ASC37 Showed 6-Fold Longer Half-life Than Retatrutide in NHP and Marked Weight Loss in DIO Mice

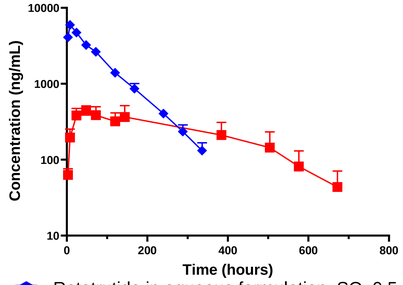
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Introduction: ASC37, a potent GLP-1R, GIPR and GCGR triple peptide agonist, was discovered and developed in-house utilizing Ascletis' Artificial Intelligence-Assisted Structure-Based Drug Discovery (AISBDD) and Ultra-Long-Acting Platform (ULAP) technologies. ASC37 is designed and engineered for a longer half-life and higher bioavailability per milligram of peptide, compared to once-weekly administered retatrutide, to support once-monthly SQ dosing, with injection volume of one milliliter or less. These engineered properties also allow for scalability advantages in manufacturing.

Methods: Pharmacokinetic profile of ASC37 in proprietary formulations developed Ascletis' ULAP technology was evaluated in non-human primates. To assess the agonistic efficacy of ASC37 in stimulating insulin secretion, *in vitro* insulin secretion assays were performed using INS-1 832/3 cells. *In vivo* weight-loss efficacy of ASC37 was evaluated in DIO mouse model. 5-week-old C57BL/6J mice were fed a high-fat diet for 16 weeks to induce obesity. ASC37 was subcutaneously (SQ) injected every day at the dose of 1,10 and 30 nmol/kg, respectively. On Day 12, all the mice were sacrificed. Body weight and food intake were recorded daily.

Results

PK Studies in Non-human Primate (NHP)



Retatrutide in aqueous formulation, SQ, 0.5 mg/kg, 0.2 mL/kg, 2.5 mg/mL
ASC37 in Self Assembly Lipid Depot formulation, SQ, 0.5 mg/kg, 0.2 mL/kg, 2.5 mg/mL

Group	Monkey	ROA	dose (mg/kg)	Observed $T_{1/2}$ (h)
Retatrutide in aqueous formulation	n=3	SQ	0.5	57.8
ASC37 in Self Assembly Lipid Depot formulation	n=3	SQ	0.5	372

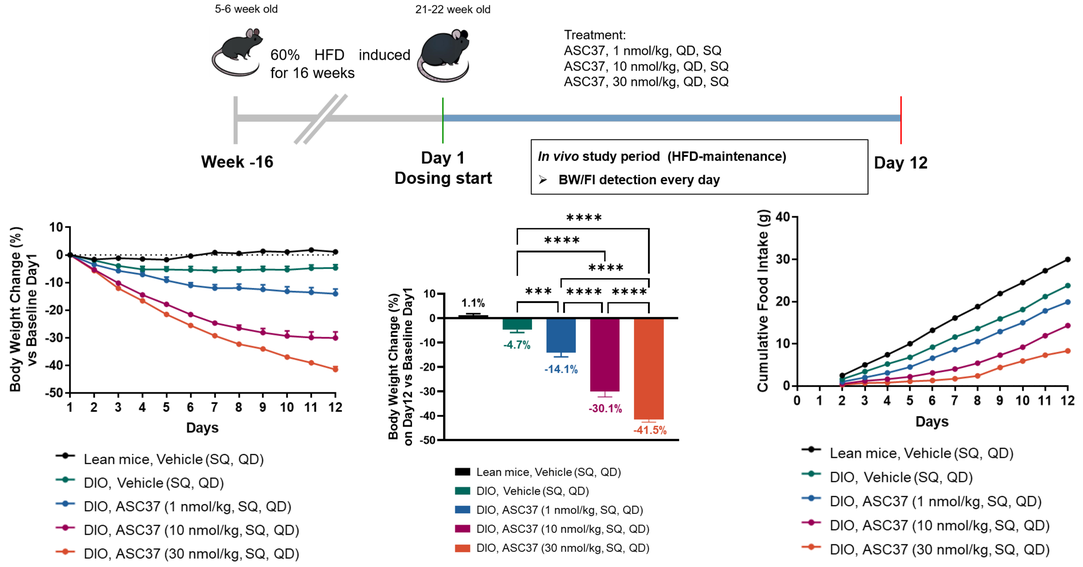
- ASC37 showed 6-fold longer half-life than retatrutide in NHP.

In vitro Insulin Secretion Assay

Compound ID	EC_{50}(nM)	E_{max}(%)
ASC37	0.9858	106.75
Retatrutide	23.03	108.84

- ASC37 exhibited a 23.4-fold higher potency than retatrutide in the insulin secretion assay.

In vivo Study Illustration in DIO mouse



- ASC37 reduced body weight by suppressing appetite in a dose-dependent manner.

Conclusions: As a potent GLP-1R, GIPR and GCGR triple peptide agonist, ASC37's longer half-life and significant weight loss in animal model demonstrate its potential as a first-in-class and best-in-class once-monthly SQ treatment for obesity.

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Disclosure:
Jinzi Jason Wu: Employee of Ascletis Pharma (China) Co., Limited;
Chengfei Wu: Employee of an affiliate of Ascletis Pharma (China) Co., Limited

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