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The Surge of Glp-1 Receptor Agonists: A Comprehensive Analysis of The Global Obesity Therapeutics Market

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Abstract

Background: Obesity, classified as a chronic disease with a global prevalence exceeding 1 billion individuals, represents one of the most significant and costly public health crises of the twenty-first century. Glucagon-like peptide-1 receptor agonist (GLP-1 RAs) have emerged as transformative pharmacological agents in obesity management, demonstrating unprecedented efficacy in weight reduction and cardiometabolic risk mitigation. The approval of semaglutide 2.4 mg (Wegovy) in 2021 and tripeptide (Zepbound) in 2023 has catalysed an extraordinary expansion of the obesity therapeutics market.

Objectives: This review analyses the mechanism of action, clinical efficacy, safety profile, and health economic impact of GLP-1 RAs, alongside a comprehensive evaluation of the global obesity therapeutics market its current valuation, competitive dynamics, access challenges, and projected trajectory through 2030.

Methods: A narrative review of pivotal clinical trials (STEP, SURMOUNT, SCALE programmes), regulatory filings, post-marketing surveillance data, and commercial market analyses published between 2018 and 2024 was conducted.

Results: Semaglutide 2.4 mg achieves mean weight loss of 14.9% from baseline (STEP-1), while tirzepatide 15 mg demonstrates mean weight reduction of 20.9% (SURMOUNT-1). The global GLP-1 RA market, valued at USD 18.4 billion in 2023, is projected to reach USD 145 billion by 2030 at a compound annual growth rate (CAGR) of 34.2%. Cardiovascular outcome data (SELECT trial) confirm semaglutide reduces major adverse cardiovascular events by 20% in obese patients with established cardiovascular disease. Significant access barriers driven by cost, supply constraints, and coverage variability remain substantial.

Conclusions: GLP-1 RAs represent the most significant pharmacological advance in obesity medicine since bariatric surgery, with clinical efficacy approaching surgical weight loss outcomes. Market growth is being driven by expanding indications, oral formulation development, and recognition of obesity as a treatable chronic disease. Equitable access and long-term adherence remain the defining challenges for realising the population health potential of this therapeutic class.

Keywords: Glp-1 Receptor Agonists; Semaglutide; Tirzepatide; Obesity; Weight Management; Cardiometabolic Disease; Pharmaceutical Market; Health Economics; Incretin; Adiposity.

Introduction

Obesity has attained pandemic proportions with devastating global health and economic consequences. The World Health Organization (WHO) reported that in 2022, more than 1 billion people worldwide were living with obesity, including 650 million adults, 340 million adolescents, and 39 million children more than double the 1990 prevalence [1]. Obesity is a chronic, progressive, and relapsing disease associated with over 200 comorbidities, including g type 2 diabetes mellitus, cardiovascular disease, hypertension, obstructive sleep apnoea, non-alcoholic fatty liver disease, and multiple malignancies [2,3]. The global economic cost of obesity-related productivity losses and healthcare expenditure is estimated to reach USD 4.3 trillion annually by 2035 [4].

For decades, pharmacological management of obesity remained largely ineffective, limited to agents with modest efficacy (2–5% weight loss), significant safety concerns (cardiovascular toxicity, neuropsychiatric effects), and high attrition rates. The approval of liraglutide 3 mg (Sax Enda) in 2014 marked the first evidence of clinically meaningful weight loss (8% mean reduction) from a pharmacological agent with an acceptable safety profile, establishing the GLP-1 receptor agonist class as the dominant paradigm in obesity pharmacotherapy [5,6].

The subsequent development of semaglutide and the dual GLP-1/glucose-dependent insulinotropic polypeptide (GIP) agonist tirzepatide has fundamentally altered the therapeutic and commercial landscape of obesity medicine. These agents achieve weight loss outcomes (15–21%) previously associated exclusively with bariatric surgery, while simultaneously demonstrating cardiovascular, renal, and hepatic protective effects that extend their clinical value far beyond cosmetic weight reduction [7,8]. The commercial impact has been extraordinary: semaglutide's manufacturer (Novo Nordisk) briefly became Europe's most valuable company in 2023, and the obesity drug market is now projected among the fastest-growing therapeutic categories globally [9].

Mechanisms of Action and Pharmacology

GLP-1 Receptor Agonist Pharmacology

Glucagon-like peptide-1 (GLP-1) is an incretin hormone secreted by L-cells in the distal small intestine and colon in response to nutrient ingestion. Endogenous GLP-1 exerts multiple metabolic effects through GLP-1 receptor (GLP-1R) activation: stimulation of glucose-dependent insulin secretion from pancreatic beta-cells, suppression of glucagon release, delayed gastric emptying, and satiety signalling via GLP-1Rs in the hypothalamus, brainstem, and vagal afferents [10,11]. Native GLP-1 has a plasma half-life of only 1–2 minutes due to rapid degradation by dipeptidyl peptidase-4 (DPP-4), necessitating the engineering of DPP-4-resistant analogues for therapeutic application [12].

Semaglutide, developed by Novo Nordisk, is a GLP-1 analogue with amino acid substitutions at positions 8 and 34 and C-18 fatty diacid attachment to lysine-26, conferring DPP-4 resistance and albumin binding that extends plasma half-life to approximately 165 hours, enabling once-weekly subcutaneous or once-daily oral administration [13]. Tirzepatide, developed by Eli Lilly, is a "Tw incretin" a 39-amino acid synthetic peptide that functions as a dual GIP/GLP-1 receptor co-agonist, with higher affinity for GIPR than GLP-1R. The synergistic activation of both incretin receptors appears to underlie tirzepatide's superior weight loss efficacy compared to selective GLP-1 Ras [14].

Mechanisms of Weight Loss

The weight loss effects of GLP-1 RAs are mediated through central and peripheral mechanisms. Central nervous system GLP-1R activation in the hypothalamic arcuate nucleus, paraventricular nucleus, and nucleus tactus solitarius suppresses appetite and reduces food intake, increasing satiety and decreasing caloric consumption by 20–30% [15]. Peripheral effects include delayed gastric emptying, reduced gastrointestinal motility, and altered nutrient sensing all contributing to reduced caloric intake and enhanced satiety [16]. Evidence from neuroimaging studies indicates that GLP-1 RAs also reduce reward-motivated food intake by modulating dopaminergic signalling in the ventral tegmental area and nucleus accumbent, potentially addressing hedonic eating behaviours [17].

Clinical Efficacy in Obesity

Semaglutide: Step Programme

The Semaglutide Treatment Effect in People with obesity (STEP) clinical trial programme evaluated semaglutide 2.4 mg subcutaneous weekly for weight management across four pivotal Phase 3 studies [18]. STEP 1 (n=1,961) demonstrated a mean weight loss of 14.9% from baseline versus 2.4% with placebo at 68 weeks ($p<0.001$), with 69.1% of participants achieving ≥10% weight loss and 50.5% achieving ≥15% weight loss [19]. STEP 2 evaluated semaglutide in patients with type 2 diabetes, achieving 9.6% weight loss (vs 3.4% placebo), acknowledging the attenuated response observed in this population [20].

The SELECT cardiovascular outcomes trial (n=17,604) demonstrated that semaglutide 2.4 mg reduced the risk of major adverse cardiovascular events (MACE) by 20% (HR 0.80, 95% CI 0.72–0.90) in non-diabetic obese adults with established cardiovascular disease, establishing a cardioprotective indication that substantially broadens the therapeutic rationale beyond weight reduction per se [21].

Tirzepatide: SURMOUNT Programme

Tirzepatide demonstrated superior weight loss efficacy in the SURMOUNT clinical programme. SURMOUNT-1 (n=2,539, non-diabetic adults with obesity) showed mean weight reductions of 15.0%, 19.5%, and 20.9% for 5 mg, 10 mg, and 15 mg doses respectively, versus 3.1% with placebo at 72 weeks [22]. Remarkably, 37.0% of participants receiving tirzepatide 15 mg achieved ≥25% weight loss a threshold historically achievable only through bariatric surgery. SURMOUNT-2 in patients with type 2 diabetes reported mean weight loss of 15.7% for tirzepatide 15 mg versus 3.3% for placebo [23].

Comparative weight loss performance across approved and emerging agents is summarised in Figure 2, illustrating the markedly superior efficacy of tirzepatide over predecessors and benchmarked against the non-GLP-1 agent orlistat [24].

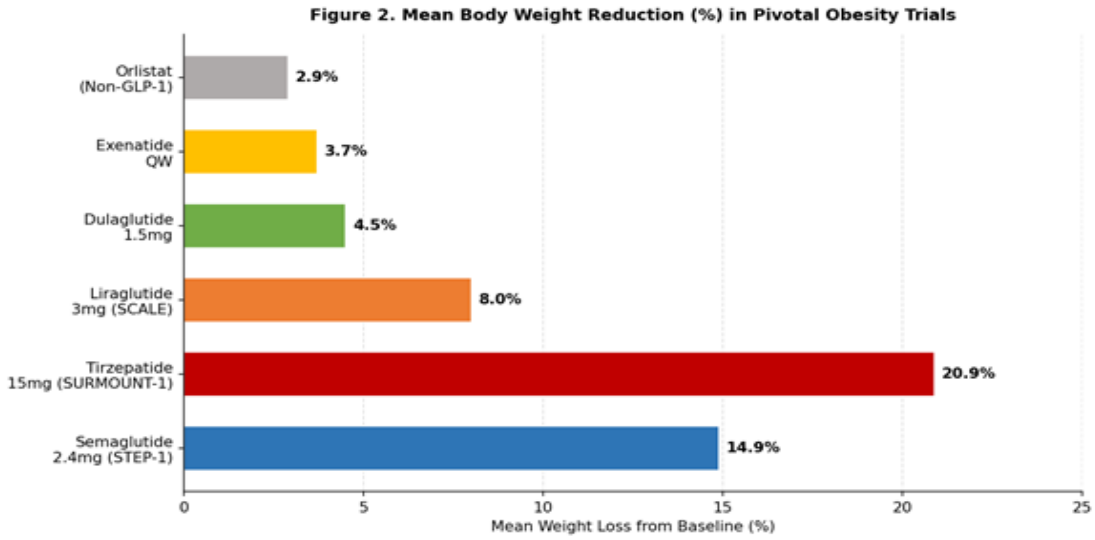

Figure 2. Comparative mean body weight reduction (%) from baseline across pivotal obesity pharmacotherapy trials. Data represent primary endpoint weight loss at trial completion.

Global Obesity Therapeutics Market Analysis

Market Size and Growth Trajectory

The global GLP-1 receptor agonist market comprising both diabetes and obesity indications was valued at approximately USD 18.4 billion in 2023, with obesity-specific revenues constituting a rapidly growing proportion. Market projections from multiple independent commercial intelligence firms forecast a compound annual growth rate (CAGR) of 32–37% through 2030, driven by label expansions, oral formulation approvals, and new entrant competition [25,26].

As illustrated in Figure 1, the market trajectory reflects an inflection point following semaglutide and tirzepatide obesity approvals, with forecasts ranging from USD 130–160 billion by 2030. This would represent an approximately 8-fold increase from 2023 levels and position obesity pharmacotherapy among the five largest pharmaceutical therapeutic categories globally [27].

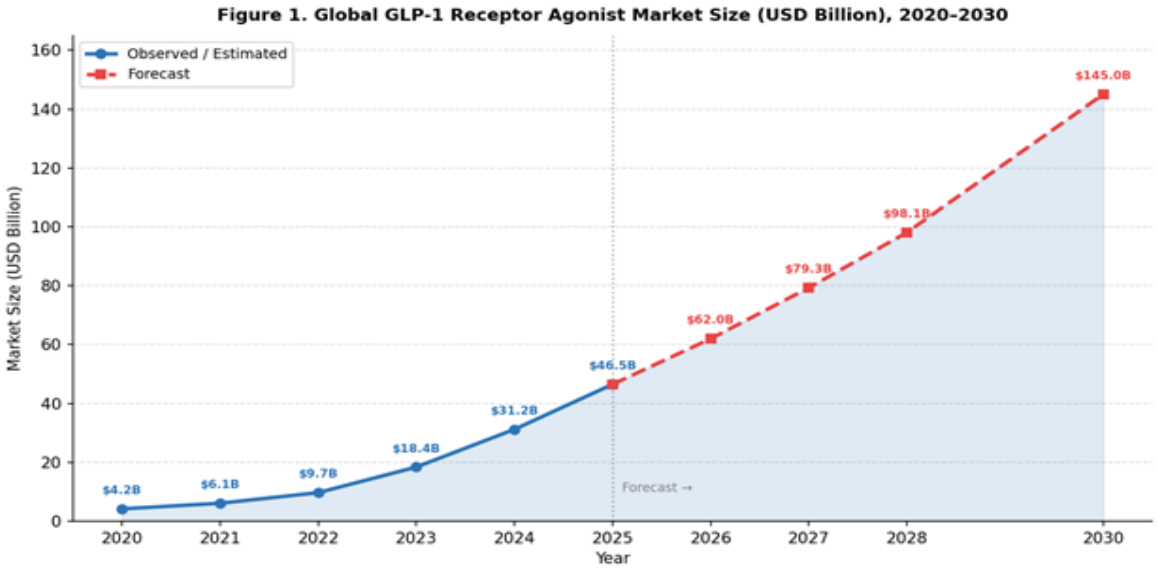

Figure 1. Global GLP-1 receptor agonist market size trajectory (USD billions), 2020–2030. Observed/estimated values (2020–2025) and consensus forecast range (2026–2030).

Competitive Landscape

The obesity pharmacotherapy market is currently dominated by two global players: Novo Nordisk (semaglutide: Wegovy for obesity, Ozempic for T2DM) and Eli Lilly (tirzepatide: Zepbound for obesity, Mounjaro for T2DM). Together, these products generate approximately 63% of the current GLP-1 RA market revenue [28]. The competitive landscape is rapidly expanding as multiple pharmaceutical organisations advance late-stage obesity programmes, with at least 11 agents in Phase 2/3 development as of mid-2024, including amycretin (Novo Nordisk, GLP-1/amylin dual agonist), retatrutide (Eli Lilly, triple GIP/GLP-1/glucagon agonist), orforglipron (Eli Lilly, oral GLP-1 RA), and survodutide (Boehringer Ingelheim, GLP-1/glucagon agonist) [29].

Table 1. Key Approved GLP-1 Receptor Agonists for Obesity Management (2024)

Agent	Brand	Developer	Route/Frequency	Mean wt loss	Indication
Liraglutide 3mg	Saxenda	Novo Nordisk	SC daily	~8.0%	Obesity ≥BMI 30
Semaglutide 2.4mg	Wegovy	Novo Nordisk	SC weekly	14.9%	Obesity ≥BMI 30
Tirzepatide 5/10/15mg	Zepbound	Eli Lilly	SC weekly	Up to 20.9%	Obesity ≥BMI 30
Semaglutide (oral)	Rybelsus (T2DM)	Novo Nordisk	Oral daily	4–5%	T2DM (obesity label pending)

BMI: body mass index; SC: subcutaneous; T2DM: type 2 diabetes mellitus; wt: weight.

Market Segmentation and Regional Analysis

The obesity therapeutics market is dominated by injectable GLP-1 RAs (42% of 2024 market share), followed by GLP-1/GIP dual agonists (21%) and the emerging oral GLP-1 category (11%). North America generates the largest regional revenue (approximately 60% of global sales), reflecting US-specific pricing dynamics, insurance landscape, and prescribing culture, followed by Europe (23%) and Asia-Pacific (12%) (Figure 3) [30].

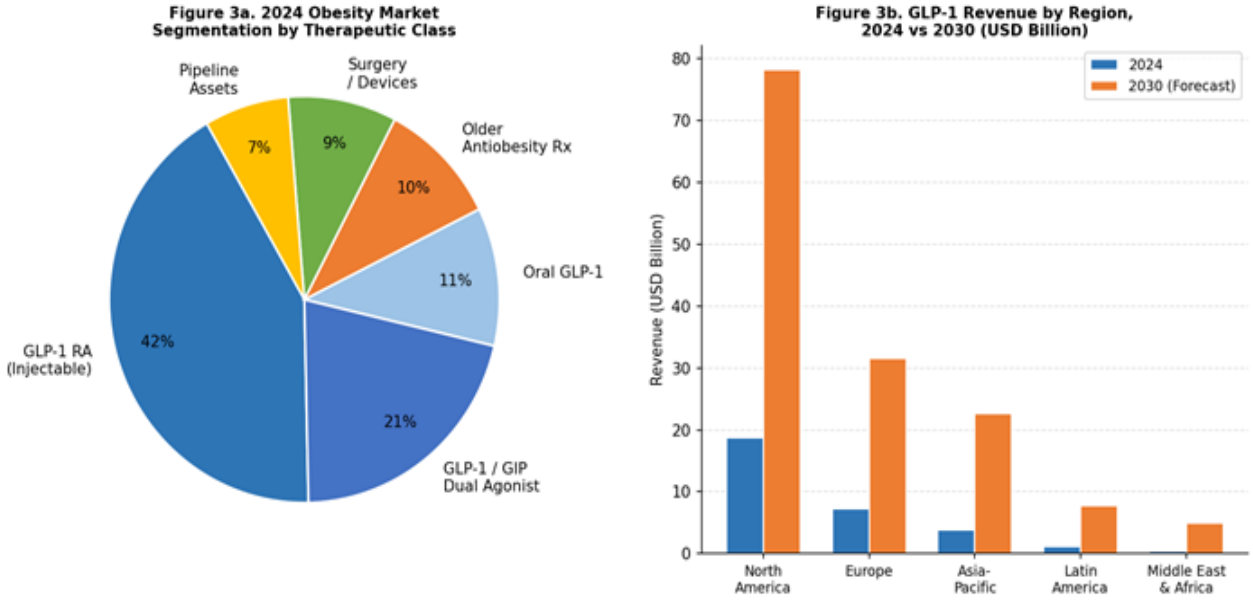

Figure 3. (a) Global obesity therapeutics market segmentation by therapeutic class, 2024. (b) GLP-1 agonist revenue by geographic region, 2024 vs 2030 forecast (USD billions).

Safety, Tolerability and Long-Term Outcomes

Adverse Effect Profile

The safety and tolerability profile of GLP-1 RAs in obesity is generally well-characterised and consistent across the class, with gastrointestinal adverse events constituting the predominant concern. Nausea is reported in 20–44% of patients initiating therapy, vomiting in 10–24%, and diarrhoea in 8–30%, with symptoms predominantly occurring during dose escalation phases and typically self-limiting within 4–8 weeks [31,32]. In the STEP and SURMOUNT programmes, gastrointestinal adverse events were the primary driver of treatment discontinuation, occurring in 4.5–7.0% of participants in active arms. [33].

More serious but less frequent adverse events include pancreatitis (relative risk vs placebo approximately 1.5–2.0, absolute risk low at 0.1–0.3%), gallbladder disease (cholelithiasis and cholecystitis are increased, likely related to rapid weight loss), and injection site reactions [34]. While rodent studies demonstrated GLP-1R expression in thyroid C-cells and medullary thyroid carcinoma (MTC) induction in rodent models at supratherapeutic doses, human clinical data and post marketing surveillance have not established a causal relationship between GLP-1 RAs and MTC in humans [35].

Cardiovascular Outcomes

The cardiovascular safety and potential protective effects of GLP-1 RAs have been extensively evaluated in large outcomes trials [36]. The SELECT trial (n=17,604) demonstrated a 20% relative risk reduction in MACE (non-fatal MI, non-fatal stroke, cardiovascular death) with semaglutide 2.4 mg compared to placebo in obese, non-diabetic adults with established CVD over a mean follow-up of 33 months [37]. This landmark finding has catalysed regulatory approval updates and guideline revisions that now recommend semaglutide as a first-line intervention in obese patients with cardiovascular risk [38].

Health Economics and Access Considerations

Cost-Effectiveness Analysis

The cost-effectiveness of GLP-1 RAs for obesity management is contingent on treatment duration, long-term cardiovascular event reduction, and comorbidity mitigation. Pharmacoeconomic analyses of semaglutide 2.4 mg from a US payer perspec-

tive estimate incremental cost-effectiveness ratios (ICERs) of USD 175,000–270,000 per quality-adjusted life year (QALY) gained at current list prices (USD 1,349/month), substantially exceeding conventional willingness-to-pay thresholds of USD 50,000–150,000/QALY [39,40]. However, when cardiovascular event reduction from SELECT trial data is incorporated into modelling, ICERs decrease substantially toward USD 100,000–150,000/QALY for high cardiovascular-risk populations, approaching cost-effectiveness thresholds [41].

Access Barriers and Coverage Landscape

Despite compelling clinical evidence, access to GLP-1 RA therapy for obesity remains highly restricted globally. In the United States, Medicare Part D historically excluded coverage for obesity pharmacotherapy, with the Treat and Reduce Obesity Act (TROA) proposed but not enacted as of 2024. Medicaid coverage varies by state. Commercial insurance coverage is inconsistent, with many plans requiring prior authorisation, step therapy mandates, or excluding obesity-specific indications [42]. Supply chain shortages driven by unprecedented demand outstripping manufacturing capacity for semaglutide created significant access disruptions throughout 2022–2024, affecting millions of patients and prompting FDA drug shortage designations [43].

Future Outlook and Emerging Developments

The obesity pharmacotherapy landscape is poised for continued rapid evolution across multiple fronts. Oral GLP-1 RA development represented by oral semaglutide (Novo Nordisk, Phase 3 for obesity), orforglipron (Eli Lilly, oral small molecule GLP-1 RA), and danuglipron (Pfizer, oral GLP-1 RA) offers the prospect of dramatically expanding access by eliminating injection barriers and potentially reducing manufacturing complexity and cost [44,45].

Triple agonism targeting GIP, GLP-1, and glucagon receptors simultaneously (retatrutide) has demonstrated weight loss of 24% at 48 weeks in Phase 2 trials, suggesting further incremental efficacy gains beyond dual agonism [46]. Emerging mechanisms including amylin analogues (amycretin), melanocortin-4 receptor agonists, and bimagrumab (anti-activin IIB antibody for selective muscle preservation during weight loss) offer complementary pathways that may be combined with GLP-1 RAs in future combination regimens [47].

The potential expansion of GLP-1 RA indications beyond obesity and diabetes is a major driver of market projections. Ongoing and planned clinical programmes in non-alcoholic steatohepatitis (NASH)/metabolic dysfunction-associated steatohepatitis (MASH), Alzheimer's disease (EVOKE trial), addiction medicine (alcohol, nicotine, opioid use disorders), polycystic ovary syndrome, and obstructive sleep apnoea could substantially broaden the addressable patient population and further accelerate market growth [48,49].

Conclusion

GLP-1 receptor agonists represent the most consequential pharmacological innovation in obesity medicine in decades, achieving weight loss outcomes (15–21%) that rival bariatric surgery and conferring cardiovascular protection in high-risk populations. The global GLP-1 RA market, currently undergoing exponential growth from USD 18.4 billion (2023) toward a projected USD 145 billion by 2030, represents one of the most significant commercial transformations in pharmaceutical history [50].

The clinical and market evidence collectively establishes GLP-1 RAs as the new standard of care for obesity management, with tirzepatide presently at the efficacy frontier. However, the full population health potential of this therapeutic class is circumscribed by profound access inequities rooted in price, supply constraints, and inconsistent insurance coverage. Sustainable healthcare system integration requires value-based pricing frameworks, expanded coverage mandates recognising obesity as a chronic disease, and long-term adherence support infrastructure. The next decade will determine whether the GLP-1 revolution translates into equitable and durable population health impact [51].

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Author Contributions: All authors contributed equally. All authors approved the final manuscript.

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