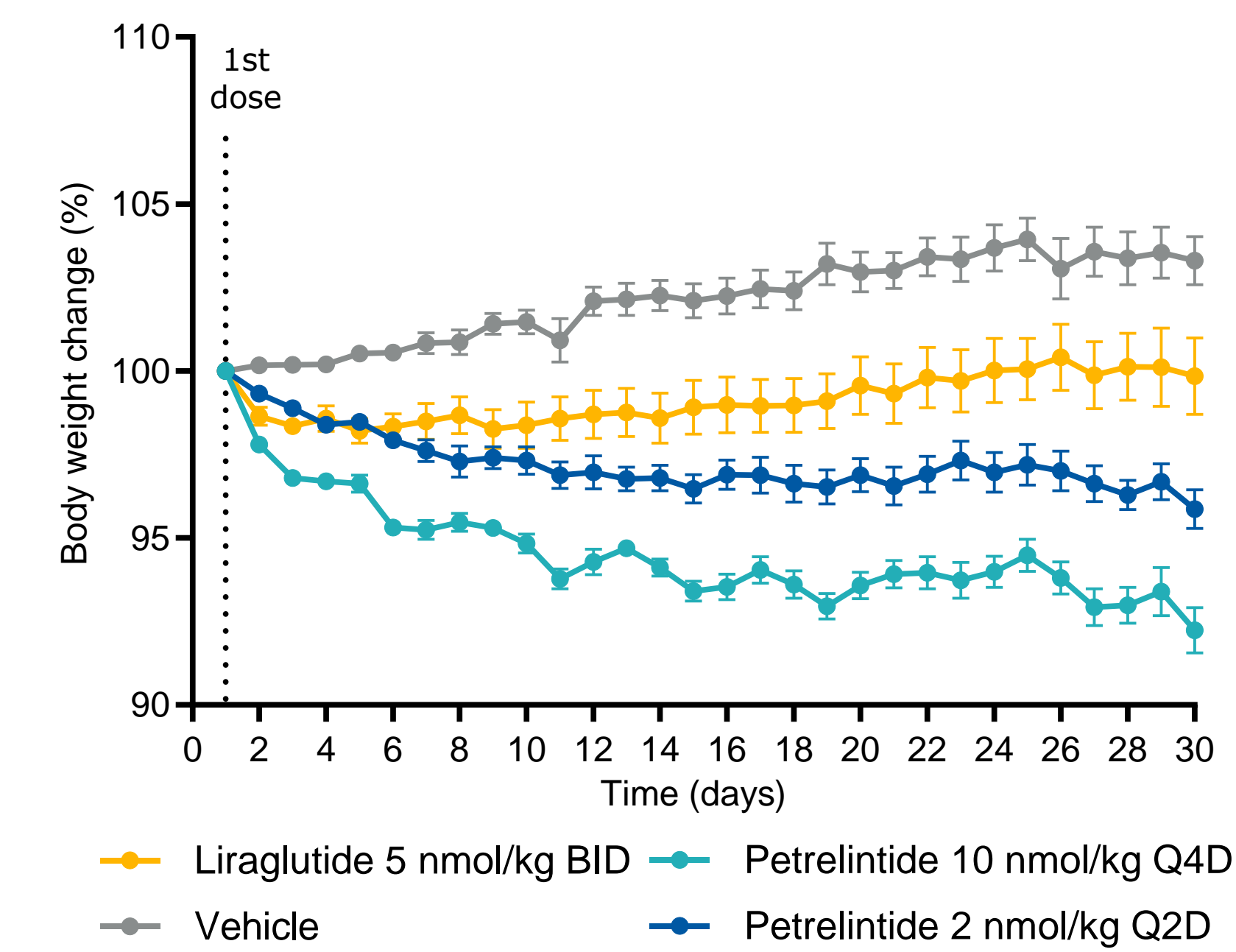
## Change in lean mass



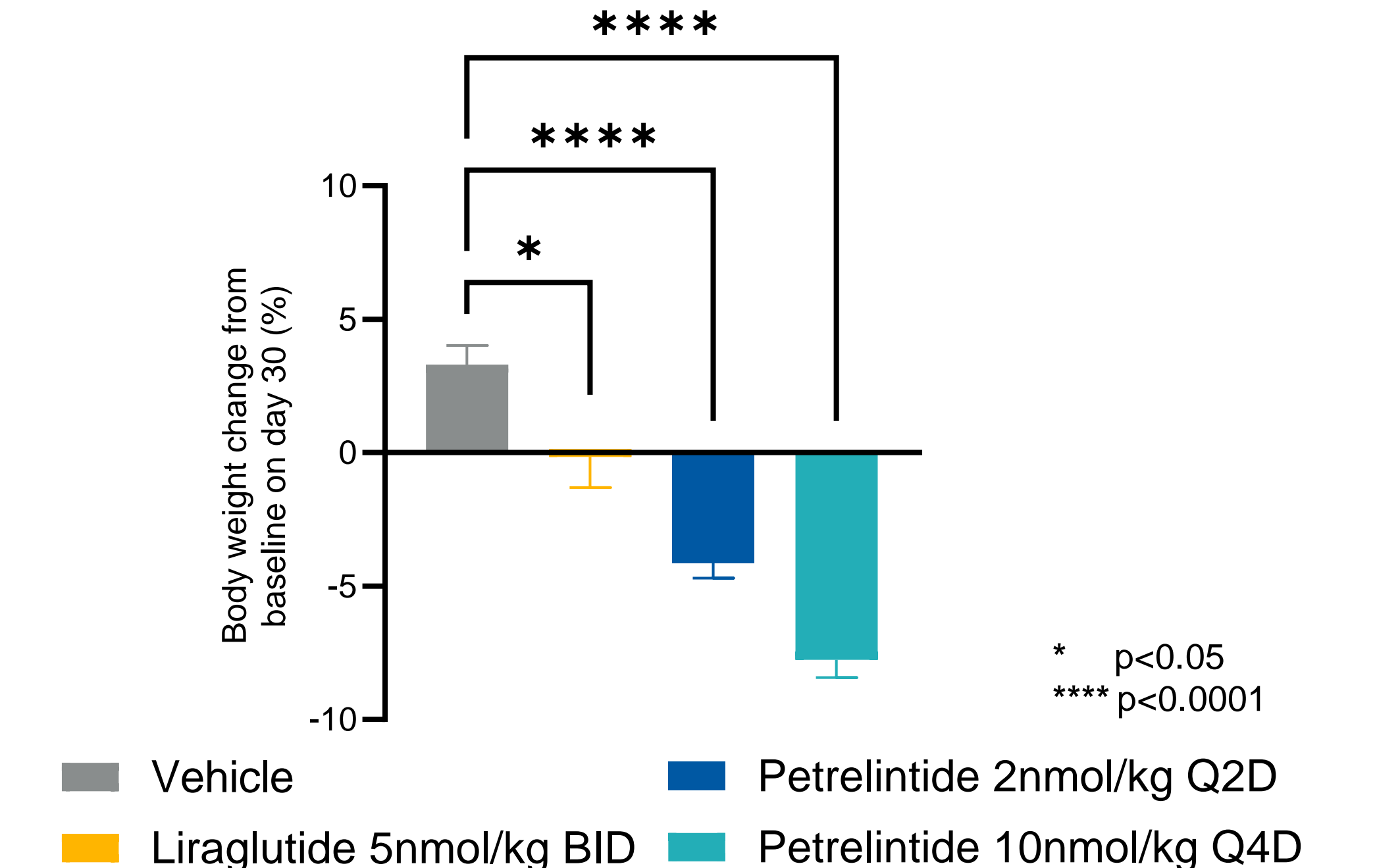
## Change in fat mass



## Change in body weight



## Change in body weight at day 30



## Conclusions

- Petrelintide shows preferential fat mass loss and preservation of relative lean mass during weight loss in DIO rats.
- Petrelintide could hold the potential to reduce the loss of lean body mass associated with weight loss in humans.
- Petrelintide is currently being explored in a phase 1 trial to assess the potential for the management of obesity.