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PHYSICIAN SUMMARY

Orforglipron: The First Practical Oral GLP-1 Pill

Evidence-informed review of the ATTAIN program, oral bioavailability, Phase 2 efficacy data, and development status.

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Content reviewed against published clinical literature

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Executive Summary

KEY TAKEAWAYS

- ✓ First small-molecule GLP-1 receptor agonist — taken as a daily pill, no injection required
- ✓ No food or water timing restrictions (unlike oral semaglutide/Rybelsus)
- ✓ Phase 2: ~14.7% average weight loss at 36 weeks (120 mg dose)
- ✓ Phase 3 ATTAIN program underway; results expected 2025–2026
- ✓ Estimated FDA approval: 2026–2027 if Phase 3 confirms Phase 2 efficacy
- ✓ Would be the first oral GLP-1 medication indicated specifically for obesity

MECHANISM
Oral GLP-1
Non-peptide small molecule agonist

PHASE 2 WEIGHT LOSS
~14.7%
At 36 weeks, 120 mg dose

ADMINISTRATION
Daily Oral Pill
No food restrictions

DEVELOPMENT STATUS
Phase 3
ATTAIN program ongoing

APPROVAL ESTIMATE
2026–2027
Pending Phase 3 results

COMPARISON
~14.9% (Wegovy)
Comparable via injectable route

What Is Orforglipron?

Orforglipron (LY3502970) is an investigational daily oral GLP-1 receptor agonist by Eli Lilly. Unlike oral semaglutide (Rybelsus), orforglipron is a non-peptide small molecule with substantially better oral bioavailability at any time of day.

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Sources & References

Wharton S et al. Daily oral GLP-1 receptor agonist orforglipron for adults with obesity. NEJM 2023; 389(10):877–888.

Eli Lilly. ATTAIN Phase 3 Program. ClinicalTrials.gov. Accessed 2026.