

Eli Lilly vs. Novo Nordisk

Next-Generation Obesity Market

Investment Thesis 2026–2028

May 14, 2026

Operator Intelligence™

- ▶ **Verdict: Lilly BUY / Novo HOLD** — orforglipron's frictionless oral profile structurally widens Lilly's addressable market vs. Novo's food-restricted pill.
- ▶ CagriSema's head-to-head miss (~20% vs. Zepbound's 24%+) meaningfully narrows Novo's near-term catalysts; amycretin is the credible recovery asset but is Phase 3-stage, not yet de-risked.
- ▶ Retatrutide and eloralintide give Lilly a staged pipeline optionality no single Novo program currently matches.
- ▶ Oral GLP-1 pricing corridor (\$149–\$349/month) is the single largest commercial variable; adherence uplift from orals could expand total market 35–55% by 2030.
- ▶ BD/M&A: Novo must acquire or license next-generation convenience assets; Lilly is more likely a disciplined tuck-in buyer than a seller.

1. Executive Snapshot

The 2026–2028 obesity market is undergoing a structural bifurcation: injectable GLP-1 incumbents built on weekly pen devices are being challenged by orally administered small-molecule and peptide alternatives that remove the needle, the refrigerator, and — critically in Lilly's case — the meal-timing restriction. This bifurcation is not merely a formulation upgrade; it is a patient-acquisition event. The estimated 110–130 million Americans who qualify for pharmacologic obesity treatment but have never initiated therapy represent a latent demand pool whose primary stated barriers are injection aversion and lifestyle inconvenience. The company that cracks frictionless oral dosing at scale will likely dominate the 2028–2032 market cycle.

The investment thesis resolves clearly: **Eli Lilly is the stronger buy at this stage of the cycle**, driven by orforglipron's superior oral convenience profile, a deep and staged pipeline (retatrutide, eloralintide), manufacturing scale-up ahead of Novo, and a narrowing window for Novo to respond with a comparably positioned oral asset. Novo Nordisk remains a hold — not a sell — because oral semaglutide's brand equity, CagriSema's eventual injectable niche, and amycretin's Phase 3 data readout in late 2026 all represent real optionality. But Novo's near-term commercial trajectory has been materially impaired by the CagriSema efficacy miss and the structural inferiority of food-restricted oral dosing relative to orforglipron's label.

Decision implied: Allocate overweight to Lilly through the 2026–2027 orforglipron launch window; maintain market-weight Novo with a defined trigger (amycretin Phase 3 readout) that could justify an upgrade.

2. Pipeline Deep-Dive: Positioning, Convenience & Efficacy

2a. Eli Lilly — The Oral Convenience Thesis

Orforglipron is the central asset. As a small-molecule, non-peptide GLP-1 receptor agonist, it requires no food or water restrictions at the time of dosing — a distinction that is commercially underappreciated in current sell-side models. Novo's oral semaglutide (Rybelsus/Wegovy pill) requires fasting for 30 minutes post-dose with limited water; in clinical adherence studies of comparable oral formulations, meal-timing restrictions account for 20–30% of early discontinuations. Orforglipron eliminates this friction entirely. FDA approval in Q2 2026 with a broad obesity label positions it to capture the "oral-curious" patient who previously declined injectable GLP-1s, as well as the subset of Rybelsus users who are dissatisfied with the dosing protocol. Efficacy in pivotal trials demonstrated approximately 8–9% body weight loss at higher doses — below tirzepatide's 22%+ ceiling but meaningfully above historical oral semaglutide and directly competitive with injectable semaglutide (Ozempic/Wegovy).

Retatrutide (GLP-1/GIP/glucagon triple agonist) is the efficacy ceiling play. Phase 3 readouts expected throughout 2026–2027 could demonstrate 24–26% weight loss — potentially setting a new class-high benchmark above tirzepatide. The asset's Phase 2 data (~24% at 48 weeks) generated significant investor attention; if Phase 3 confirms this, retatrutide becomes the go-to "maximum efficacy" injectable for patients who need it, while orforglipron handles the broadened oral market. This staged segmentation — convenience oral at the base, maximum-efficacy injectable at the apex — is a textbook portfolio architecture that Lilly is executing deliberately.

Eloralintide (oral amylin agonist) addresses satiety via a complementary mechanism. Amylin slows gastric emptying and reduces glucagon secretion independently of GLP-1 receptor activation, which positions eloralintide as either a standalone for GLP-1-intolerant patients or a combination partner. Phase 2 data and timeline specifics are not fully available in current sources (see Information Limits), but the existence of an oral amylin asset is strategically important: if approved, Lilly would offer the only oral/oral combination obesity regimen, dramatically expanding the non-injectable adherent population.

2b. Novo Nordisk — Managing a Narrowing Window

Oral semaglutide (Wegovy pill) launched January 2026 with strong brand recognition but a structurally compromised convenience profile relative to orforglipron. The food restriction requirement is not a minor

inconvenience — it is a daily behavioral demand placed on a population that is already struggle with adherence. Novo's brand equity from Ozempic and injectable Wegovy will drive initial uptake, and payer formulary positioning may favor semaglutide given established coverage frameworks (Medicare coverage determinations for anti-obesity medications remain in flux, per CMS Medicare Coverage Database; payers with existing semaglutide pathways may default to the oral form on prior authorization grounds). Nevertheless, the structural ceiling on oral semaglutide market share is lower than orforglipron's absent a label change.

CagriSema (cagrilintide/semaglutide combination — GLP-1/amylin) was the marquee Novo pipeline asset entering 2026. Its Phase 3 head-to-head result of approximately 20% weight loss vs. tirzepatide's 24%+ is a material miss. The gap matters not because 20% is clinically irrelevant — it is not — but because it undercuts the premium positioning argument and reduces CagriSema to a "Zepbound-adjacent" injectable at best. Payers and prescribers who expected CagriSema to leapfrog tirzepatide will now maintain tirzepatide/Zepbound formulary priority. Novo's remaining argument for CagriSema is cardiovascular and renal outcomes data, which could differentiate the asset in guideline-driven prescribing — but that story requires 2027–2028 outcomes readouts that are not yet confirmed.

Amycretin is Novo's most credible next-generation asset: an oral dual GLP-1/amylin agonist entering Phase 3 in 2026. If Phase 3 replicates Phase 1/2 signals showing 13–15% weight loss (oral, no food restriction in early data), amycretin would directly compete with orforglipron on convenience while offering dual-mechanism differentiation. This is the single most important binary for Novo investors in the 2026–2027 window. A positive readout re-establishes Novo's oral leadership claim and materially upgrades the investment case; a negative or merely "me-too" result confirms Lilly's oral dominance through the decade.

Summary Positioning Table

Asset	Company	Stage / Status	Mechanism	Oral Convenience	Est. Weight Loss	Commercial Timing
Orforglipron	Lilly	FDA Approved (Q2 2026)	GLP-1 (small molecule)	✅ No food/water restriction	~8–9%	Launching now
Oral Semaglutide (Wegovy pill)	Novo	Approved, Launched Jan 2026	GLP-1 peptide (oral)	⚠️ 30-min fast required	~10–15%	Launched
Retatrutide	Lilly	Phase 3 (readouts 2026–27)	GLP-1/GIP/Glucagon triple	❌ Injectable	~24–26% (est.)	2027–2028 approval est.
CagriSema	Novo	Phase 3 (data in)	GLP-1 + Amylin (injectable)	❌ Injectable	~20%	2027 approval est.

Amycretin	Novo	Phase 3 starting 2026	GLP-1 + Amylin (oral)	✅ (early signals, TBC)	~13–15% (Phase 1/2 est.)	2028–2029 est.
Eloralintide	Lilly	Phase 2	Amylin (oral)	✅ Oral	TBD	2028+ est.

So what / Decision implied: Lilly holds both the near-term commercial launch (orforglipron) and the pipeline high-card (retatrutide). Novo's competitive recovery is binary on amycretin. Investors with a 12–18 month horizon should position asymmetrically toward Lilly; those with a 3-year view should maintain Novo exposure for the amycretin option.

3. rNPV / Valuation Scenarios & Sensitivity Analysis

The table below models peak annual obesity franchise revenues for each company across bear, base, and bull cases for the 2028–2032 period, incorporating oral pricing sensitivity (\$149–\$349/month range), market share dynamics from oral GLP-1 adoption, and adherence-driven market expansion assumptions. The "oral adherence uplift" row captures the market-expanding effect of removing injection barriers — estimated at 35–55% total addressable patient expansion by 2030 relative to the injectable-only baseline. This table is the central valuation artifact: modest pricing or adherence assumptions generate enormous revenue ranges, underscoring why the oral execution call is the primary investment variable.

Scenario Parameter	Bear Case	Base Case	Bull Case
Oral GLP-1 price (\$/month net)	\$149	\$229	\$349
Total obesity Rx market size (2028, patients on therapy, M)	8.5M	13M	18M
Oral adherence uplift vs. injectable baseline	+20%	+38%	+55%
Lilly oral share (orforglipron, 2028)	18%	27%	36%
Novo oral share (oral sema + amycretin, 2028)	12%	18%	22%
Lilly total obesity franchise peak revenue (2030, \$B)	\$14B	\$26B	\$42B

Novo total obesity franchise peak revenue (2030, \$B)	\$11B	\$19B	\$31B
Lilly obesity rNPV contribution (risk-adj., \$B)	\$85B	\$155B	\$230B
Novo obesity rNPV contribution (risk-adj., \$B)	\$65B	\$115B	\$180B
Key swing variable	Medicare coverage denial + price compression	Partial payer coverage, stable pricing	Medicare broad coverage, premium pricing holds
Novo amycretin Phase 3 outcome impact on Novo rNPV	Miss: -\$25B	Neutral: baseline	Win: +\$40B
Retatrutide approval impact on Lilly rNPV	Delayed/label restricted: -\$15B	On-time approval: baseline	Broad label + CV indication: +\$35B

The pricing corridor deserves particular emphasis. At \$149/month net, oral GLP-1s become accessible to a large commercially insured population without robust payer coverage — a dynamic that expands volume but compresses margin. At \$349/month, the value proposition for payers requires demonstrated outcomes data (cardiovascular mortality reduction, hospitalization avoidance) that neither oral semaglutide nor orforglipron has yet generated for obesity specifically. The base case at \$229/month assumes a payer negotiated rate consistent with CMS NCD-adjacent coverage frameworks and commercial plan tiering, neither of which has been definitively resolved as of May 2026 (per CMS Medicare Coverage Database; authoritative determinations remain pending).

Competitive Share Shift Sensitivity (2028)

Scenario	Lilly Obesity Share	Novo Obesity Share	Share Delta vs. 2025 Baseline	Primary Driver
Orforglipron dominates oral, amycretin delayed	42%	28%	Lilly +12pp / Novo -8pp	Oral convenience gap widens
Base: Both orals coexist, amycretin Phase 3 reads mid-2027	34%	32%	Lilly +4pp / Novo -4pp	Amycretin data pending; prescribers split

Amycletin Phase 3 strong, price war triggers	28%	36%	Novo +8pp / Lilly -4pp	Novo recaptures oral narrative; price compression hits both
Medicare broad coverage unlocked (all GLP-1s)	36%	31%	Market expands 40%+; both gain absolute revenue	Volume surge; Lilly benefits more from oral convenience

So what / Decision implied: The bear-to-bull revenue range for Lilly (\$14B–\$42B peak) is wider than for Novo (\$11B–\$31B), reflecting both greater upside and greater execution dependence. Lilly's risk is commercial execution; Novo's risk is pipeline binary. Conservative investors should weight Novo's more predictable (if lower) floor; growth investors should weight Lilly's superior ceiling, particularly if Medicare NCD resolution comes in H2 2026.

4. Operator Precedents: Oral vs. Injectable Launch Dynamics

History offers three directly relevant oral-vs.-injectable launch comparisons in chronic cardiometabolic disease, each with distinct lessons for the current GLP-1 transition.

Oral semaglutide (Rybelsus) vs. injectable GLP-1s in T2D (2019–2023): Rybelsus launched with strong Phase 3 PIONEER data but captured only 8–12% of the GLP-1 class in T2D despite oral convenience — primarily because the 30-minute fasting requirement and once-daily demand conflicted with patient behavior in a polymedicated population. The lesson: oral formulation alone is insufficient; dosing convenience must be genuinely frictionless. Orforglipron has directly internalized this lesson; oral semaglutide for obesity is repeating the same structural error. Novo appears not to have resolved this for the Wegovy pill launch.

Oral vs. injectable anticoagulants (DOACs vs. warfarin, 2010–2018): The DOAC transition took 6–8 years to reach 70%+ oral share despite clear convenience and safety advantages over INR monitoring. The acceleration driver was payer formulary normalization, not clinical superiority alone. The obesity analog: oral GLP-1 dominance will require 3–5 years of formulary infrastructure building, prior authorization protocol evolution, and prescriber habit change. Early movers (Lilly with orforglipron, Novo with oral semaglutide) who establish formulary position in 2026–2027 will structurally defend it against later oral entrants.

Oncology oral-to-IV transitions (e.g., oral targeted therapy vs. IV chemotherapy): Patient preference data consistently shows 70–80% preference for oral dosing when efficacy is within 15–20% of injectable comparators — the threshold at which prescribers also accept oral alternatives. Orforglipron's ~8–9% weight loss versus injectable semaglutide's ~12–15% falls within this "acceptable gap" for the convenience-motivated patient segment. Retatrutide, if approved, would serve the efficacy-maximizing segment — a clean two-tier market architecture.

So what / Decision implied: Oral market share build will be non-linear — slow in 2026, accelerating sharply in 2027–2028 as formulary positioning locks in. Companies that secure prior authorization pathways and payer tier-2 positioning in the first 12–18 months post-launch will disproportionately capture the adherence-driven market expansion. Lilly's manufacturing scale-up and orforglipron's frictionless label give it a structural edge in this formulary race.

Operator Insight 1 — Commercial Execution: The orforglipron launch window (Q2–Q4 2026) is not primarily a sales force execution challenge — Lilly's existing GLP-1 infrastructure from Mounjaro/Zepbound means prescriber relationships are established. The real execution test is payer contracting: securing favorable tier-2 formulary status without excessive rebating that erodes net pricing below \$200/month. The company that wins the first 6 major PBM negotiations in 2026 will set the pricing floor for the entire oral category. Lilly should resist the temptation to buy formulary position with deep discounts; a premium-maintained \$220–\$250 net price preserves margin architecture for the retatrutide launch cycle.

Operator Insight 2 — BD / M&A Implications: Novo Nordisk faces a structural BD imperative that Lilly does not. The CagriSema efficacy miss and oral semaglutide's convenience deficit mean Novo must either accelerate amycretin internally or acquire an oral convenience asset in the next 18–24 months. Target profile: an oral small-molecule GLP-1 or GIP/GLP-1 dual agonist in Phase 2 or later, without food restriction, from a mid-cap biotech. Novo's balance sheet supports a \$15–25B acquisition; the scarcity of qualifying assets means premium multiples (8–12x revenue for any de-risked oral GLP-1 Phase 2 asset). Lilly, conversely, is more likely to selectively acquire amylin mechanism assets or novel delivery platforms that extend the oral franchise — tuck-in deals in the \$2–5B range — rather than transformative M&A.

Operator Insight 3 — Investment Implications & Reversibility: The Lilly-over-Novو thesis has a reversibility score of 6/10 — meaning the lead could plausibly change within 24–30 months if two conditions are met simultaneously: (1) amycretin Phase 3 demonstrates $\geq 12\%$ weight loss without food restriction, and (2) Medicare broad obesity coverage is granted to all approved GLP-1s, reducing the formulary differentiation that currently favors the first-to-market oral player. Neither condition alone is sufficient to reverse the thesis; both together would materially narrow Lilly's oral market share advantage and upgrade Novo to a buy. Investors should monitor the amycretin Phase 3 interim analysis (expected H1 2027) and any CMS NCD policy signals from CMMI as the primary thesis-change triggers. Until then, the structural commercial advantage favors Lilly.

5. Risks & Catalysts

Key Risks — Lilly

- **Efficacy ceiling constraint:** Orforglipron's ~8–9% weight loss may be insufficient for patients with BMI ≥ 40 or significant comorbidities, creating a prescriber hesitation in high-acuity patients who would default to tirzepatide or, eventually, retatrutide. This creates a self-competition dynamic within Lilly's own portfolio.
- **Manufacturing execution:** Lilly's prior GLP-1 supply constraints (Mounjaro, Zepbound) demonstrated that manufacturing ramp is a real execution risk. If orforglipron demand significantly exceeds supply in H2 2026, competitor oral alternatives benefit disproportionately.
- **Retatrutide Phase 3 safety signal:** Triple agonism adds glucagon receptor activity, which carries theoretical risks (hepatic fat mobilization, glucose variability). An unexpected safety finding in Phase 3 would materially impair the pipeline valuation, potentially by \$15–20B rNPV.
- **Pricing compression from policy:** Any executive or legislative action on drug pricing in 2026 that establishes a precedent below \$200/month net for oral GLP-1s would compress Lilly's base case

revenue trajectory by 20–30%.

Key Risks — Novo

- **Amycretin Phase 3 binary:** As noted above, a failure or "me-too" result from amycretin effectively locks Novo into second-tier oral positioning through at least 2029. This is the highest-probability single-asset risk in the competitive landscape.
- **CagriSema label and commercial positioning:** Even a 20% weight loss label requires Novo to build a compelling "why CagriSema over Zepbound" prescriber narrative. Without cardiovascular outcomes differentiation, this is a difficult commercial story in an increasingly crowded injectable field.
- **Wegovy pill adherence data in real world:** If 12-month adherence data from the Wegovy pill launch (expected late 2026/early 2027) shows discontinuation rates meaningfully above orforglipron (where no food restriction removes a key friction point), Novo faces a real-world credibility problem with payers and prescribers.

Key Catalysts — Both

Catalyst	Timing	Impact: Lilly	Impact: Novo
Medicare NCD for obesity pharmacotherapy	H2 2026 – H1 2027	Very High positive (volume surge)	High positive (volume surge, but Lilly benefits more from oral access)
Retatrutide Phase 3 primary endpoint	Late 2026 – Q1 2027	Very High positive if confirmed	Negative (competitor bar raised)
Amycretin Phase 3 interim/primary data	H1 2027	Negative if strong (thesis pressure)	Very High positive if strong; thesis-defining
Orforglipron 12-month real-world adherence data	Q1–Q2 2027	High positive if adherence >65%	Negative (competitive benchmark set)
CagriSema CV outcomes data	2027–2028	Neutral	High positive if mortality benefit shown
Novo BD/M&A (oral asset acquisition)	2026–2027	Neutral to mildly negative	High positive; upgrades oral competitive position immediately

So what / Decision implied: The catalyst calendar favors Lilly in H2 2026 (retatrutide readout, orforglipron commercial ramp, Medicare NCD optionality) and Novo in H1 2027 (amycretin interim). Investors should position for Lilly's near-term catalyst density and reassess Novo exposure in Q4 2026 ahead of amycretin data.

6. Strategic Implications for BD / M&A

The obesity market's oral transition is creating a three-tier BD dynamic. Tier 1 targets are oral small-molecule GLP-1 or dual agonist assets in Phase 2+ without food restriction — the scarcest and most competitively pursued assets. Tier 2 targets are delivery technology platforms (oral peptide formulation, nanoparticle oral delivery) that could enable Novo to convert existing peptide assets to food-restriction-free oral formats — an approach that addresses the Wegovy pill's structural weakness at lower development cost than de novo programs. Tier 3 targets are complementary mechanism assets (amylin, GIP standalone, PYY agonists) that extend the obesity franchise beyond GLP-1 class limitations.

Novo is the more pressured acquirer in Tier 1 and Tier 2, given the amycretin Phase 3 binary. A failed amycretin trial in mid-2027 would trigger an immediate M&A mandate; Novo's business development team almost certainly has a shortlist of Phase 2 oral assets already under NDA. The strategic question is whether Novo moves preemptively (before amycretin data, at lower multiples) or reactively (after a miss, at elevated multiples in a bidding environment). Preemptive BD is the correct strategic call, but large pharma rarely executes it with sufficient urgency.

Lilly's BD calculus is different: with orforglipron launched, retatrutide Phase 3 ongoing, and eloralintide in Phase 2, the pipeline is well-populated. The most strategic Lilly BD move is not pipeline acquisition but platform acquisition — manufacturing technology (e.g., novel oral peptide delivery that bypasses first-pass hepatic metabolism) or companion diagnostics that enable precision patient selection for GLP-1 vs. amylin vs. triple-agonist therapy. This positions Lilly as the obesity medicine platform company, not merely the GLP-1 leader.

So what / Decision implied: Monitor Novo's BD activity as a leading indicator of pipeline confidence. Silence on BD through 2026 implies Novo's internal teams are confident in amycretin — a modestly positive signal. Aggressive BD in H1 2026 implies hedging, which itself signals internal concern about amycretin's Phase 3 trajectory.

7. Investment Thesis: Buy / Hold / Sell with Reversibility Score

Eli Lilly — BUY | Reversibility Score: 6/10

The Lilly buy thesis rests on three compounding advantages: first-mover oral convenience positioning (orforglipron, no food restriction), the highest near-term efficacy ceiling in the pipeline (retatrutide 24–26% weight loss), and a manufacturing and commercial infrastructure already calibrated to GLP-1 blockbuster scale. The obesity franchise, on a base case, contributes \$26B in peak revenue by 2030 — enough to sustain a premium valuation multiple even if diabetes and non-obesity indications grow modestly. The bull case at \$42B peak would represent one of the largest single-franchise revenue achievements in pharma history.

The reversibility score of 6/10 reflects genuine, if lower-probability, risks: amycretin delivering a surprise strong Phase 3, Medicare pricing action compressing net revenue below \$200/month, or a retatrutide Phase 3 safety signal. None of these is the base case, but all are plausible within the 24-month investment window. Investors should treat the thesis as a 12–18 month core position with defined exit or reduce triggers: (1) orforglipron real-world adherence data below 55% at 12 months, or (2) retatrutide Phase 3 primary endpoint miss.

Novo Nordisk — HOLD | Reversibility Score: 7/10

Novo remains a hold, not a sell, for three reasons. Oral semaglutide's brand equity will generate substantial initial uptake among Ozempic loyalists and physicians who prefer a known peptide backbone. CagriSema's 20% weight loss, while not class-leading, serves a real clinical need and will find its market — particularly if cardiovascular outcomes data arrives. And amycretin represents a genuine "fund the option" argument: a Phase 3 success would materially re-rate the stock and restore Novo's oral leadership narrative.

The reversibility score of 7/10 — higher than Lilly's — reflects the binary nature of Novo's near-term path. The downside scenario (amycretin miss + oral semaglutide real-world adherence disappointment) is a meaningful de-rating event; the upside scenario (amycretin success + CagriSema CV data) is a material re-rating. Investors with higher risk tolerance and a 2-year horizon who believe in amycretin's probability of success above 50% should hold a larger Novo position; those with 12-month horizons or who assign amycretin Phase 3 success probability below 40% should underweight.

Information limits: Specific orforglipron post-approval label language, current PBM formulary negotiation status, Novo's formal amycretin Phase 3 protocol design, and very recent BD activity for both companies (post-January 2026) are not captured in the sources available for this analysis. Conclusions in those areas reflect structural inference from public program designs and historical analogs rather than confirmed current-week data. Readers should supplement with live investor relations disclosures and CMS policy trackers.

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