A full analysis of 28-Day MAD Study of Oral GLP-1R Biased Small Molecule Agonist ASC30 for obesity

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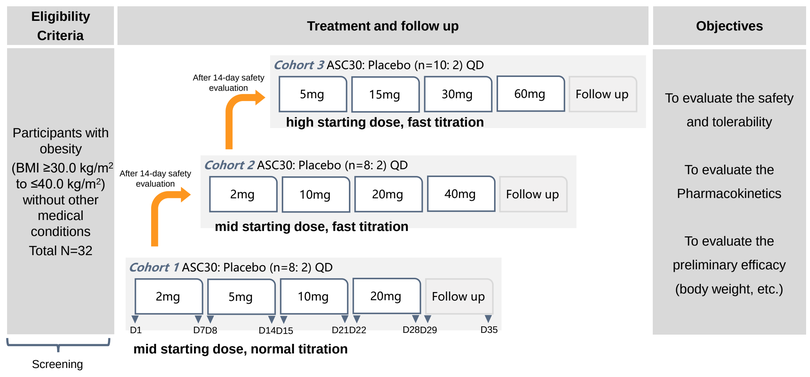
Introduction & Objective

ASC30 is a GLP-1R fully biased small molecule agonist without β arrestin recruitment, discovered and developed in-house at Ascletis. ASC30 has unique and differentiated properties that enable the administration of one small molecule as both a once daily oral tablet and a once-monthly subcutaneous injection. We report here a full analysis of all three cohorts of the 28-day multiple ascending dose (MAD) study using once-daily oral ASC30 tablet in participants with obesity to evaluate safety, tolerability, pharmacokinetics, and preliminary efficacy across all three cohorts. (NCT06680440).

Materials and Methods

A 28-day randomized, double-blind, placebo-controlled MAD trial in participants with obesity (BMI 30–40 kg/m²), conducted in the United States. Study design shown in Figure 2.

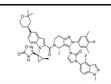
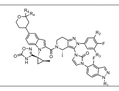
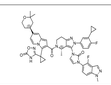
Figure 2 Study Design



Results

- Body weight changes from baseline were –6.3% (MAD 2, n=8), –4.3% (MAD 1, n=7), and +0.2% (placebo, n=6). The maximum body weight changes from baseline were -7.6% and -9.1% for MAD 1 and MAD 2, respectively. No plateau observed at Day 29.
- Body weight change from baseline was -4.8% for MAD 3 (N=7), with the maximum body weight change being -9.3%. Excluding two outliers, the mean body weight change from baseline was -5.9% (Figure 3).
- GI Tolerability**:** In the MAD study, MAD 1 showed no vomiting, while MAD 2 had events, indicating weekly titration from 2 mg to 5 mg was appropriate. Compared with MAD 2, MAD 3 showed no increasing trend in severity or incidence, despite 2 discontinuations due to PI decisions, and 1 discontinuation due to subject withdrawal (Figure 4).
- No SAEs or Grade ≥3 AEs, including GI events, were observed. Labs, vitals, ECGs (QTc), and physical exams were normal. No hepatic safety signals were detected across all MAD Cohorts (Figure 5).

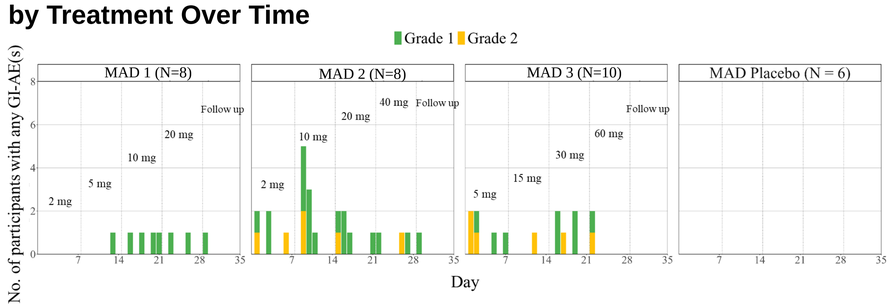
Figure 1 "Chugai Scaffold": Only four players in the clinical development*

Drug	Sponsor	Structure	Clinical Status
Orforglipron	Eli Lilly		Phase III
ASC30**	Ascletis		Phase II
Aleniglipron (GSBR-1290)	Structure Therapeutics		Phase II
Elecoglipron (AZD5004)	AZ/Eccogene		Phase I

*From www.clinicaltrials.gov as of 1 Aug 2025;
**ASC30 is protected by two granted U.S. patents (US12234236B1& US12291530B1) and multiple rest-of-world patent applications.

Figure 4 ASC30 tablets MAD GI tolerability over 28-day treatment and 7-day follow-up: no vomiting incidence in MAD 1 due to 2mg to 5 mg weekly titration strategy; no increasing trend in severity or incidence in MAD 3 compared to MAD 2.

(A) Severity of GI-AEs (Nausea, Vomiting, Diarrhoea and Constipation) by Treatment Over Time



(B) Incidences of GI-AEs by Treatment Over Time

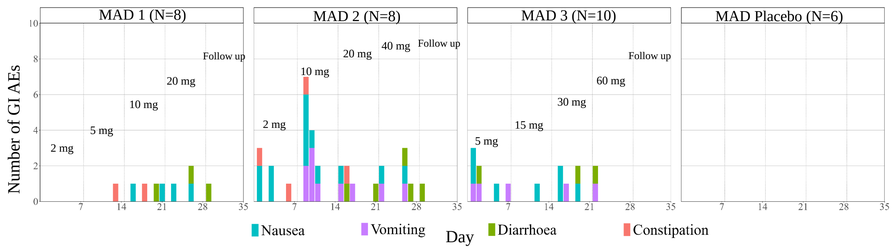
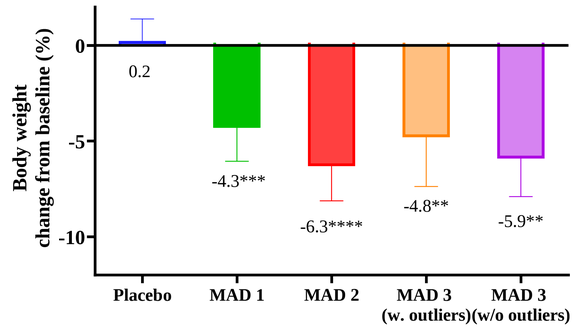
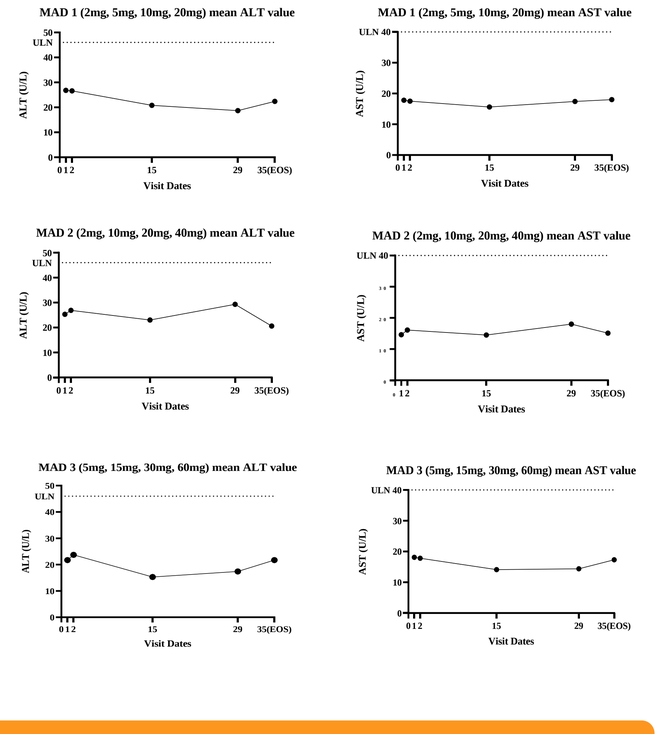


Figure 3 Body Weight Change from Baseline at Day 29



*p<0.05, **p<0.01, ***p<0.001, ****p<0.0001

Figure 5 Changes in liver enzymes



Conclusion

- **ASC30 once-daily oral tablet demonstrated up to 6.5% placebo-adjusted mean body weight reduction from baseline after 28-day treatment.**
- **The highest dose level, designed to validate the optimal combination of tolerability and efficacy, exhibited up to 9.3% body weight loss, showed no increasing trend in severity or incidence in GI AEs.**
- **ASC30 is safe and well tolerated with only mild-to-moderate GI AEs across all MAD cohorts. The safety profile of the ASC30 tablet was consistent with or better than that of the GLP-1 receptor agonist class.**
  - **We believe that GI AEs can further be reduced by "lower starting dose, slower titration" trial design for the ongoing ASC30 tablet 13-week Phase II study in U.S.**