EXECUTIVE INSIGHTS

Beyond Peak Weight Loss: The Next Battleground in Obesity

GLP-1 therapies have cracked the efficacy ceiling. The competition thatmatters now is being fought on tolerability, convenience, personalization, the long arc of chronic disease management and the bility to seamlessly get medicines to the patients who need them.

The anti-obesity medication (AOM) market has rapidly evolved from an emerging category into one of the preeminent biopharma markets. Wegovy's FDA approval in June 2021 catalyzed the modern obesity therapeutics market, delivering approximately 15% mean weight loss at 68 weeks in STEP 1. Tirzepatide's GIP/GLP-1 dual agonism raised the efficacy bar further, with the 15 mg dose of Zepbound (FDA-approved in November 2023) achieving approximately 21% mean weight loss at 72 weeks. Novo Nordisk subsequently extended the semaglutide franchise with Wegovy HD 7.2 mg (FDA-approved 2026), which achieved approximately 19% mean weight loss at 72 weeks in STEP UP and closed much of the efficacy gap with tirzepatide. Each efficacy step-change has driven substantial sponsor value creation, culminating in Novo Nordisk and Eli Lilly reaching combined market capitalizations exceeding $1 trillion at their peak.

Phase 3 data for retatrutide, Lilly's GLP-1/GIP/glucagon agonist, announced in May 2026 represent the latest inflection. TRIUMPH-1 (n=2,339; 80 weeks) showed mean body weight

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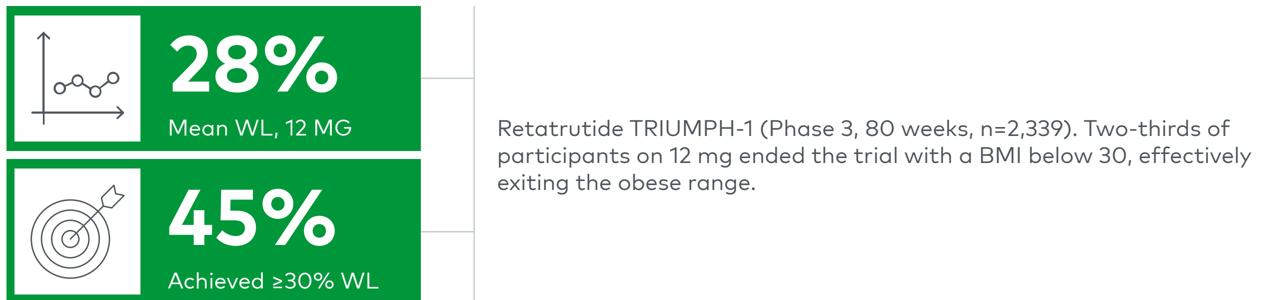
reductions of 19.0% at the lowest dose (4 mg) and 28% at the highest dose (12 mg), versus 2% on placebo. Notably, the lowest dose produced weight loss that is highly competitive with the best available weekly injectable semaglutide and tirzepatide regimens. At 12 mg, 45% of participants achieved at least 30% body weight reduction and 27% achieved at least 35% reduction, outcomes that effectively normalize body weight for a meaningful subset of patients with severe obesity (see Figure 1).

Figure 1

Retatrutide Phase 3 headline results



Note: WL=weight loss; BMI=body mass index; GLP-1=glucagon-like peptide-1
Source: Eli Lilly (TRIUMPH-1 Phase 3 data, 2026); L.E.K. research and analysis

The implication is significant: With retatrutide, the AOM class now addresses much of the upper range of physiologic weight-loss need, approaching outcomes historically associated with gastric bypass surgery. For many patients, this degree of weight loss could move BMI below 30, the clinical threshold for obesity. While higher efficacy could support uptake among severe obesity patients with BMI >40, this population is unlikely to materially alter broader market dynamics. As incremental weight loss becomes less differentiating for most patients, future winners will need to address the remaining clinical unmet needs in the broader obesity market (see Figure 2).

Figure 2

Remaining unmet needs in obesity pharmacotherapy (2026)

Need	Description	Status
Tolerability	GI adverse events (vomiting, diarrhea) remain a primary driver of premature discontinuation; there is a clear competitive white space for assets with a credible advantage that preserve efficacy	UNRESOLVED
Convenience	Weekly injectables face needle aversion and administration burden; oral semaglutide has proven non-injectable demand is large, and monthly dosing (Amgen MariTide, Phase 3) could extend the frontier further.	EVOLVING
Personalization	No approved paradigm exists for titrating therapy toward an individual weight-loss target and managing tolerability; fixed escalation to maximum tolerated dose ignores meaningful heterogeneity in patient goals, biology and treatment experience.	UNRESOLVED
Maintenance	Weight regain on discontinuation is well-documented, yet no protocol guides transition from induction to lower-intensity maintenance; Lilly's ATTAIN-MAINTAIN (topline December 2025) is the first prospective attempt.	EVOLVING
Treatment-refractory obesity	Up to 17% of patients fail to achieve even 5% weight loss on GLP-1 therapy; no second-line regimen or clinical algorithm exists, and with a treatment population of tens of millions, this subpopulation is commercially material.	UNRESOLVED
Obesity-related comorbidities	Cardiovascular, renal and metabolic benefits are increasingly becoming class expectations rather than durable sources of clinical differentiation. The opportunity has shifted to identifying ORCs where asset-specific benefit is credible and outcomes data can support a distinct label claim, payer argument or role in the treatment pathway.	EVOLVING
Weight loss "quality"	Patients on GLP-1-based therapy lose lean mass alongside fat, yet the field lacks a consensus definition of "weight loss quality," validated endpoints, standardized body composition measures, and a clear regulatory pathway for muscle-preservation claims. While lean mass loss is clinically relevant, particularly given concerns around sarcopenia and physical decline in older patients, it remains unclear whether lean mass preservation translates into outcomes compelling enough to support FDA action or differential payer reimbursement.	UNRESOLVED

Note: GI=gastrointestinal; GLP-1=glucagon-like peptide-1
Source: Published clinical trial data; L.E.K. research and analysis

Beyond these clinical gaps sits an equally consequential commercial requirement: providing patients with frictionless access to the medicines they need. That will require channel strategies that leverage telehealth and direct-to-consumer (DTC) platforms, enabling patients to start therapy more easily, stay on treatment longer, and choose the payment pathway that best fits their needs. Winners will also need to secure market access with insurers, increasingly through portfolio-level contracting leverage that can drive preferred placement. Strategic inclusion of obesity-related comorbidities into product labels may further reduce access friction, as coverage tied to cardiometabolic and other obesity-related risks may prove more durable than coverage for weight loss alone. The expected availability of generic semaglutide in the early 2030s will only intensify these pressures.

So what — implications for market participants

For incumbents:

The magnitude-of-weight-loss arms race may be nearing its end as the primary battleground for the injectable class. Differentiation will increasingly depend on treatment protocols that support persistence, options for treatment-experienced patients, and the ability to build frictionless access from initiation to ongoing therapy. Oral Wegovy's DTC launch and LillyDirect's telehealth-integrated dispensing model signal that channel strategy is becoming a core competitive asset, enabling patients to start therapy more easily and choose between insurance-based and self-pay pathways. Market access will also be central: portfolio-level contracting may be needed to secure preferred placement, while obesity-related comorbidities can help reduce coverage friction where weight-loss-only indications face resistance. As generic semaglutide approaches in the early 2030s, incumbents with the strongest combination of clinical lifecycle management, contracting leverage and omnichannel reach will be structurally advantaged.

For challengers and emerging biopharmas:

Winning with a single undifferentiated obesity asset will become increasingly difficult. Emerging companies should focus on a clearly defined unmet need, with precise positioning and a clear source-of-business thesis that makes the asset strategically relevant to partners or acquirers. Larger challengers will need to start with a differentiated beachhead asset and build from there, adding the evidence base, access capabilities, channel infrastructure and portfolio breadth required to compete at scale. As the basis of competition expands beyond efficacy to include market access, channel presence and lifecycle management, entrants must be prepared to make the substantial commercial investment required to challenge entrenched incumbents.

For financial sponsors and acquirers:

Valuation frameworks built around peak weight loss magnitude require recalibration. With the efficacy ceiling now set at 28%, durable value creation will depend less on incremental weight loss and more on the ability to address persistent clinical unmet needs (tolerability, convenience, personalization, maintenance, refractory obesity and weight-loss quality) in ways that translate into real-world adherence, payer relevance and chronic care scalability. Assets with demonstrated tolerability advantages, validated oral formulations, credible maintenance strategies or mechanistic rationale

in refractory settings may merit premium scrutiny. Platform companies in telehealth, digital therapeutics and patient support that can serve as the access layer for AOM therapy at scale also warrant attention. Single-asset obesity stories without a clear clinical differentiation thesis and channel strategy will face increasing headwinds.

For payers and health systems:

The clinical case for coverage of AOMs is now increasingly difficult to dispute from an efficacy standpoint. Going forward, the policy debate will center on access, adherence infrastructure and cost-effectiveness in the maintenance phase, not on whether the drugs work. Managed care organizations that develop population management frameworks for obesity now will be better positioned than those that treat it as a one-line formulary decision.

For further insights, see our recent piece exploring how AOMs are changing DTC pharmaceutical platforms.[1]

Contact us for more information.

Endnotes

[1]LEK.com, "The Emergence of Direct-to-Consumer Pharmaceutical Platforms: Strategic Implications for Biopharma." https://www.lek.com/insights/life-sciences-pharma/emergence-direct-consumer-pharmaceutical-platforms-strategic

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