



Retatrutide: Clinical Overview & Weight Loss Data

Evidence-informed review of mechanism, Phase 2/3 efficacy data, development status, safety considerations, and clinical context.

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Content reviewed against published clinical literature

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Executive Summary

KEY TAKEAWAYS

- ✓ Investigational triple agonist (GLP-1, GIP, glucagon receptors) — not FDA approved
- ✓ Phase 2: ~24.2% average body weight loss at 48 weeks (12 mg dose)
- ✓ Approximately 26% of Phase 2 participants achieved $\geq 30\%$ body weight loss
- ✓ TRIUMPH Phase 3 program is currently underway (results expected 2025–2026)
- ✓ Earliest realistic FDA approval estimate: 2027 — timelines may shift
- ✓ No published cardiovascular outcomes data; CV endpoints included in Phase 3

MECHANISM

Triple Agonist

GLP-1 + GIP + Glucagon

PHASE 2 WEIGHT LOSS

~24.2%

At 48 weeks, 12 mg dose

ADMINISTRATION

Weekly Injection

Once subcutaneous (investigational)

DEVELOPMENT STATUS

Phase 3

TRIUMPH program ongoing

APPROVAL ESTIMATE

2027-2028

Pending Phase 3 results

CV OUTCOMES DATA

Pending

Phase 3 includes CV endpoints

What Is Retatrutide?

Retatrutide (LY3437943) is an investigational weight-loss medication developed by Eli Lilly. It is a triple receptor agonist — activating the GLP-1, GIP, and glucagon pathways simultaneously. This triple-mechanism approach distinguishes it from currently approved dual agonists (tirzepatide) and single GLP-1 agonists (semaglutide).

Phase 2 Trial Results

The Phase 2 trial enrolled adults with obesity (BMI ≥ 30 or ≥ 27 with comorbidities). Key results at 48 weeks for the 12 mg dose:

- **Mean weight loss:** ~24.2% of initial body weight
- **Responders $\geq 20\%$ weight loss:** approximately 63% of participants
- **Responders $\geq 30\%$ weight loss:** approximately 26% of participants
- **Tolerability:** consistent with GLP-1 class (nausea, vomiting predominantly during dose escalation)

Phase 3: The TRIUMPH Program

The TRIUMPH Phase 3 program is evaluating retatrutide across multiple populations. Phase 3 trials are designed to confirm Phase 2 efficacy findings, characterize the long-term safety profile, and include cardiovascular endpoints. Retatrutide is not available outside clinical trials.

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Sources & References

Jastreboff AM et al. Triple-Hormone-Receptor Agonist Retatrutide for Obesity. *NEJM* 2023; 389(6):514–526.

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