ASC36, a Once-Monthly Next-Generation Amylin Receptor Agonist Peptide, Demonstrated 32-day Average Observed Half-life, 6-fold Longer than Petrelintide, in NHP Model and 91% and 32% More Relative Weight Loss than Petrelintide and Eloralintide in DIO Rat Model

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Introduction

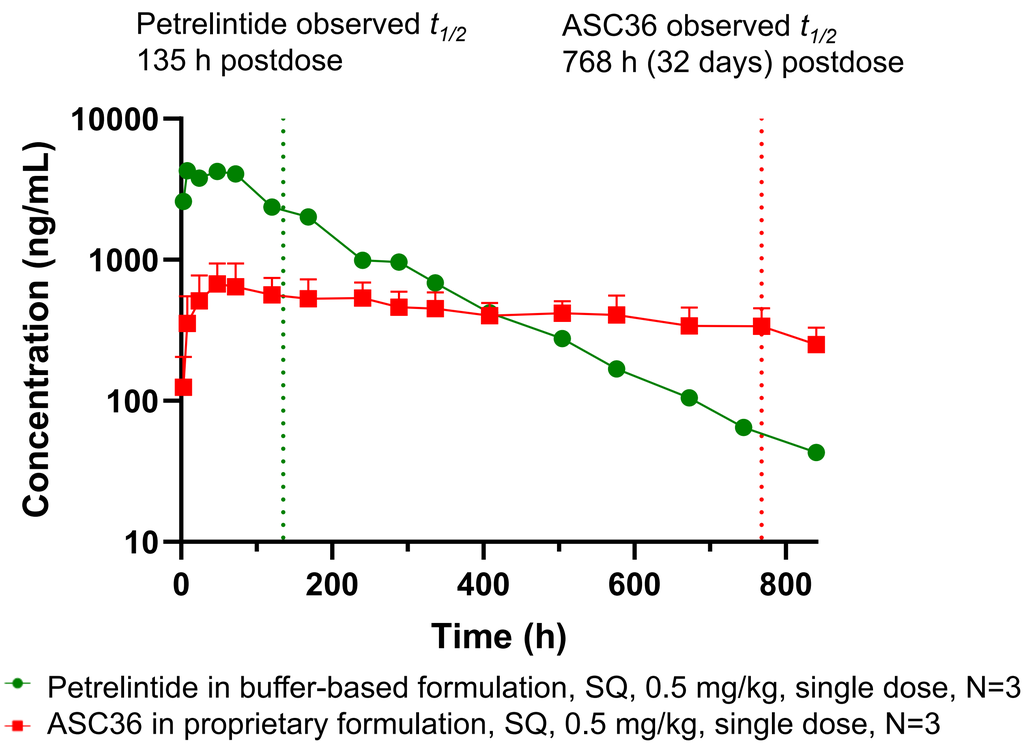
ASC36, a next generation amylin receptor agonist peptide, was discovered and developed in-house utilizing Ascletis' Artificial Intelligence-Assisted Structure-Based Drug Discovery (AISBDD) and Ultra-Long-Acting Platform (ULAP) technologies. ASC36 is engineered for a longer observed half-life (as measured by time to 50% C_{max}) and greater efficacy to support once-monthly SQ dosing, with injection volume of one milliliter or less.

Methods

Pharmacokinetic profile of ASC36 in proprietary formulations developed Ascletis' ULAP technology was evaluated in non-human primates, in vivo efficacy of ASC36 was evaluated in DIO rat model.

Results

PK Study in Non-human Primate (NHP)

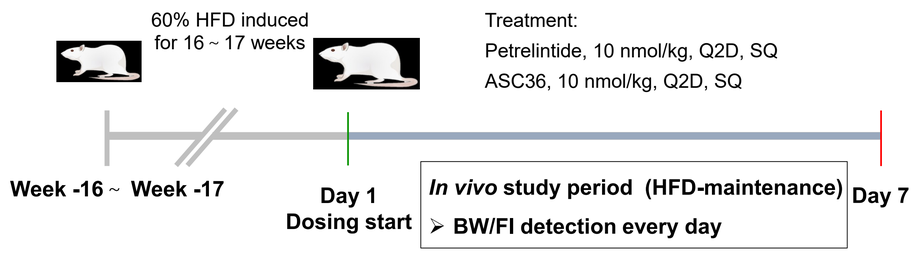


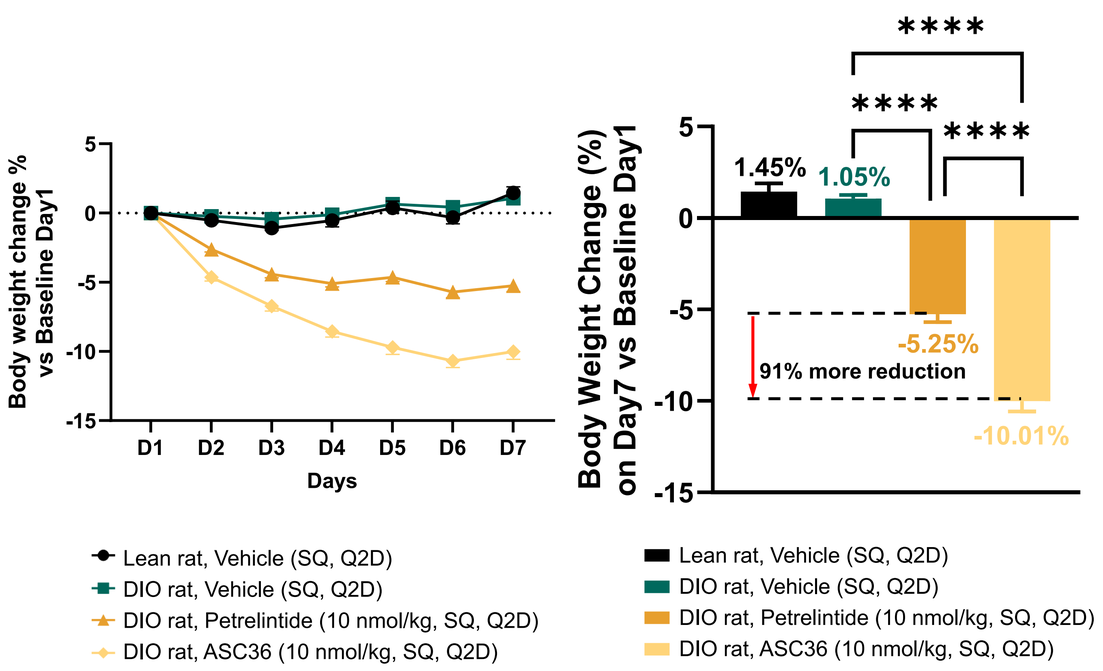
- In head-to-head non-human primate (NHP) studies, ASC36 slow-release SQ depot formulation had an average observed half-life of approximately 32 days, 6-fold longer than petrelintide.

In vivo Efficacy Study

Study 1: ASC36 Induced Greater Weight Loss than Petrelintide

Study Illustration

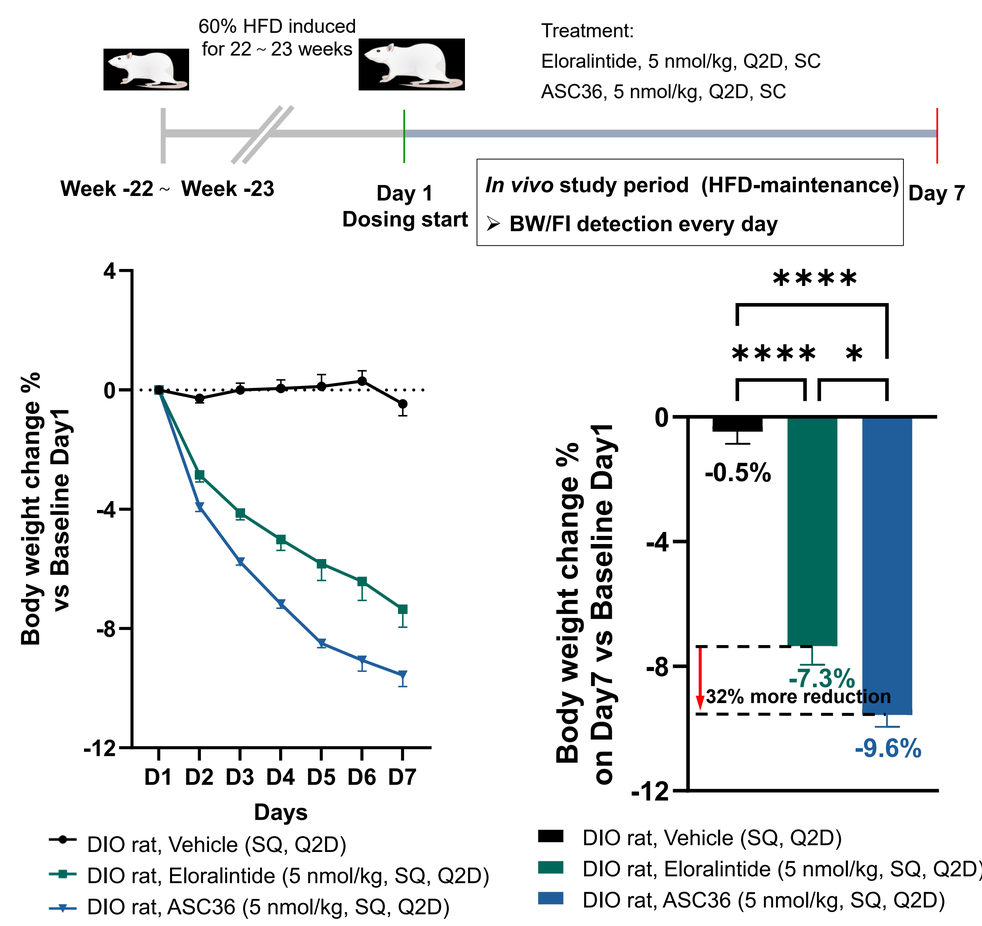




- ASC36 reduced body weight by 10.01%, compared to 5.25% for petrelintide, a relative increase in efficacy of 91%.

Study 2: ASC36 Induced Greater Weight Loss than Eloralintide

Study Illustration



- ASC36 reduced body weight by 9.6%, compared to 7.3% for eloralintide, a relative increase in efficacy of 32%.

Tabulated summary

Table 1. ASC36 demonstrated statistically and significantly more weight loss than petrelintide in DIO rats after 7-day treatment

Group	Dosing	Total body weight change from baseline	Greater relative weight loss versus petrelintide
Obese rats treated with vehicle	Vehicle, SQ, Q2D	1.05%	-
Obese rats treated with ASC36	10 nmol/kg, SQ, Q2D	-10.01% (p <0.0001 vs vehicle)	91% (p <0.0001 vs petrelintide)
Obese rats treated with petrelintide	10 nmol/kg, SQ, Q2D	-5.25% (p <0.0001 vs vehicle)	-

Table 2. ASC36 demonstrated statistically and significantly more weight loss than eloralintide in DIO rats after 7-day treatment

Group	Dosing	Total body weight change from baseline	Greater relative weight loss versus petrelintide
Obese rats treated with vehicle	Vehicle, SQ, Q2D	-0.5%	-
Obese rats treated with ASC36	5 nmol/kg, SQ, Q2D	-9.6% (significant change vs eloralintide)	32% (vs eloralintide)
Obese rats treated with eloralintide	5 nmol/kg, SQ, Q2D	-7.3% (significant change vs vehicle)	-

Note:
DIO rats/Obese rats: diet-induced obese rats;
SQ: subcutaneous; Q2D: once every two days.

Conclusions: ASC36's longer observed half-life and greater weight loss demonstrate its potential as a best-in-class once-monthly amylin receptor agonist for the treatment of obesity.