NEWSLETTER 23

ADA 2026 GLP-1 Pipeline: Retatrutide, CagriSema, Orforglipron

The next wave of incretin therapies unveiled in New Orleans

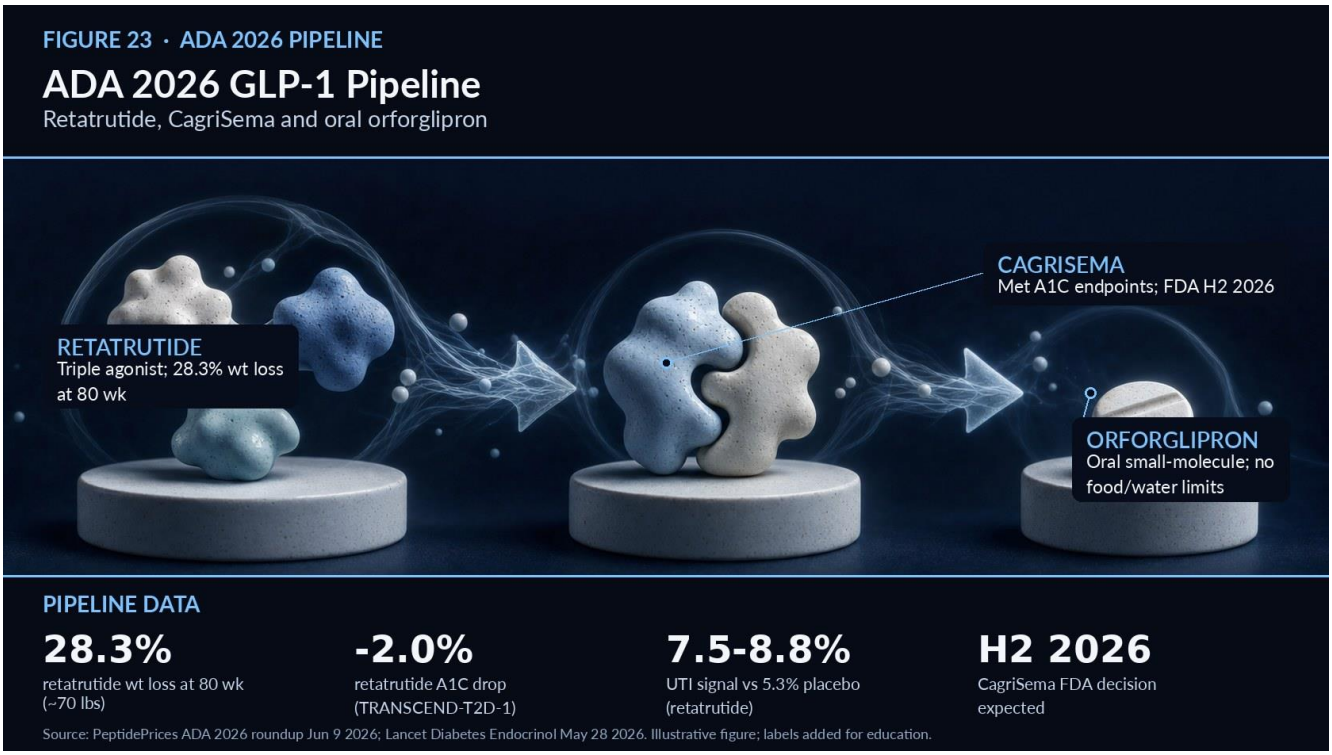

Figure 23. ADA 2026 GLP-1 Pipeline: Retatrutide, CagriSema, Orforglipron — mechanism overview (illustrative; labels added for education).

At the ADA's 86th Scientific Sessions in New Orleans (June 5–8, 2026), the GLP-1 pipeline dominated the agenda. Retatrutide, a once-weekly GLP-1/GIP/glucagon triple agonist, delivered headline TRIUMPH-1 data: 28.3% average body-weight loss (about 70.3 lbs) at 80 weeks, with 45.3% of top-dose participants losing at least 30% of body weight.[1] These figures approach the range historically associated with bariatric surgery.

Glycaemic and metabolic effects were equally strong. In TRANSCEND-T2D-1, retatrutide lowered A1C by up to 2.0% and cut weight by up to 16.8% (about 36.6 lbs) at 40 weeks.[1] A new safety signal emerged, however: urinary tract infections appeared in roughly 7.5–8.8% of retatrutide participants versus 5.3% on placebo, and Lilly is expected to file in 2026 with likely 2027–2028 approval.[1]

CagriSema, combining cagrilintide with semaglutide, advanced on multiple fronts. Its REIMAGINE-1, -2, and -3 trials met primary A1C endpoints and confirmed secondary weight-loss endpoints; Novo Nordisk filed in late 2025, with an FDA decision expected in the second half of 2026.[1]

Oral therapy also took the stage. Orforglipron, Lilly's oral small-molecule GLP-1 (brand Foundayo), can be taken without food or water restrictions and received its own ADA symposium on June 8, 2026, though no specific efficacy numbers were stated in this roundup.[1] An effective oral option could substantially improve access and adherence.

The pipeline also signals a shift in the efficacy ceiling. Retatrutide's roughly 28% average weight loss narrows the historical gap between pharmacotherapy and bariatric surgery, while an effective oral agent like orforglipron

could transform access in settings where injectables are impractical.[1] Yet the emerging UTI signal with retatrutide is a reminder that each incremental gain in potency arrives with its own safety profile, reinforcing the need for careful post-marketing surveillance as these agents reach large, real-world populations.[2]

The pipeline's breadth is reflected in the literature. The *Lancet* 2026 review lists retatrutide, cagrilintide-semaglutide, survodutide, mazdutide, and amycretin among the newer GLP-1-based and multiagonist agents under evaluation.[2] For CKM practice, this next wave promises greater efficacy and more convenient formulations—but the retatrutide UTI signal is a reminder that each new agent will require careful post-marketing surveillance as it reaches broader populations.[6]

References

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