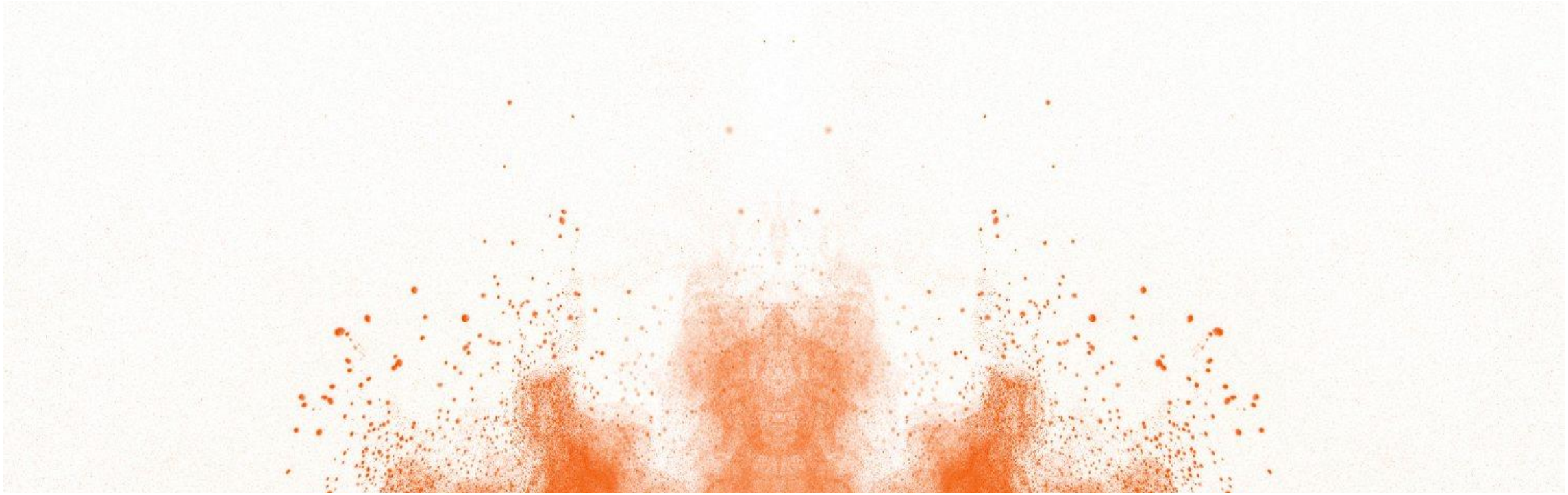


ASC30, an Oral GLP-1R Biased Small Molecule Agonist Demonstrated Superior Weigh Loss in Participants with Obesity: A 28-Day Multiple Ascending Dose Study

Jinzi Jason Wu

Vanessa Wang

Ascletis Pharma (China) Co., Limited, Hong Kong

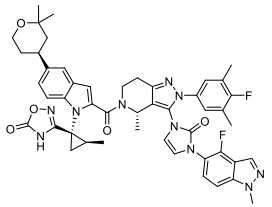
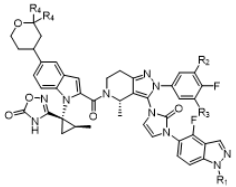
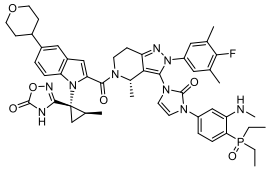
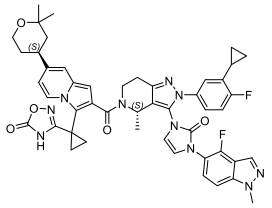
Disclosure

Dr. Jinzi Jason Wu, presenter, is an employee of Ascletis Pharma (China) Co., Limited, Hong Kong

Overview of ASC30

- **ASC30 is discovered and developed in-house at Ascletis as a first and only investigational small molecule GLP-1R fully biased agonist designed to be administered:**
  - **Once-daily oral tablet**
  - **Once-monthly SQ injection as a treatment therapy**
  - **Once-quarterly SQ injection as a maintenance therapy**
- **ASC30 once-daily oral tablet demonstrated a 6.5% placebo-adjusted mean body weight reduction from baseline after 28-day treatment in multiple ascending dose (MAD) cohort 2 (weekly titrations of 2 mg, 10 mg, 20 mg, and 40 mg).**
- **ASC30 once-daily oral tablet also demonstrated a 4.5% placebo-adjusted mean body weight reduction from baseline after 28-day treatment in MAD cohort 1 (weekly titrations of 2 mg, 5 mg, 10 mg, and 20 mg).**

“Chugai Scaffold”: Only four players in the clinical development*

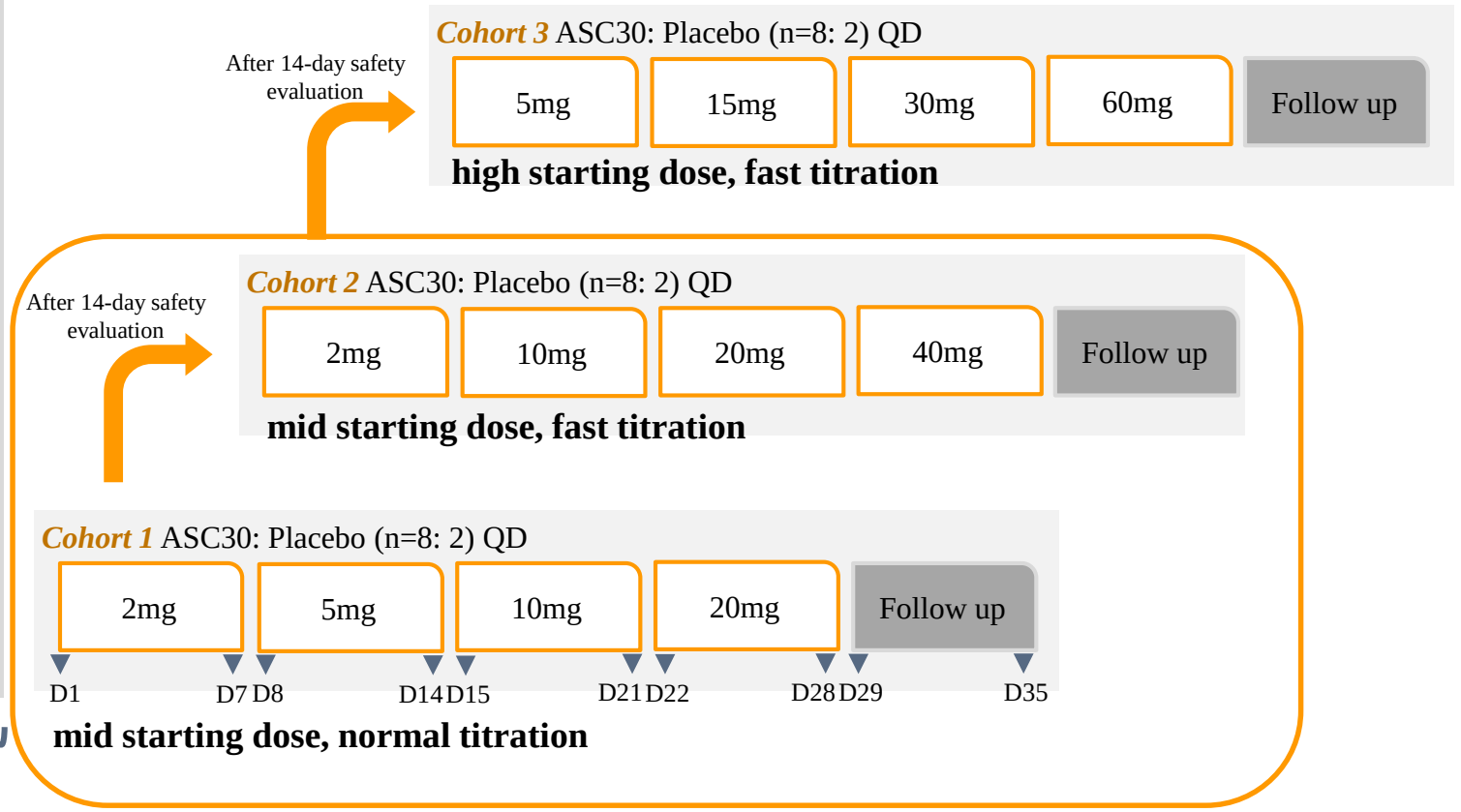
Drug	Sponsor	Structure	Clinical Status
Orforglipron	Eli Lilly		Phase III
ASC30**	Ascletis		Phase II
Aleniglipron (GSBR-1290)	Structure Therapeutics		Phase II
Elecoglipron (AZD5004)	AZ/Eccogene		Phase I

*From www.clinicaltrials.gov as of 1 Aug 2025;
**ASC30 is protected by two granted U.S. patents (US12234236B1& US12291530B1)

ASC30 oral exposure is much higher than orforglipron in NHP (Head-to-head comparison)

Oral dosing	5 mg/kg in Rat, $AUC_{0\text{-}48h}$, h*ng/mL	15mg/kg in NHP, $AUC_{0\text{-}24h}$, h*ng/mL
ASC30	91,858	8,097
Orforglipron	6,346	1,661
AUC ratio of ASC30 to orforglipron	14	5

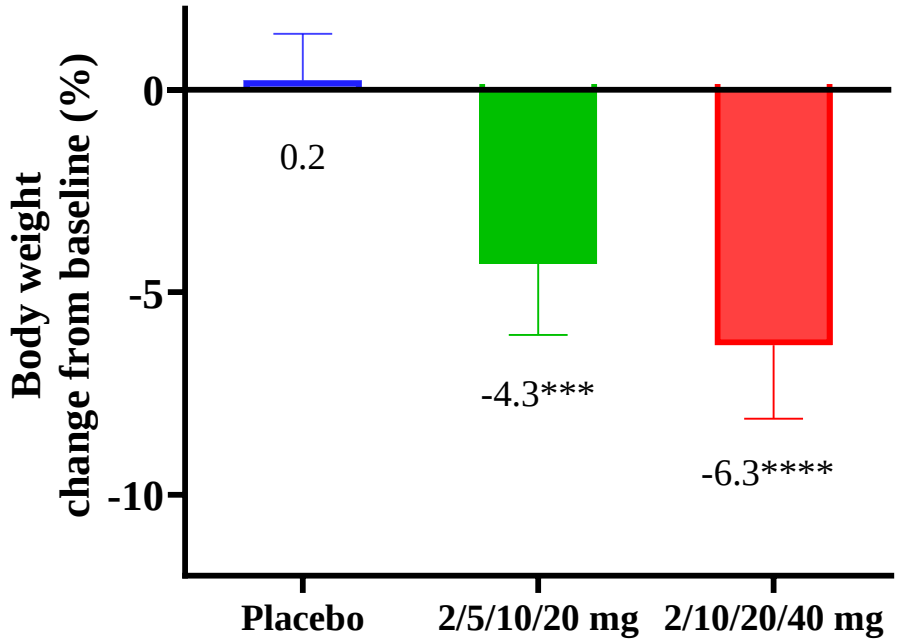
ASC30 tablets MAD (28 days) in obese patients explored various titrations (conducted in U.S.)

Eligibility Criteria	Treatment and follow up	Objectives
Participants with obesity (BMI ≥30.0 kg/m^2 to ≤40.0 kg/m^2) without other medical conditions Total N=30		To evaluate safety and tolerability To evaluate the pharmacokinetics To evaluate preliminary efficacy (body weight etc.)

Screening

ASC30 once-daily tablets demonstrated superior weight loss at Day 29

% body weight change from baseline at Day 29



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

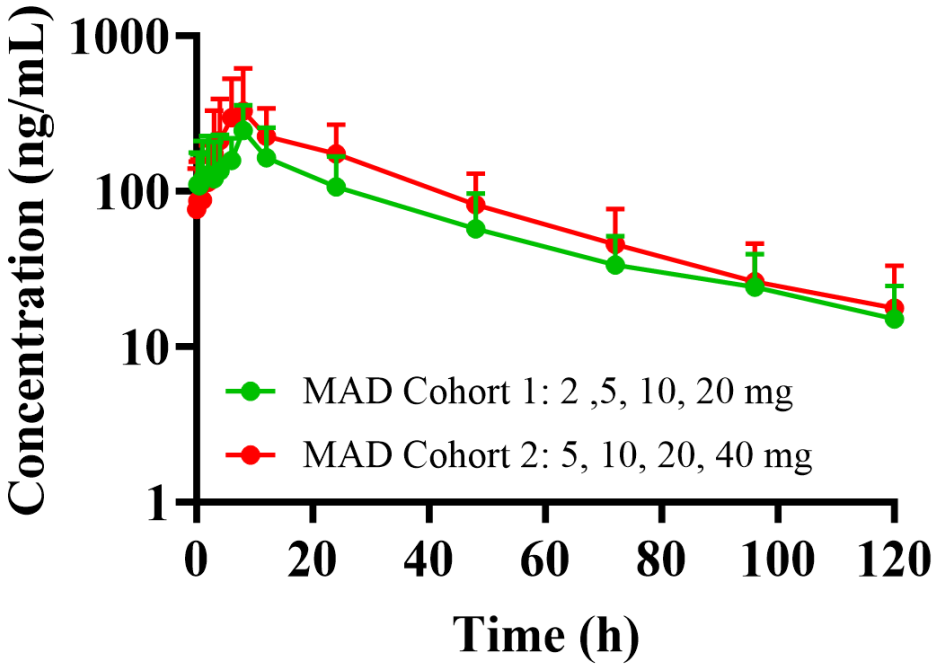
ASC30 MAD Cohorts 1 and 2 weight change at day 29 from baseline (Day 1 prior to first dose):

- ASC30 MAD2 = -6.3% (n=8);
- ASC30 MAD1 = -4.3% (n=7);
- Placebo = +0.2% (n=6).
- No sign of plateau observed at Day 29.

20 mg and 40 mg ASC30 demonstrated superior oral PK profile at steady state

■ **Higher AUC positively correlated with greater body weight reduction**

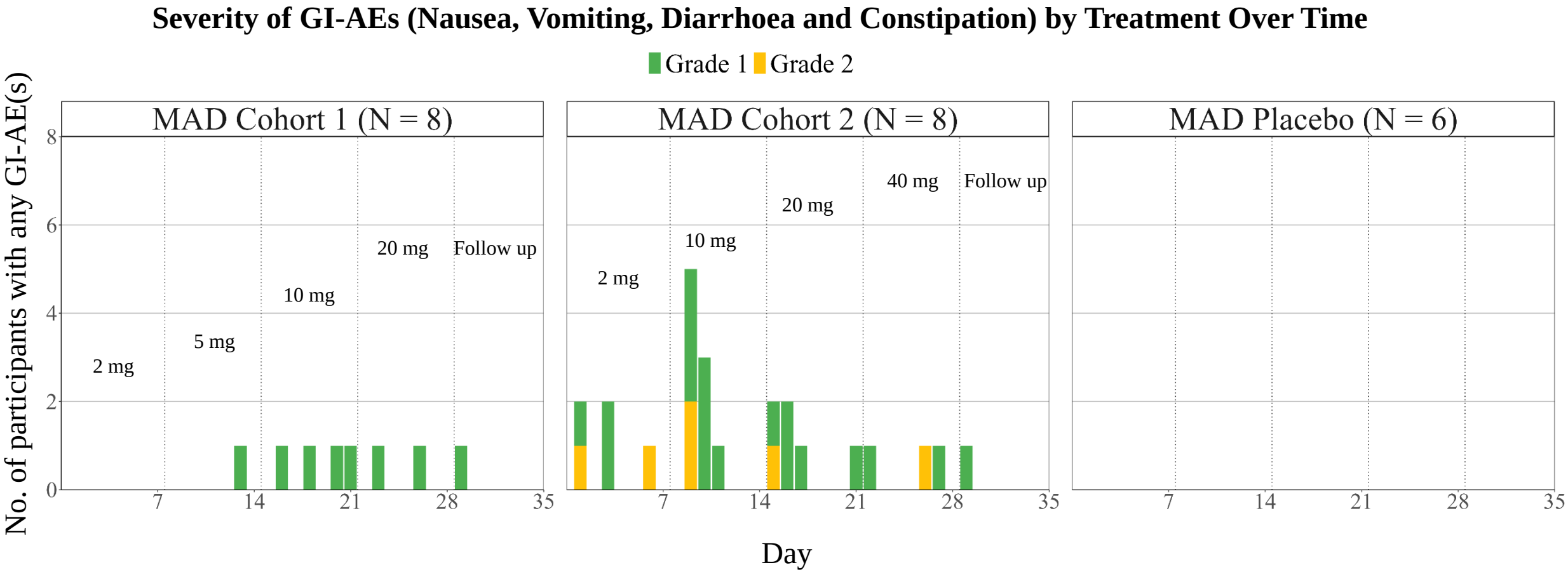
Concentration-time curves of ASC30 Day 28



		MAD Cohort 1 (N = 8)	**MAD Cohort 2** (N = 8)
Dose level (mg)		2, 5, 10, 20	2, 10, 20, 40
Day 28 (steady state)	T_{max} (h)	8.000 (2.00-8.00)	8.000 (3.00-24.00)
	C_{max} (ng/mL)	272±101	397±274
	$AUC_{0\text{-}24h}$ (h*ng/mL)	3,560±1,440	5,060±2,080
	$T_{1/2}$ (h)	41.9±12.9	35.7±13.7

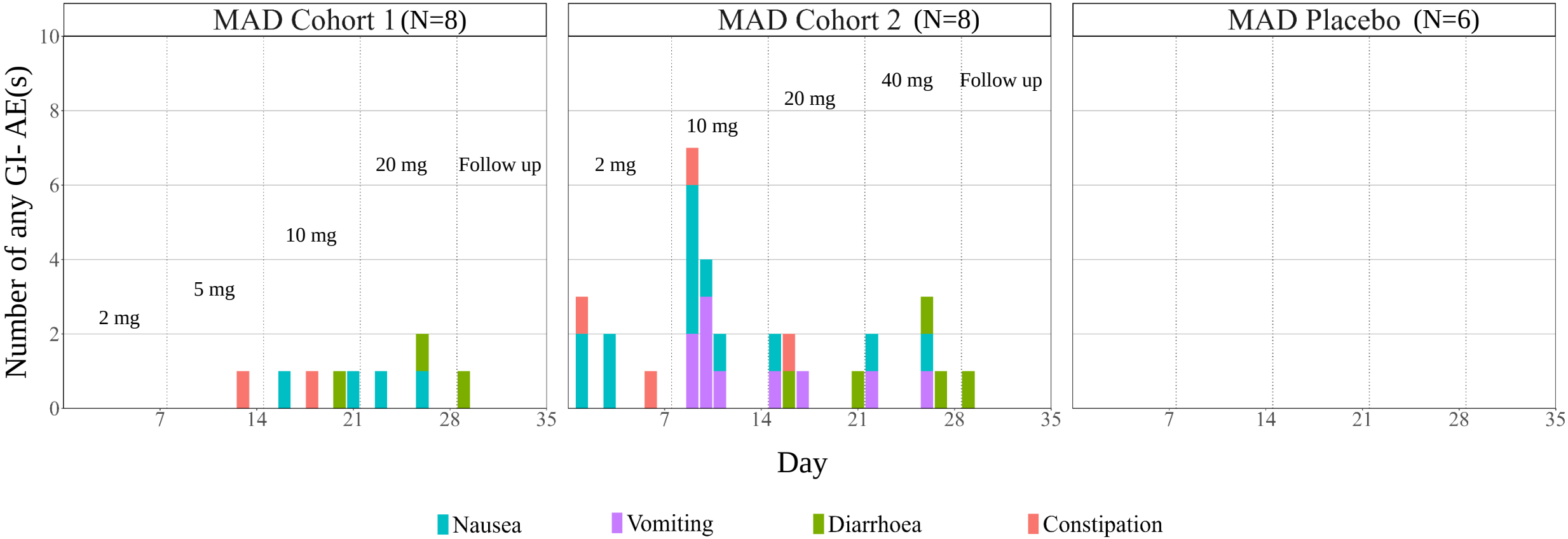
T_{max} is shown as median (range); C_{max}, $AUC_{0–24h}$, and $T_{1/2}$ are shown as mean ± standard deviation.

ASC30 tablets MAD GI tolerability over 28-day treatment and 7-day follow-up: no vomiting incidence in MAD cohort 1 due to 2 mg to 5 mg weekly titration strategy



During 28-day treatment and 7-day follow up, zero incidence of vomiting was reported in MAD cohort 1, whereas vomiting events occurred in MAD cohort 2, suggesting weekly titration from 2 mg to 5 mg represents an appropriate escalation pace and provides key evidence to inform the titration regimen for phase II.

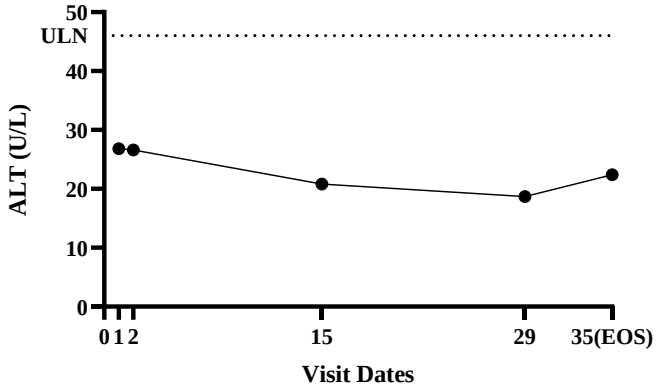
Incidences of GI-AEs by Treatment Over Time



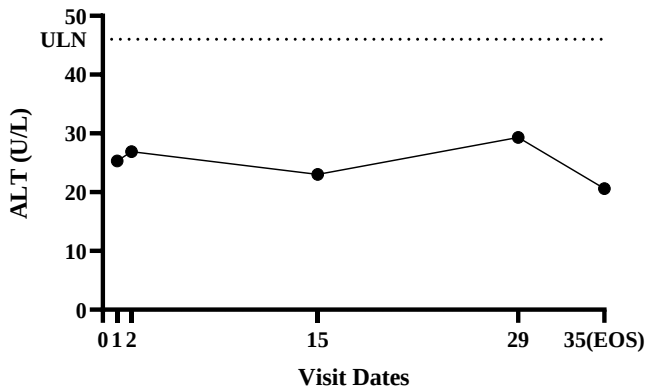
GI-AEs: Nausea, Vomiting, Diarrhoea and Constipation

ASC30 MAD Cohorts 1 and 2 had no hepatic safety signals

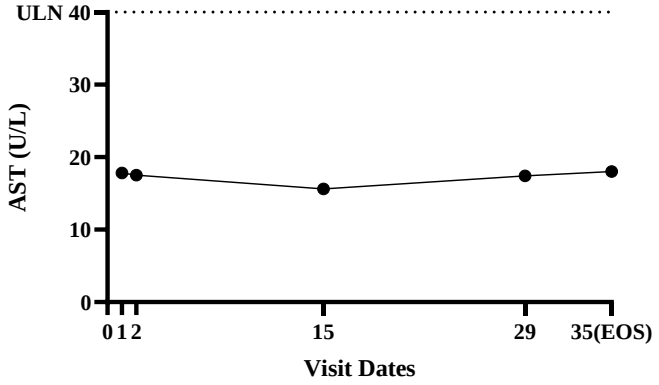
MAD Cohort 1 (2mg, 5mg, 10mg, 20mg) mean ALT value



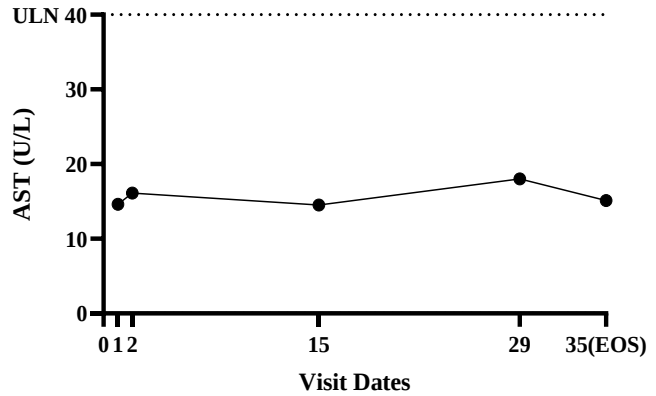
MAD Cohort 2 (2mg, 10mg, 20mg, 40mg) mean ALT value



MAD Cohort 1 (2mg, 5mg, 10mg, 20mg) mean AST value



MAD Cohort 2 (2mg, 10mg, 20mg, 40mg) mean AST value



No SAEs were reported. No Grade 3 or higher AEs were observed. There were no abnormal findings in laboratory tests, vital signs, ECGs (electrocardiograms, including QTc intervals), or physical exams.

ASC30 Summary

- **ASC30 once-daily oral tablets demonstrated up to 6.5% placebo-adjusted mean body weight reduction from baseline after 28-day treatment**
- **ASC30 tablet's higher efficacy is supported by its higher oral drug exposures**
- **ASC30 is safe and well tolerated with only mild-to-moderate GI AEs**
  - **We believe that GI AEs can further be reduced by "lower starting dose, slower titration" trial design for the ongoing ASC30 tablets 13-week Phase II study in U.S.**

E-poster

Presentation number: 827

ASC30, an Oral GLP-1R Biased Small Molecule Agonist Demonstrated Superior Weigh Loss in Participants with Obesity: A 28-Day Multiple Ascending Dose Study

Jinzi Jason Wu, Vanessa Wang
Ascletis Pharma (China) Co., Limited, Hong Kong

EASD 2025 VIENNA

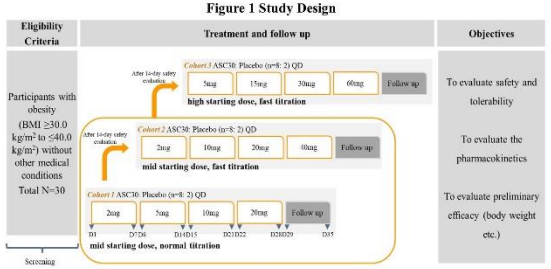
Introduction & Objective

ASC30 is an oral GLP-1R biased small molecule agonist without β-arrestin recruitment, with unique and differentiated properties that enable the drug administration as both a once-monthly subcutaneous injection and a once-daily oral tablet. The completed single ascending dose (SAD) study of ASC30 oral tablet demonstrated a favorable tolerability profile and dose-proportional pharmacokinetics characteristics. We present here the weight loss, pharmacokinetics and tolerability of ASC30 once-daily oral tablet in the first two cohorts of a 28-day multiple ascending dose (MAD) study to treat patients with obesity (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 1.

Figure 1 Study Design



Results

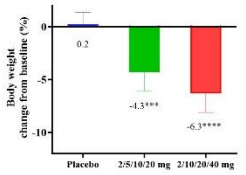
- Weight change from baseline was –6.3% (MAD2, n=8), –4.3% (MAD1, n=7), and +0.2% (placebo, n=6). No plateau observed at Day 29 (Figure 2).
- 20 mg and 40 mg ASC30 demonstrated superior steady-state oral pharmacokinetics(Figure 3 and Table 1).
- GI Tolerability: In the MAD study, Cohort 1 showed no vomiting, while Cohort 2 had events (Figure 4), indicating weekly titration from 2 mg to 5 mg was appropriate.
- 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 in MAD Cohorts 1 and 2 (Figure 5).

Table 1 Higher AUC positively correlated with greater body weight reduction

		MAD Cohort 1 (N = 8)	MAD Cohort 2 (N = 8)
Dose level (mg)		2, 5, 10, 20	2, 10, 20, 40
Day 28 (steady state)	T_{max} (h)	8.000 (2.00-8.00)	8.000 (3.00-24.00)
	C_{max} (ng/mL)	272±101	397±274
	AUC_{0-24h} (h*ng/mL)	3560±1440	5060±2080
	$T_{1/2}$ (h)	41.9±12.9	35.7±13.7

T_{max} is shown as median (range), C_{max}, AUC_{0-24h} and $T_{1/2}$ are shown as mean ± standard deviation.

Figure 2 Body Weight Change from Baseline at Day 29



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

Figure 3 Concentration-time curves of ASC30 Day 28

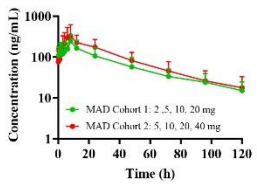
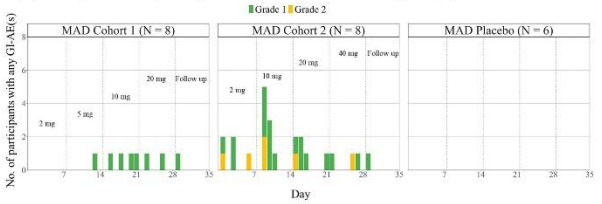


Figure 4 ASC30 tablets MAD GI tolerability over 28-dday treatment and 7-day follow-up: no vomiting incidence in MAD cohort 1 due to 2mg to 5 mg weekly titration strategy

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



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

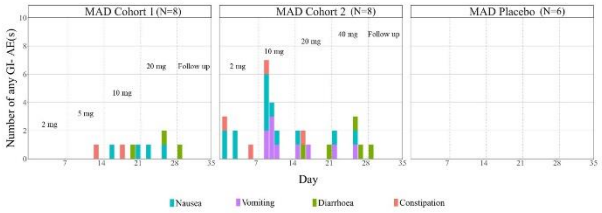
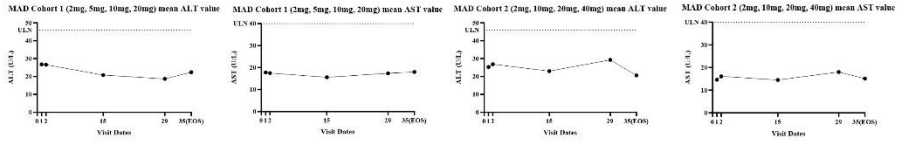


Figure 5 Changes in liver enzymes



Conclusion

- ASC30 once-daily oral tablet demonstrated up to 6.5% placebo-adjusted mean body weight reduction from baseline after 28-day treatment
- ASC30 tablet's higher efficacy is supported by its higher drug exposures
- ASC30 is safe and well tolerated with only mild-to-moderate GI AEs
  - 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.

Thanks