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ASC37 Oral Tablets, GLP-1R/GIPR/GCGR Triple Agonist Peptide, Achieved Average Absolute Oral Bioavailability of 4.2% in Nonhuman Primate Studies

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Introduction

ASC37 is an oral GLP-1R/GIPR/GCGR triple agonist peptide, discovered and developed in-house at Ascletis. Peptide Oral Transport ENhancement Technology (POTENT) is a proprietary technology developed by Ascletis for oral peptide delivery. POTENT offers the following advantages: impedes enzymatic degradation of peptides; increases gastrointestinal permeability of peptides; is able to increase oral bioavailability of peptides from <1% to 3–5%. In non-human primates (NHPs), the absolute oral bioavailability of semaglutide in Ascletis' POTENT formulation is 3-fold of that of semaglutide in its commercial SNAC formulation; and the absolute oral bioavailability of tirzepatide in Ascletis' POTENT formulation is 9-fold of that of tirzepatide in the SNAC formulation (Table 1).

Methods

ASC37 oral tablets were developed utilizing Ascletis' POTENT technology. The absolute oral bioavailability and drug exposure of ASC37 tablets were evaluated in NHP models. ASC37 *in vitro* activity was also evaluated.

Table 1. Absolute oral bioavailability: POTENT formulation vs SNAC formulation

	Semaglutide		Tirzepatide	
Dose and route	**14 mg per monkey, oral**	**14 mg per monkey, oral**	**14 mg per monkey, oral**	**14 mg per monkey, oral**
Formulation	SNAC formulation*,details : 14mg Semaglutide, 300mg SNAC, 80mg MCC, 8mg PVPK90, 9.7mg Magnesium stearate	Ascletis proprietary POTENT formulation	SNAC formulation*,details: 14mg Tirzepatide, 300mg SNAC, 80mg MCC, 8mg PVPK90, 9.7mg Magnesium stearate	Ascletis proprietary POTENT formulation
Absolute oral bioavailability based on $AUC_{0\text{-}72h}$ after dose and body weight normalized	0.92%	2.78%	0.14%	1.29%

*Extrapolated from Novo Nordisk's patents, oral semaglutide FDA and Japanese regulatory filings

Results

- Utilizing Ascletis' POTENT, ASC37 oral tablets achieved average absolute oral bioavailability of 4.2%, approximately 30- and 60-fold higher than tirzepatide and retatrutide in the SNAC formulation, respectively, in head-to-head NHP studies. (Table 2)
- Average observed half-life of ASC37 oral tablets was approximately 56 hours in NHP studies, supporting once daily and less frequent oral dosing.

Table 2. Absolute oral bioavailability: ASC37 in POTENT formulation vs Tirzepatide and Retatrutide in SNAC formulation

	ASC37	Tirzepatide	Retatrutide
Dose and route	**14 mg per monkey, oral**	**14 mg per monkey, oral**	**14 mg per monkey, oral**
Formulation	Ascletis proprietary POTENT formulation	SNAC formulation*, details: 14mg Tirzepatide, 300mg SNAC, 80mg MCC, 8mg PVPK90, 9.7mg Magnesium stearate	SNAC formulation*, details: 14mg Retatrutide, 300mg SNAC, 80mg MCC, 8mg PVPK90, 9.7mg Magnesium stearate
Absolute oral bioavailability based on $AUC_{0\text{-}inf}$ after dose and body weight normalized	4.18%	0.14%	0.07%

Conclusions

ASC37 is a promising oral GLP-1R/GIPR/GCGR triple agonist peptide for clinical development

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