ASC30, a Once-Monthly SQ Injected Small Molecule GLP-1RA in Participants with Obesity: A Ph Ib Study

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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 once-monthly to once-quarterly subcutaneous (SQ) injections.

ASC30 slow-release SQ depot treatment and maintenance formulations were optimized and developed utilizing Ascletis' Ultra-Long-Acting Platform (ULAP) technology. Based on the properties of small molecules and peptides, Ascletis can design and optimize, through its proprietary ULAP technology, various slow-release constants (*k*) for small molecules and peptides in SQ depots to precisely release injected small molecules and peptides over desired dosing intervals to reduce peak-to-trough ratios and improve clinical outcomes.

The current study in U.S. assessed the pharmacokinetics and tolerability of ASC30, a potentially first-in-class SQ-injected small molecule GLP-1R agonist (NCT06679959).

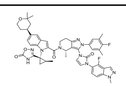
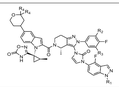
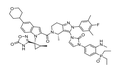
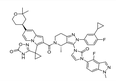
Materials and Methods

This randomized, double-blind, placebo-controlled Phase Ib study was conducted in the U.S. to assess the pharmacokinetics and tolerability of the ultra-long-acting subcutaneous (SQ) formulations of ASC30 (100 mg) in participants with obesity (BMI 30–40 kg/m²). In either treatment formulation (Injection A) cohort or maintenance formulation (Injection B) cohort, 8 participants with obesity received a single SQ injection of ASC30 and was followed for 12 weeks.

Results

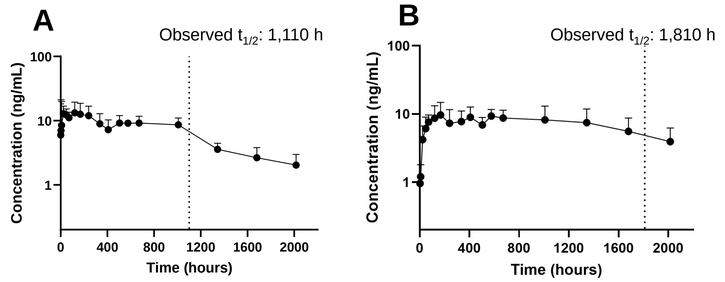
- Observed half-lives, time for ASC30 concentrations to reduce to fifty percent (50%) of ASC30's C_{max}, reached 46 days and 75 days, for ASC30 SQ treatment formulation (Injection A) and ASC30 SQ maintenance formulation (Injection B), respectively (Figure 2).
- C_{max}-to-C_{day29} ratio of 1.5:1, supported ASC30 SQ treatment formulation monthly dosing, while C_{max}-to-C_{day85} ratio of 2.5:1, supported ASC30 SQ maintenance formulation quarterly dosing.
- No SAEs or Grade ≥3 AEs. GI-related AEs were mild to moderate. Labs, vitals, ECGs (QTc), and physical exams were normal. No hepatic safety signals were detected across all Cohorts (Table 2).

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

Figure 2 Observed $t_{1/2}$ for ASC30 SQ treatment formulation (A) and maintenance formulation (B) after a single injection



(A) ASC30 SQ treatment formulation Observed $t_{1/2}$: 46 days (1,100 h) post-dose in participants with obesity, supporting monthly treatment dosing;

(B) ASC30 SQ maintenance formulation Observed $t_{1/2}$: 75 days (1,810 h) post-dose in participants with obesity, supporting quarterly maintenance dosing.

Table 1 PK parameters for ASC30 SQ treatment and maintenance formulations

Formulation	ASC30 treatment formulation	ASC30 maintenance formulation
Condition	Fasted	Fasted
Dose level (mg)	100	100
Observed $t_{1/2}$ (hr)	1,100	1,810
T_{max} (range) (hr)	168.5 (3.0, 529.6)	407.6 (119.3, 1,007.6)
C_{max} (ng/mL)	18.9±10.0	13.2±3.34
AUC_{inf} (hr*ng/mL)	15,500±2,750	21,200±8,850

Note: Abstract data updated; data presented used Mean ± SD

Table 2 Safety and tolerability profiles of ASC30 SQ treatment and maintenance formulations compared to pooled placebo

Category	ASC30 treatment formulation 100 mg (N=8) n (%)	ASC30 maintenance formulation 100 mg (N=8) n (%)	Placebo (N=16) n (%)
Number of participants reporting at least one TEAE	8 (100.0)	8 (100.0)	14 (87.5)
Number of participants reporting TEAEs by severity			
Grade 1	4 (50.0)	7 (87.5)	12 (75.0)
Grade 2	4 (50.0)	1 (12.5)	2 (12.5)
Grade 3	0 (0.0)	0 (0.0)	0 (0.0)
Grade 4	0 (0.0)	0 (0.0)	0 (0.0)
Number of participants reporting SAEs	0 (0.0)	0 (0.0)	0 (0.0)
Overall discontinuation	0 (0.0)	0 (0.0)	0 (0.0)
Common GI-related TEAEs			
Vomiting	3 (37.5)	0 (0.0)	0 (0.0)
Nausea	3 (37.5)	0 (0.0)	2 (12.5)
Diarrhea	1 (12.5)	1 (12.5)	1 (6.3)
Constipation	2 (25.0)	1 (12.5)	0 (0.0)

Notes: TEAE(s): treatment-emergent adverse event (s); SAEs: serious adverse events; GI: gastrointestinal.

Conclusion

- **ASC30 ultra-long-acting, slow-release SQ depot formulations demonstrated 46-day observed $t_{1/2}$ (treatment formulation) and 75-day observed $t_{1/2}$ (maintenance formulation), supporting both once-monthly treatment and once-quarterly maintenance therapies.**
- **ASC30 SQ formulations were well tolerated, with only mild-to-moderate TEAEs, comparable or superior to those observed with GLP-1 receptor agonists.**
- **Developed with Ascletis' ULAP technology, ASC30 treatment and maintenance formulations represent a potential breakthrough in chronic weight management by improving treatment convenience, adherence, and quality of life.**