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# ASC39: An Eloralintide-like Selective and Potent Oral Small Molecule Amylin Receptor Agonist for the Treatment of Obesity

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## Introduction & Objective

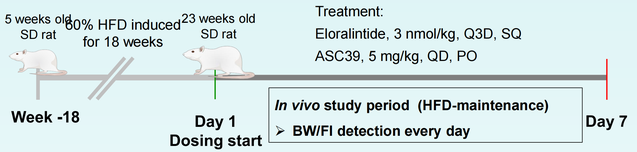
Amylin is an attractive target for obesity therapy. Eloralintide is a selective and potent once-weekly subcutaneously administered amylin analog peptide, which has demonstrated promising efficacy and safety profile in a 48-week clinical trial for obesity. ASC39 is a novel oral small molecule amylin receptor agonist development candidate. This study evaluates *in vitro* and *in vivo* pharmacological properties of ASC39 vs eloralintide.

## Methods

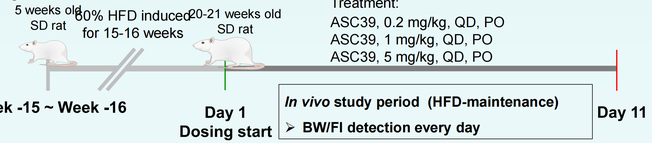
The cAMP activation of ASC39 vs eloralintide was assessed for human amylin receptors and human calcitonin receptor (hCTR). The weight-loss efficacy evaluation of ASC39 was conducted in DIO rats across two batches of studies. In the first batch, 5 mg/kg ASC39 (QD, PO) was compared head-to-head with 3 nmol/kg eloralintide (Q3D,SQ). The second batch consisted of once-daily oral dosing of ASC39 at 0.2 mg/kg, 1 mg/kg and 5 mg/kg.

### Study Illustration

**Study 1**




**Study 2**




## Results

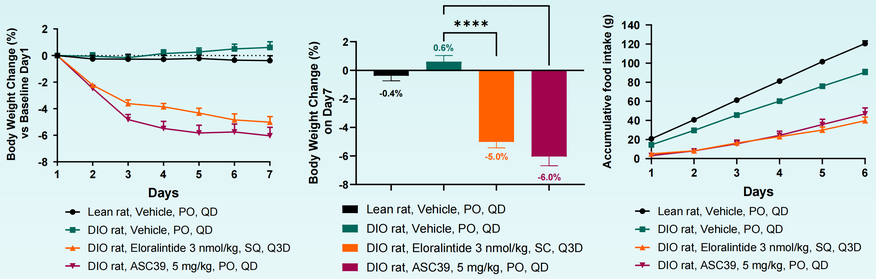
### *In vitro* cAMP Production Assay

| Compound ID | HEK293 AMY1R $EC_{50}$(pM) | HEK293 CTR $EC_{50}$(pM) | Selectivity (hAMY1R / hCTR) |
|---|---|---|---|
| ASC39 | 21.4 | 846.1 | 40 |
| Eloralintide | 21.2 | 1350.8 | 64 |

- ASC39 and eloralintide have 40-fold and 64-fold selectivity, respectively for hAMY1R over hCTR

### *In vivo Efficacy Study*

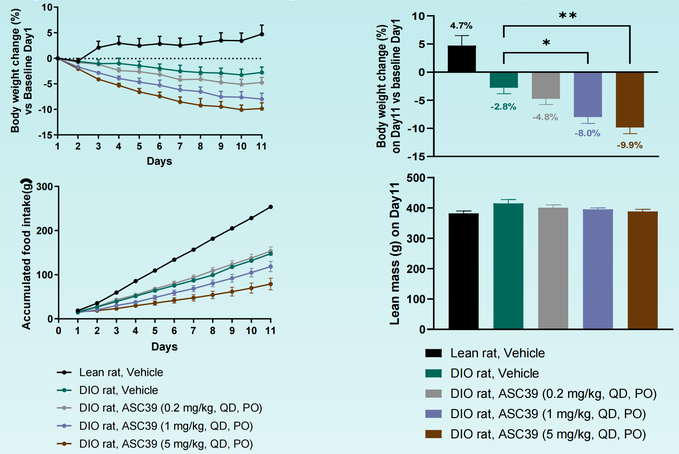
**Study 1: ASC39 Induced Comparable Weight Loss to Eloralintide**




- Oral administration of ASC39 resulted in significant weight loss which was as good as eloralintide.

Note: one-way ANOVA test was used for significance comparison. **, p<0.05; **, p<0.01; ****, p<0.0001; p<0.05* is considered statistically significant. GraphPad Prism 10 was used for data visualization.

**Study 2: ASC39 Induced Weight Loss in a Dose-Dependent Manner**




- Oral administration of ASC39 elicited significant weight loss in a dose-dependent manner, with no reduction in lean mass.

## Conclusions

ASC39 is an eloralintide-like selective and potent oral small molecule amylin receptor agonist development candidate with a novel scaffold. Both ASC39 and eloralintide demonstrated a strong selectivity towards hAMY1R over hCTR and a comparable preclinical efficacy in DIO rats. Oral ASC39's attractive pharmacological profile supports its advancement into human clinical trials, alone and in combination to offer a novel, convenient, accessible and differentiated obesity therapeutic option.

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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