

Oral Small Molecule GLP-1, ASC30, Demonstrated Placebo-Adjusted Weight Loss of 7.7% with Better Gastrointestinal Tolerability in Its 13-Week U.S. Phase II Study in Participants with Obesity

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ASC30 Introduction

ASC30 is an orally administered small-molecule glucagon-like peptide-1 receptor agonist (GLP-1 RA) discovered by Ascletis. The chemical structure of ASC30 is presented in Figure 1.

ASC30 has differentiated pharmacological properties vs. orforglipron in head-to-head studies

Compared with OFG, ASC30 demonstrated differentiated pharmacologic activity, including approximately two- to threefold greater *in vitro* potency, as reflected by lower EC₅₀ values for human GLP-1 receptor activation and β -arrestin 2 recruitment (Table 1). In cell-based GLP-1R receptor binding assay, ASC30 is threefold more potent than OFG. In nonhuman primate (NHP) intravenous glucose tolerance testing (IVGTT), ASC30 administered at 1.5 mg/kg stimulated statistically significant and substantially greater insulin secretion than OFG administered at 6 mg/kg (Figure 2). In an NHP study, ASC30 achieved approximately fivefold higher oral exposure than OFG.

Table 1. Head-by-head comparison

Compound	cAMP activation EC ₅₀ , pM (mean±SD)	β -arrestin 2 EC ₅₀ , pM (mean±SD)
Orforglipron (OFG)	18.0 ± 4.3	>30,000,000
ASC30	8.8 ± 1.7	>30,000,000

ASC30 Phase I SAD and MAD Studies in U.S.

ASC30 showed dose-proportional pharmacokinetics, with a peak-to-trough ratio below 2:1.

In a 4-week phase I study, ASC30 demonstrated favorable safety and tolerability across all doses (20, 40, and 60 mg), with no hepatic safety signals or elevations in ALT, AST, or total bilirubin.

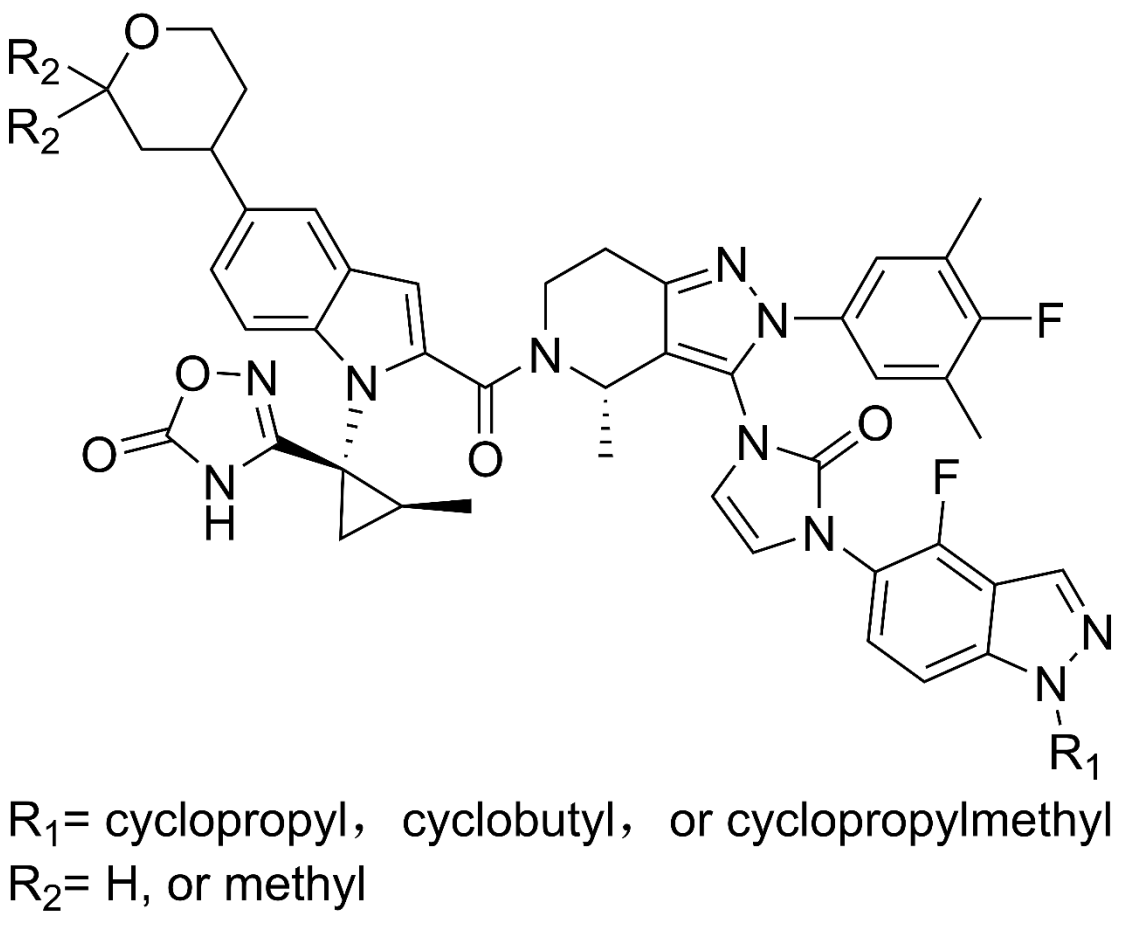
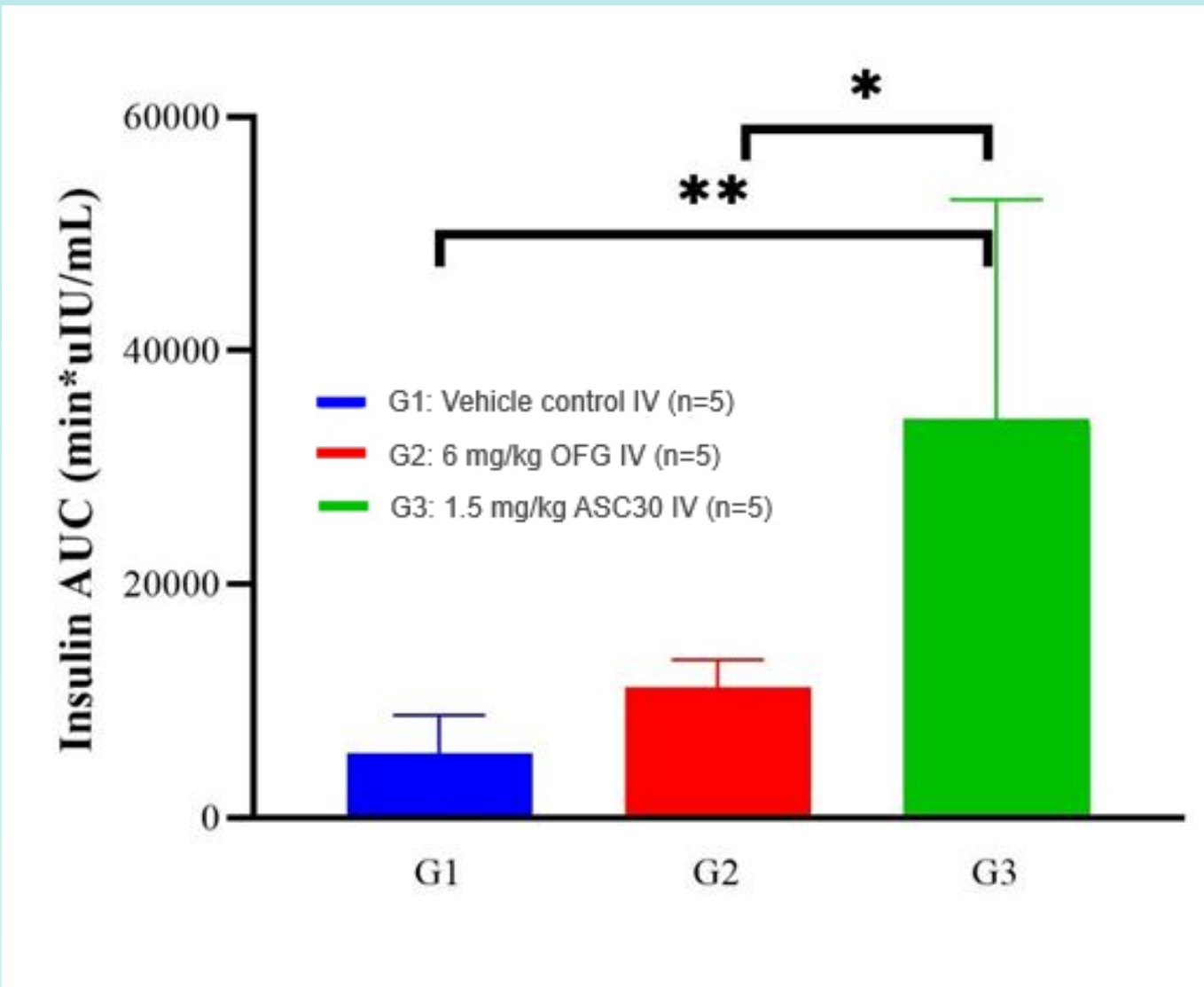


Figure 1. ASC30 structure

Figure 2. Head-to-head comparison between ASC30 and OFG



ASC30 Phase II Study In U.S.

This 13-week, randomized, double-blind, placebo-controlled, multicenter Phase II study was conducted at U.S. sites. A total of 125 participants were randomized to placebo or ASC30 oral tablet with target doses of 20, 40, or 60 mg once daily via weekly titration.

Table 2. Vomiting rate of ASC30 titrated weekly was approximately half of the published vomiting rate of orforglipron titrated weekly – topline data

Cross-trial comparison	ASC30 13-week study			Orforglipron 12-week study ^[1]	Orforglipron ATTAIN-1 72-week study ^[2]
Titration schedule	Weekly			Weekly	Every four weeks
Target dose	20 mg	40 mg	60 mg	45 mg	36 mg
Vomiting	22%	25%	30%	56%	24%
Nausea	49%	63%	40%	78%	34%
Diarrhea	15%	13%	20%	11%	23%
Constipation	12%	18%	10%	Not published	25%

References: [1]. Diabetes Obes Metab. 2023;25:2642–2649; [2]. N Engl J Med. 2025;393:1796-1806

Topline Results

- ASC30 once-daily tablets showed statistically significant and clinically meaningful dose-dependent placebo-adjusted mean body weight reductions with no observed plateau for weight loss. At Week 13, ASC30 showed placebo-adjusted weight reductions of 5.4%, 7.0%, and 7.7% for 20, 40 and 60 mg maintenance doses, respectively. Mean baseline body weight and BMI were 107.3 kg and 38.6 kg/m².
- ASC30 titrated weekly to the target dose demonstrated approximately one-half the rate of vomiting observed with orforglipron titrated weekly. The gastrointestinal (GI) tolerability of ASC30 titrated weekly was comparable to that reported for orforglipron titrated every four weeks in the Phase III ATTAIN-1 study (Table 2). In the ASC30 Phase II study, all GI adverse events (AEs) were grade 1 (mild) and grade 2 (moderate) in severity and mostly occurred during the dose titration period. There were no grade 3 (severe) or above GI AEs. There were no drug-related AEs of grade 3 (severe) or higher. No drug-related serious AEs (SAEs).
- The AEs leading to treatment discontinuations were only mild-to-moderate GI AEs (nausea, vomiting and constipation). No treatment discontinuation due to AEs in 60 mg cohort.
- No hepatic safety signal was observed, and there were no elevations of ALT, AST, or TBL.

Conclusion and Outlook

- ASC30 oral tablets showed dose-dependent weight loss with a favorable GI tolerability profile compared with orforglipron, supporting its potential as a best-in-class oral GLP-1 RA.
- ASC30 is a Phase III-ready, one-pill-once-daily oral small-molecule GLP-1R agonist. The two ASC30 Phase III trials in participants with obesity or overweight, with or without T2DM, are 72-week studies with 20 mg, 40 mg, or 60 mg maintenance doses and up to a 20-week titration period. Initiation of global Phase III trials of ASC30 for the obesity indication is expected by the end of the third quarter of 2026.