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Are GLP-1s the magical drug?

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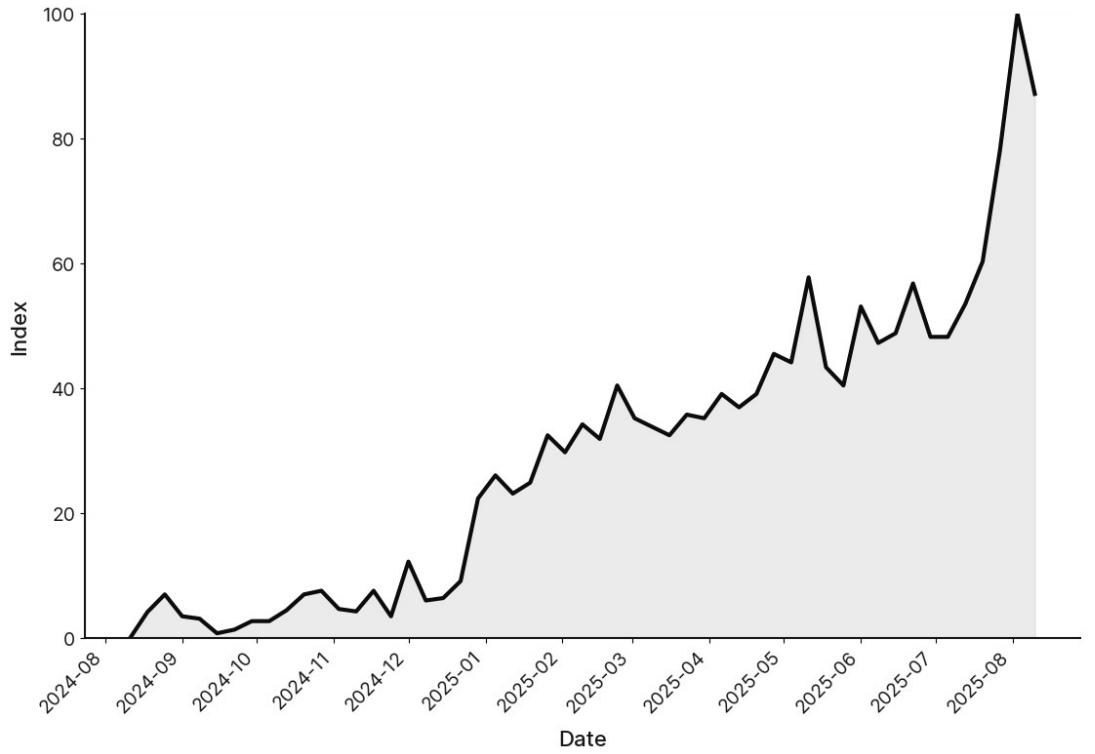
In the history of medicine, few drugs tower above all others, drugs which helped patients far beyond doctors' initial expectations and continue to benefit millions of people every day. We have such a drug for obesity & diabetes - GLP-1 receptor agonists. Glucagon-like peptide 1 receptor agonists known as GLP-1 such as semaglutide and tirzepatide are a class of medications developed to treat diabetes and obesity. GLP-1 RAs have revolutionized the approach to obesity treatment, becoming the most effective non-surgical pharmacological intervention available. Current GLP-1 RAs such as once-weekly subcutaneous semaglutide help in mean body weight reduction of approx 15% in individuals with obesity; Dual glucose-dependent insulinotropic polypeptide (GIP) and GLP-1 receptor agonists, like once-weekly tirzepatide resulted in the mean body weight changes of -17.5%.

GLP-1 is a USD150–175bn global market opportunity over the coming decade. In the United States alone, the obesity epidemic affects over 100 million adults and almost 15 million children, representing 41.9% of the adult population and 19.7% of the child population, which has quadrupled over the last 30 years. Obesity is defined as having a BMI over 30.0 kg/m² and is linked to many significant chronic diseases, including diabetes, heart disease, and some types of cancer. This epidemic contributes to $173 billion in annual healthcare costs. The global market for obesity drugs could increase by more than 15-fold by 2030 as their use expands beyond weight loss to treat a range of diseases.

Two companies dominate the GLP-1 landscape: Novo Nordisk and Eli Lilly. Novo Nordisk's portfolio includes liraglutide (Victoza® for diabetes, Saxenda® for obesity) and semaglutide (Ozempic® for diabetes, Wegovy® for obesity, and Rybelsus® as an oral tablet) – all GLP-1 analogues. Eli Lilly's offerings include dulaglutide (Trulicity®, a once-weekly GLP-1 RA for diabetes) and tirzepatide (Mounjaro® for diabetes and Zepbound® for obesity, a dual GIP/GLP-1 agonist).

Apart from obesity and T2D, GLP-1s seem to curb alcohol, cocaine, and tobacco use in people with addiction. They cut risk of strokes, heart attacks, chronic kidney disease, sleep apnea and Parkinson's. They're linked to lower rates of several cancers, including pancreatic cancer and multiple myeloma.

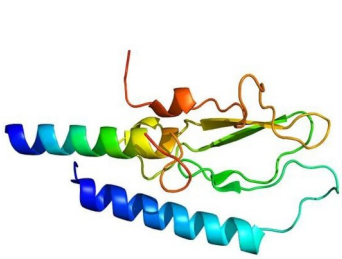
Searches for GLP-1s Have Skyrocketed in Past Few Years



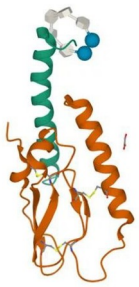
source: exploding topics

how do these drugs work?

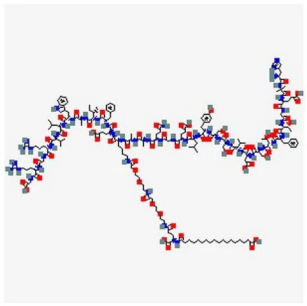
When someone digests food, their intestines release several hormones - two of the most important are GLP-1 (which stands for glucagon-like peptide 1) and GIP (which stands for “glucose-dependent insulinotropic polypeptide”). These are sensed by receptors in the brain, stomach and pancreas. When these receptors are triggered in the brain, they generate a sense of fullness and hence reduce the desire to eat; when they are triggered in the stomach, they slow the rate at which stomach empties; and when triggered in the pancreas, they help produce insulin, which controls blood sugar and hence diabetes.



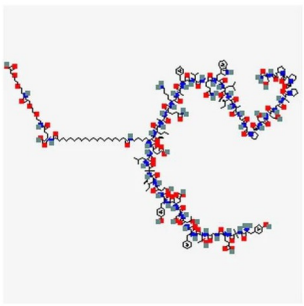
Glucagon-like peptide (GLP-1)



Gastric inhibitory polypeptide (GIP)



Semaglutide

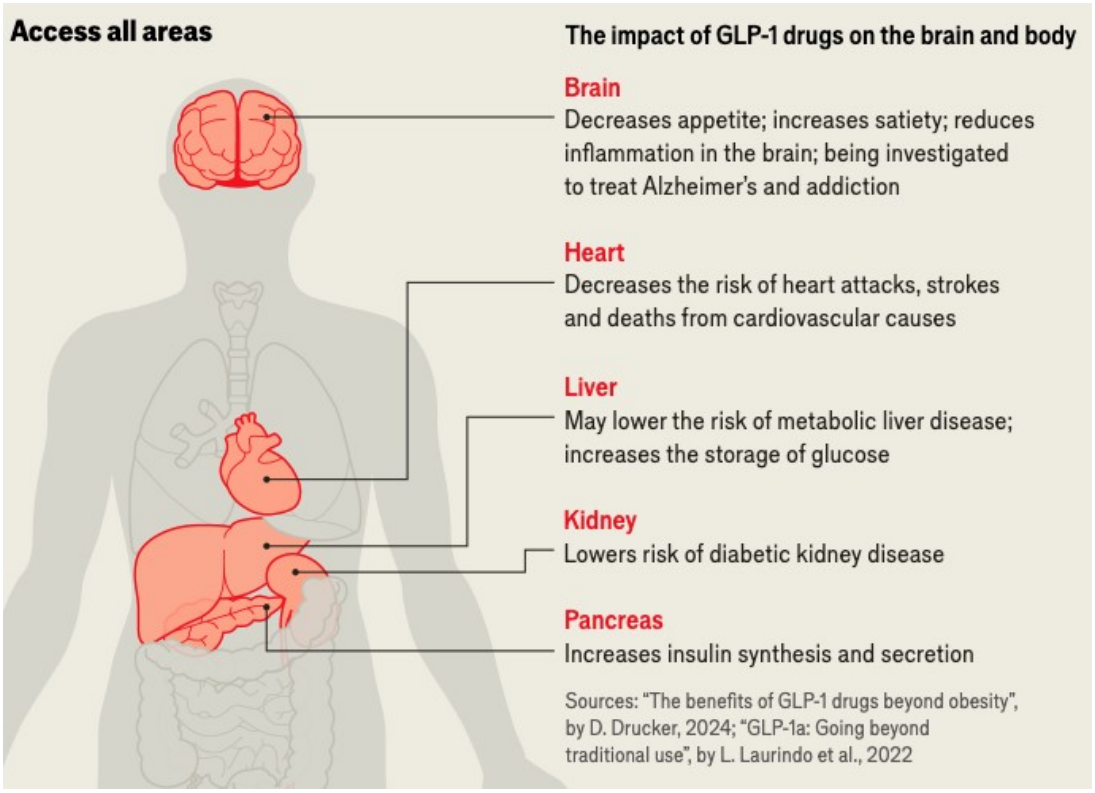


Tirzepatide

Semaglutide is a “GLP-1 agonist” which means it activates GLP-1 receptors. Tirzepatide is a “double agonist” because it activates both GLP-1 and GIP receptors. It’s not possible to use the hormone GLP-1 itself as a drug, because the body naturally breaks it down within a few minutes. Drugs like semaglutide work because they combine a fatty-acid “tail” attached to the GLP-1 “head”. The head binds to, and activates, the GLP-1 receptors. The tail protects the head, because it is tough and sticky, slowing down the rate at which the body breaks it down.

Benefits of GLPs

Several years ago, scientists took a close look at GLP-1 drugs, and learned that they were good at helping people lose weight. Then they took an even closer look and learned the drugs are also good at just about everything else.



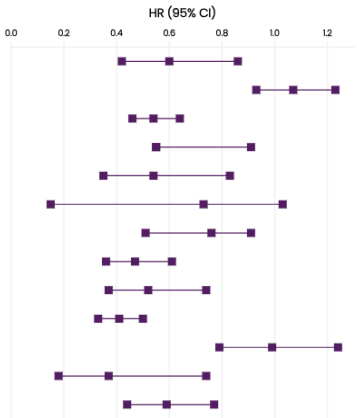
source: the economist

Cardiovascular Disease: GLP-1 receptor agonists demonstrate significant cardiovascular benefits across multiple compounds. Semaglutide reduces the risk of major adverse cardiovascular events including heart attack, stroke, and cardiovascular death by 20% in patients with established cardiovascular disease and obesity or overweight.

Diabetes Prevention: Beyond managing existing T2D, GLP-1 RAs have shown remarkable potential in preventing its onset in high-risk populations. The SURMOUNT trial revealed that for adults who are overweight or obese and have prediabetes, treatment with a dual receptor agonist like tirzepatide made them more than 90% less likely to develop type 2 diabetes compared to those receiving a placebo.

Cancers: Emerging evidence suggests a potential role for GLP-1 RAs in reducing the risk of obesity-associated cancers (OACs) such as colorectal cancer, esophageal, breast, endometrial, gallbladder, stomach, kidney, ovarian, pancreatic, and thyroid cancer, as well as hepatocellular carcinoma, meningioma, and multiple myeloma. In a large study involving over 1.6 million patients with type 2 diabetes who had no prior diagnosis of OACs, patients treated with GLP-1 RAs demonstrated a significantly lower risk for ten types of cancers associated with obesity.

Outcome (N =1651 452)	Group prescribed GLP-1RAsbut not insulin. No (%) (n= 48983)	Group prescribed insulin but not GLP-1RAs, No (%) (n= 1044745)	HR (95% CI)
Esophageal cancer (n=48437)	49 (0.10)	77 (0.16)	0.60 (0.42-0.86)
Breast cancer (n=13768)	427 (3.08)	379 (2.94)	1.07 (0.93-1.23)
Colorectal cancer (n=48443)	223 (0.46)	391 (0.81)	0.54 (0.46-0.64)
Endometrial cancer (n=25750)	160 (0.62)	210 (0.82)	0.74 (0.60-0.91)
Gallbladder cancer (n=48587)	<10 (<0.02)	19 (0.04)	0.35 (0.15-0.83)
Stomach cancer (n=48449)	56 (0.12)	75 (0.16)	0.73 (0.51-1.03)
Kidney cancer (n=48322)	223 (0.46)	284 (0.59)	0.76 (0.64-0.91)
Hepatocellular carcinoma (n=48397)	79 (0.16)	167 (0.35)	0.47 (0.36-0.61)
Ovarian cancer (n=25739)	51 (0.20)	94 (0.37)	0.52 (0.37-0.74)
Pancreatic cancer (n=48490)	123 (0.25)	290 (0.60)	0.41 (0.33-0.50)
Thyroid cancer (n=48527)	154 (0.32)	149 (0.31)	0.99 (0.79-1.24)
Meningioma (n=48518)	11 (0.02)	29 (0.06)	0.37 (0.18-0.74)
Multiple myeloma (n=48527)	80 (0.17)	131 (0.27)	0.59 (0.44-0.77)

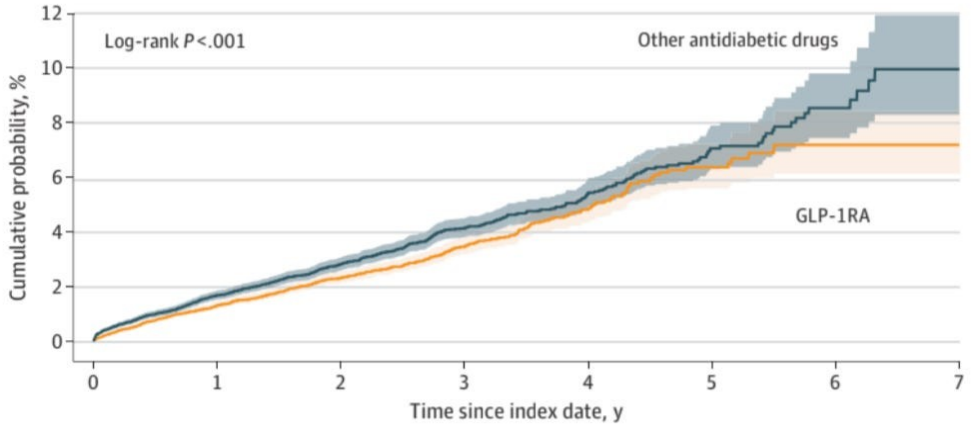


Chronic kidney disease: GLP-1 RAs provide significant kidney-protective benefits, especially for patients with type 2 diabetes and chronic kidney disease (CKD). The Flow trial had 3,500 participants who had CKD and type 2 diabetes (but were not necessarily overweight). The trial showed that semaglutide reduced the risk of major kidney disease events by 24% and the overall death rate by approximately 20% over a median follow-up of 3.4 years.

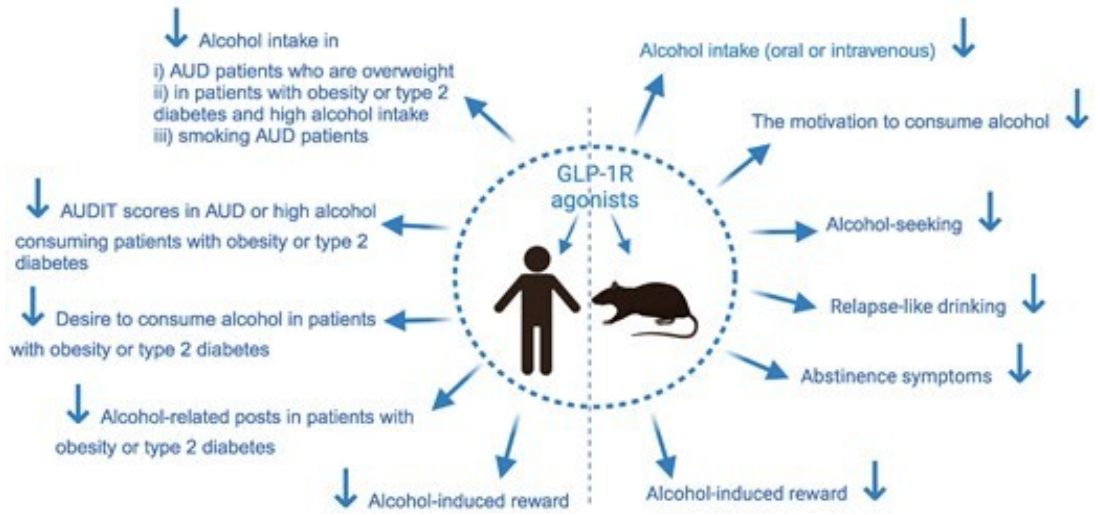
MASH/Fatty Liver Disease: In a phase 2 trial, tirzepatide demonstrated dose-dependent efficacy in patients with biopsy-confirmed MASH and moderate to severe fibrosis. After 52 weeks, resolution of MASH without worsening of fibrosis was achieved in 44% (5 mg), 56% (10 mg), and 62% (15 mg) of tirzepatide-treated participants, compared to only 10% in the placebo group.

Parkinson's: Lixisenatide is an older GLP-1, approved only for diabetes. However, in a recent Phase 2 study, it stopped the progression of Parkinson's in early-stage patients. GLP-1 RAs achieve neuroprotection by inhibiting inflammation, improving neuronal survival, maintaining synapses, and enhancing dopaminergic transmission in the brain.

Alzheimer's and Dementia: There is also evidence that GLP-1s can help with dementia. For example, a retrospective study of 130,000 diabetes patients published in July found that semaglutide was associated with a lower risk of the cognitive issues (such as memory loss) that are often an early sign of dementia. GLP-1 analogs can improve the brain's glucose metabolism by enhancing glucose transport across the blood-brain barrier. They also attenuate neuroinflammation and oxidative stress, critical factors in neurodegeneration.



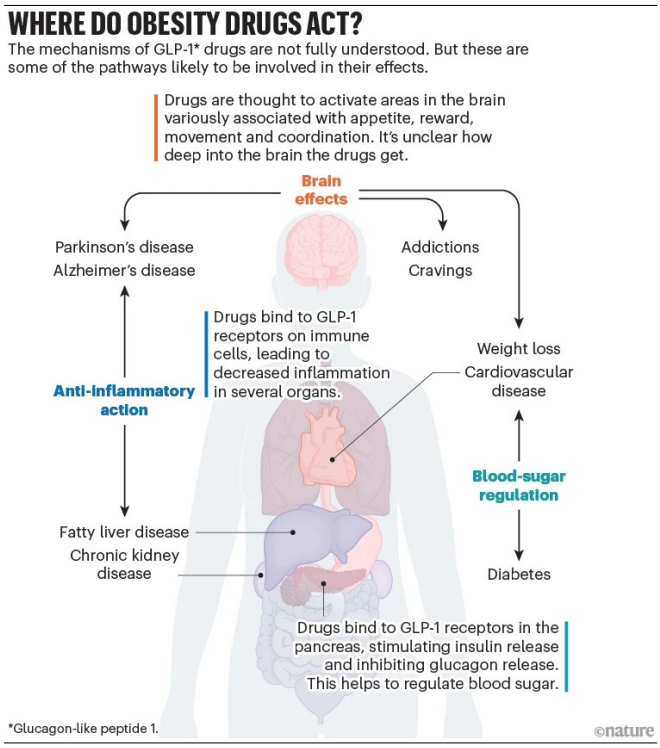
Addiction: Preliminary clinical and preclinical evidence suggests GLP-1 RAs may be therapeutic targets for addiction, including smoking and nicotine dependence. GLP-1 RAs can influence reward pathways in the brain by modulating dopamine levels and glutamatergic neurotransmission, which contributes to reducing palatable food intake, as well as decreasing the use of cocaine, amphetamines, alcohol, and nicotine.



How can a weight loss drug do everything?

GLP-1 is a hormone secreted by special gut cells in your lower intestine whenever you eat carbohydrates, fats or proteins. The primary physiological role of GLP-1 is to connect nutrient consumption with glucose metabolism, acting as a crucial signal to the body that food has been consumed and metabolic adjustments are required. In its natural form, GLP-1 rises quickly after a meal, then vanishes within minutes, so it never makes it far enough to have a sustained therapeutic effect.

Once released, GLP-1 flips three key switches. In the brain, it triggers the feeling of fullness so you naturally eat less. In the stomach, it slows down how fast food empties into your intestines, extending that satisfied-after-a-big-meal feeling. And it triggers the pancreas to release more insulin lowering blood sugar and less glucagon raising blood sugar.



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The ability of GLP-1 RAs to do everything largely stems from the activation of GLP-1 receptors across numerous organs and tissues in the body, well beyond the pancreas. When the supercharged GLP-1 RAs enter the bloodstream and persist due to their prolonged half-life, they can activate these receptors in various locations, leading to a cascade of beneficial effects.

GLP-1Rs are prominently found in:

- Pancreatic cells: Beta-cells (insulin secretion) and alpha-cells (glucagon suppression).
- Central Nervous System (CNS): Multiple brain regions, including the hypothalamus (arcuate, paraventricular, ventromedial nuclei), area postrema, brainstem (nucleus tractus solitarius), insula, amygdala, and striatum.
- Gastrointestinal Tract: Stomach (gastric pits, antrum/pylorus), small intestine (duodenum crypts, L-cells), and enteric neurons.
- Cardiovascular System: Cardiac atrium, vascular smooth muscle, and endothelium.
- Kidneys: Smooth muscle cells in the preglomerular vasculature, and potentially other renal cells.

Site	Primary receptor action	Main clinical effects
Brain/vagal (NTS, ARC)	Appetite reduction; slowed gastric empty	Lower intake; early satiety
Pancreatic β, α cells	↑ Insulin (glucose-dependent); ↓ glucagon	Lower fasting/post-meal glucose; low hypo risk
Stomach/proximal gut	Slower antral/pyloric transit (vagal)	Blunted post-prandial spikes; fullness
Kidney proximal tubule	Natriuresis/diuresis signals	Small BP/glucose benefits
Heart atrium	Direct cardiometabolic signaling (limited)	Possible CV benefit

This extensive receptor map explains why GLP-1 RAs have such a broad impact, as their activation can directly influence the function of these diverse organ systems.

Side Effects

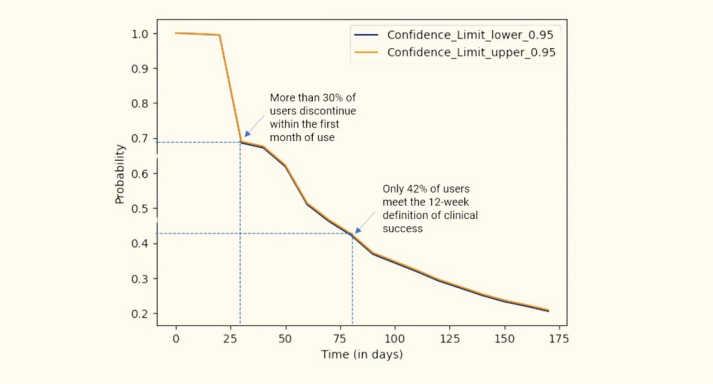
Gastrointestinal effects: Nausea affects 20-30% of patients during titration, vomiting 5-15%, diarrhea 20-30%, and constipation 5–15%. Most symptoms are transient and improve after 8–12 weeks. Real-world discontinuation rates reach 30% at 6 months and 36% at 12 months, primarily from GI intolerance. Severe cases like protracted gastroparesis or small-bowel obstruction are rare but drive most discontinuations.

Muscle-mass loss: About one-quarter to one-third of weight lost in STEP and SURMOUNT was fat-free mass. This can have adverse implications, because muscle helps with not only strength and endurance but also energy regulation and metabolism. Loss of muscle mass in older people can contribute to frailty, including an increased risk of falls.

Diabetic retinopathy: SUSTAIN-6 showed 3.0% retinopathy worsening with semaglutide vs 1.8% placebo, primarily in patients with pre-existing retinopathy. The mechanism is rapid glucose reduction (HbA1c dropped 1.9–2.5% at 16 weeks vs 0.9–1.3% placebo), causing transient osmotic and vascular changes.

Full time adherence remains poor

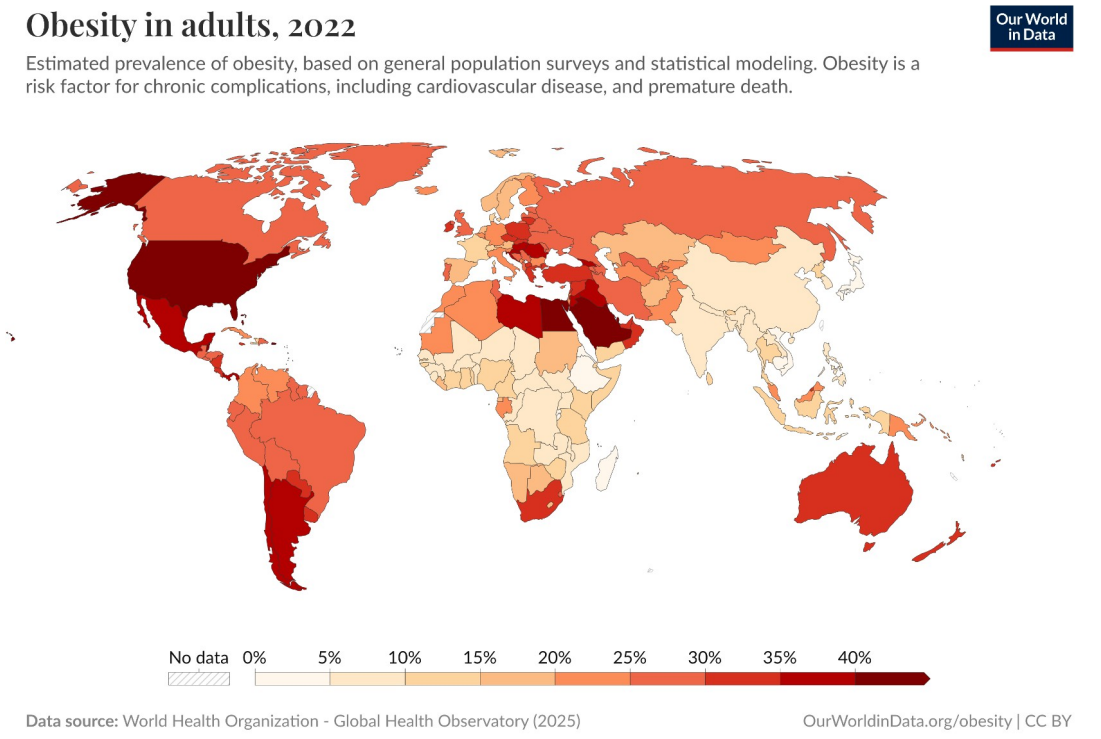
GLP-1 Drugs fall into the same category as blood pressure or cholesterol medicine; i.e they need to be taken forever or else the benefits tends to reverse if the drug is stopped. Current continuation rate remains very poor with a study reported that 50% of peope prescribed GLP1s for obesity discontinued them within six month and 80% within one year. Affordibility, GI related side effects and limited insurance coverage remains the primarly reasons for low adoption rates.



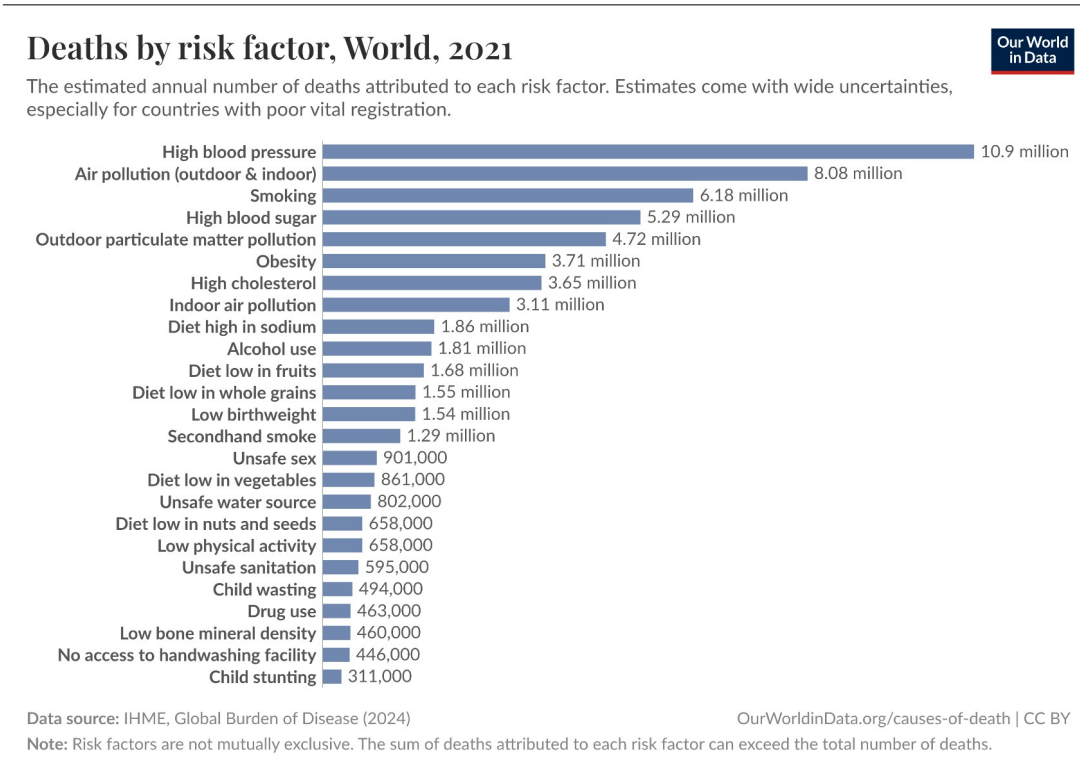
Source: Blue Cross Blue Shield

Obesity: A Global Burden

The global prevalence of obesity, defined as having a body mass index (BMI) equal to or greater than 30 kg/m2, is expected to rise from 14% of the world's population in 2020 to 25% by 2035, or 1.9 billion people. When the overweight population is included, i.e. those having a BMI equal to or greater than 25 kg/m2 but less than 30 kg/m2, prevalence more than doubles to 4 billion. This dramatic trend has a huge economic impact, estimated at $4 trillion in 2035 or 2.9% of global GDP, as a result of higher healthcare costs and lost economic productivity.



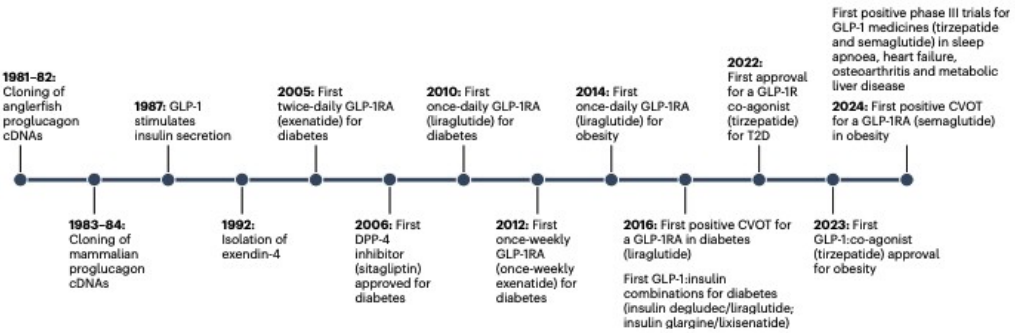
Obesity isn't a disease in itself: no one dies of obesity. However, there are a large number of obesity-related diseases, for example type 2 diabetes, chronic kidney disease and fatty liver disease. These develop through the slow build-up of what is usually irreversible damage to various systems in the body. It's estimated that around 5 million people died prematurely in 2019 as a result of obesity, which makes it one of the leading causes of death worldwide.



The arrival of the GLP-1 receptor agonists marked an inflection point for the obesity market, because for the first time pharmacological interventions delivered meaningful weight loss of 10-15%. Global obesity spending reached nearly $24bn in 2023, an over seven fold growth in value in just three years, driven by the advent of new agents, and from 2024 onwards the market is forecasted to accelerate rapidly, with a possible 24-27% CAGR to 2028, and a potential value of up to $131bn by 2028, according to the IQVIA Institute's Global Use of Medicines 2024 report. There is already evidence suggesting GLP-1s are lowering obesity rates in America. In September, the CDC published data that showed that the overall rate of adult obesity had fallen for the first time.

History of GLP-1s Drugs

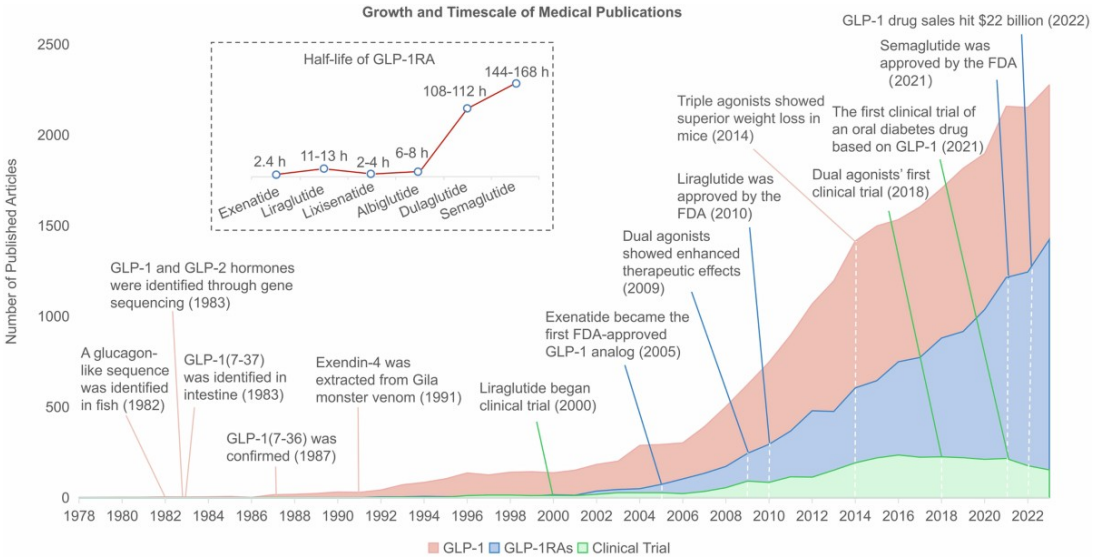
Understanding GLP-1s and their therapeutic applications began over a century ago with the incretin concept. Early in the 20th century, researchers observed that intestinal extracts could influence blood glucose levels, leading to the idea of a chemical stimulus from the gut affecting pancreatic secretions. In the 1960s, it was definitively proven that oral glucose intake stimulates insulin secretion more effectively than intravenous glucose, giving rise to the incretin hormone concept.



The first incretin hormone identified was Glucose-dependent Insulinotropic Polypeptide (GIP) in the 1970s. However, GIP did not consistently stimulate insulin secretion in patients with type 2 diabetes, which led researchers to believe another incretin might exist. The sequence of GLP-1 was identified in 1983, following the cloning of the proglucagon gene. In 1987, two research groups, one led by Svetlana Mojsov and Joel Habener and the other by Jens J. Holst, independently characterized the molecular nature of naturally occurring GLP-1 and demonstrated its insulin-stimulating effect at very low concentrations. These studies confirmed GLP-1 as an incretin hormone with potent insulinotropic activity, inhibition of glucagon secretion, and effects on appetite and gastric emptying.

Despite GLP-1's promising properties, its short half-life of 1-2 minutes in the circulation presented a significant challenge for therapeutic use, necessitating continuous intravenous infusion. A major breakthrough occurred with the serendipitous discovery of exendin-4 in the saliva of the Gila monster (Heloderma suspectum). Exendin-4 is a 39-amino acid peptide that shares about 50-53% sequence homology with human GLP-1, but is resistant to degradation by the enzyme dipeptidyl peptidase-4 (DPP-4), giving it a much

longer biological half-life. This resistance to DPP-4 cleavage made exendin-4 a highly valuable therapeutic target for activating the GLP-1 receptor.



source: nature

Synthetic exendin-4, marketed as Byetta, was approved for use in type 2 diabetes in 2005, initially administered twice daily. This marked the entry of GLP-1 receptor agonists (GLP-1RAs) into clinical evaluation. The development of GLP-1 based therapies has since focused on creating modified forms and analogues of GLP-1 that are also resistant to DPP-4 degradation and have longer durations of action. This has led to once-weekly administrations and oral preparations. Weekly dosing began with exenatide ER in 2012, followed by dulaglutide in 2014 and semaglutide in 2017; oral semaglutide arrived in 2019.

Currently Approved GLP-1 Drugs

There are six FDA-approved chronic weight-loss drugs: orlistat, phentermine–topiramate, naltrexone–bupropion, liraglutide 3.0 mg (Saxenda), semaglutide 2.4 mg (Wegovy), and tirzepatide (Zepbound). Two are GLP-1–based (liraglutide, semaglutide). Tirzepatide is a dual GIP/GLP-1 agonist with its own obesity label. Saxenda, Wegovy, and Zepbound are subcutaneous injections; the others are oral.

Approved GLP-1 Based Therapies

Drug	Target	Indication	Administration	Dose	Key trial	Year of approval
Exenatide	GLP-1R	T2D	Twice daily subcutaneously	10 µg twice daily	AMIGO	2005
Exenatide once weekly	GLP-1R	T2D	Once weekly	2 mg once weekly	EXSCEL	2012
Lixisenatide	GLP-1R	T2D	Once daily	20 µg daily	ELIXA	2016
Liraglutide	GLP-1R	T2D	Once daily	1.8 mg daily	LEADER	2010
		Obesity		3 mg daily	SCALE	2014
Dulaglutide	GLP-1R	T2D	Once weekly	4.5 mg weekly	REWIND	2014
Semaglutide	GLP-1R	T2D	Once weekly	1-2 mg weekly	SUSTAIN-6	2017
		Obesity		2.4 mg weekly	SELECT	2021
		T2D	Oral daily	14 mg daily	PIONEER-6 / SOUL	2019
Tirzepatide	GLP-1R / GIPR	T2D	Once weekly	15 mg weekly	SURPASS CVOT	2025
		Obesity			SURMOUNT MMO	2027

Exenatide (Byetta; exenatide ER/Bydureon)

Exenatide, the first GLP-1 RA (2005), is a synthetic exendin-4 that resists DPP-4. Byetta 5–10 µg BID lowered A1c with modest weight loss and inconvenient dosing. Bydureon 2 mg weekly improved adherence, but EXSCEL showed MACE noninferiority vs placebo. AstraZeneca discontinued Byetta and Bydureon BCise in the U.S. in Oct 2024.

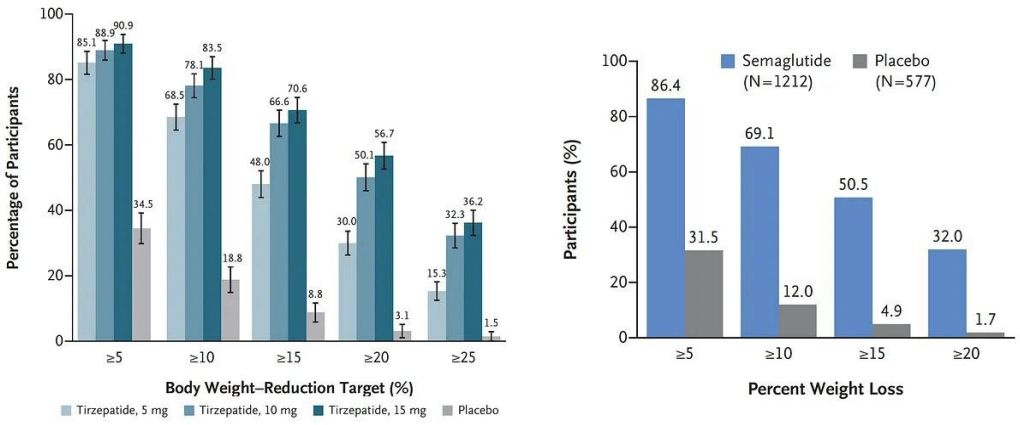
Liraglutide (Victoza; Saxenda)- Once-daily analog with proven CV benefit. LEADER: 3-point MACE HR 0.87 with significant reductions in CV and all-cause mortality. Saxenda 3.0 mg daily produces clinically meaningful weight loss (SCALE). Victoza generics entered 2024.

Dulaglutide (Trulicity)- Once-weekly 0.75–4.5 mg with broad primary-care reach. REWIND showed MACE reduction (HR 0.88) in a population with mostly multiple risk factors and ~31% established CVD; the U.S. label includes reduction of MACE in T2D with CVD or risk factors. Data support renal benefit signals (slower eGFR decline, fewer new macroalbuminuria events).

Semaglutide (Ozempic; Rybelsus; Wegovy) - Single-agent backbone across diabetes, obesity, and CV risk reduction. Ozempic weekly for T2D; Rybelsus oral for T2D; Wegovy 2.4 mg weekly for obesity and for reducing CV risk in adults with established CVD and overweight/obesity (FDA label March 2024, supported by SELECT: 20% MACE reduction, HR 0.80). SUSTAIN-6 showed MACE reduction (HR 0.74) but no significant mortality reduction; PIONEER-6 established CV safety for oral dosing. STEP-1 showed ~15% mean weight loss at 68 weeks.

Tirzepatide (Mounjaro; Zepbound) - Dual GIP/GLP-1 agonist setting the efficacy bar. In T2D, SURPASS trials beat semaglutide 1 mg on A1c and weight (e.g., SURPASS-2). In obesity, SURMOUNT-1 showed ~15–21% mean weight loss at 72 weeks and head-to-head data show greater loss than semaglutide in non-diabetic obesity. U.S. approvals: T2D (Mounjaro, 2022), obesity (Zepbound, 2023), and obstructive sleep apnea with obesity (Zepbound, 2024).

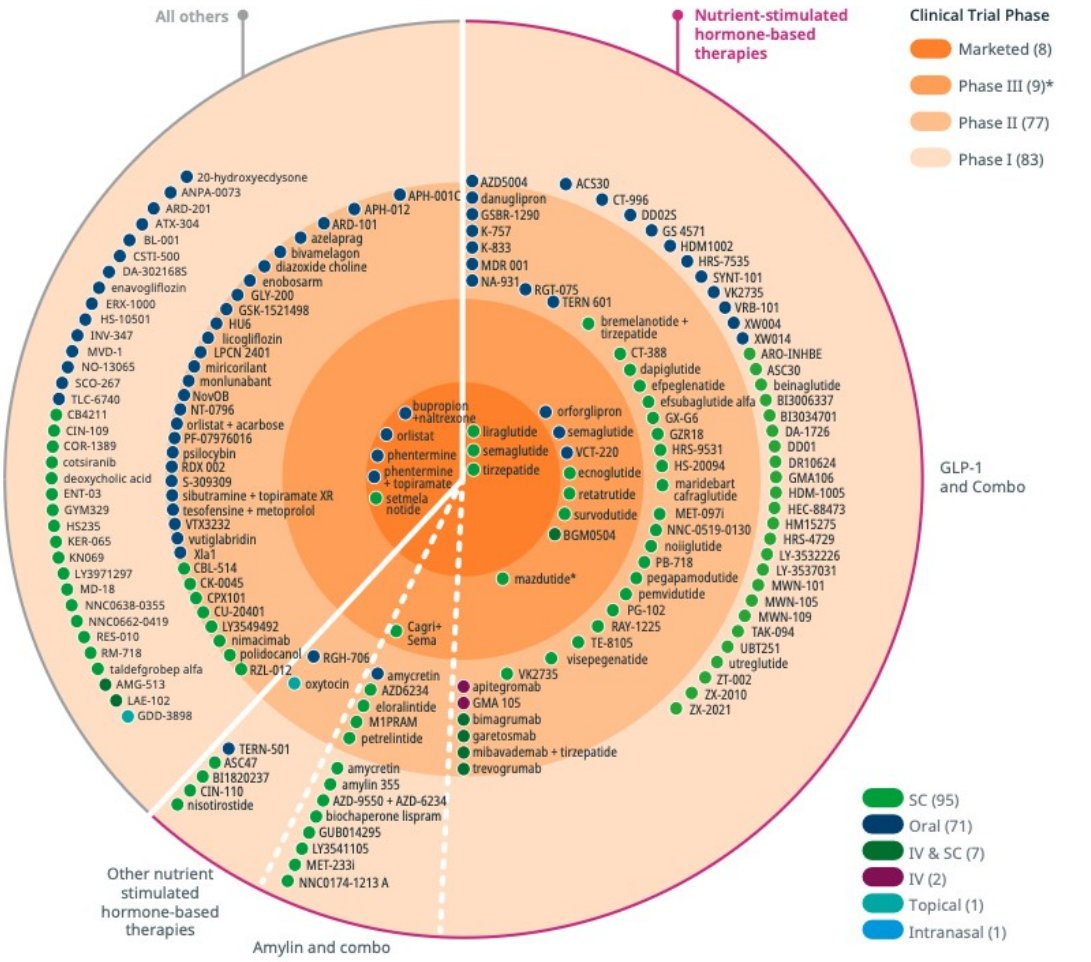
Body Weight Reduction Tirzepatide vs Semaglutide



Ongoing Innovations in GLP-1s Landscape

The race has intensified dramatically. The obesity pipeline from phase 1 to market now includes 173 drugs, with GLP-1 and combination therapies accounting for majority of trials. We are seeing innovations happening in the oral GLP-1s, dual GIP/GLP-1 and GLP-1/glucagon co-agonists, triple GIP/GLP-1/glucagon agonists, and amylin co-agonists.

Obesity pipeline by phase, target and route of administration



source: IQVIA

Oral Formulations

We expect oral GLP-1s to unlock a significant segment of the global obesity market, with an oral GLP-1 being 1) much easier to manufacture at scale compared to the current injectable GLP-1 drugs, 2) much simpler to distribute globally, given no need for cold-chain storage, 3) more attractive for needle-phobic patients who avoid the injectable GLP-1 drugs currently available, and 4) better suited to long-term maintenance therapy, given what we expect will be lower pricing (and lower costs) for orals compared to injectable GLP-1 drugs.

Oral GLP-1 Drugs Pipeline Overview (Selected Universe)

Drug	Company	Description	Current Phase	Mechanism
SMALL MOLECULES				
Orforglipron	Eli Lilly	First oral small molecule GLP-1 receptor agonist with no food/water restrictions; achieved 27.3 lbs weight loss in Phase 3	Phase 3	GLP-1 RA
Aleniglipron (GSBR-1290)	Structure Therapeutics	Small-molecule GLP-1 agonist; Phase 2b ACCESS studies fully enrolled, results by year-end 2025	Phase 2b	GLP-1 RA
AZD5004/ECC5004	AstraZeneca/ Eccogene	Oral small molecule showing 5.8% weight loss in 4 weeks; currently in global Phase 2b VISTA and SOLSTICE trials	Phase 2b	GLP-1 RA
CT-996	Roche/Genentech	Once-daily oral small molecule; 6.1% placebo-adjusted weight loss in 4 weeks; advancing to Phase 2	Phase 2	GLP-1RA (biased)
PEPTIDES				
Oral Semaglutide (Rybelsus)	Novo Nordisk	First and only FDA-approved oral GLP-1 (since 2019); 25mg version pending approval for weight management	Approved/Ph3	GLP-1 RA
HRS-953	Hengrui Pharma	Oral GLP-1 receptor agonist in late-stage development for obesity and type 2 diabetes	Phase 3	GLP-1 RA
DUAL AGONISTS				
Amycretin	Novo Nordisk	Dual GLP-1/amylin receptor agonist; 13.1% weight loss at 12 weeks; Phase 3 starts Q1 2026	Phase 3	GLP-1/Amylin
VK2735	Viking Therapeutics	Dual GLP-1/GIP agonist; oral Phase 2 fully enrolled, results expected H2 2025	Phase 2	GLP-1/GIP

Eli Lilly - Orforglipron (oral, small-molecule GLP-1 RA)

Orforglipron is an oral, non-peptide, small-molecule GLP-1 receptor agonist developed by Eli Lilly. The drug is taken once daily by mouth without food or water restrictions and has an elimination half-life of 29 to 49 hours. Eli Lilly reported phase 3 clinical data for its oral GLP-1 drug orforglipron (orfor) on 7 August 2025. That data was presented in the ATTAIN-1 trial, and measured weight loss in an obese patient population. While the ATTAIN-1 trial successfully met its predetermined weight loss endpoints versus placebo, the weight loss percentage realized in the highest dose fell modestly short of investor expectations, with average weight loss of 12.4% versus placebo at 0.9%. most common side effect were mild to moderate gastrointestinal related, treatment discontinuations due to adverse effects across the three doses were 5.1% , 7.7% and 10.3% respectively versus 2.6% for placebo.

Key Benefits	• the efficacy estimand showed an average weight reduction of 12.4% with the 36 mg dose, compared to 0.9% in the placebo group after 72 weeks • Reductions in non-HDL-C, triglycerides, systolic BP • hsCRP reduction by −47.7% at 36 mg dosage
Adverse events by dose (6 mg / 12 mg / 36 mg)	• Nausea: 28.9% / 35.9% / 33.7% • Constipation: 21.7% / 29.8% / 25.4% • Diarrhea: 21.0% / 22.8% / 23.1% • Vomiting: 13.0% / 21.4% / 24.0% • Dyspepsia: 13.0% / 16.2% / 14.1% • AE-related discontinuation: 5.1% / 7.7% / 10.3% • Overall discontinuation (any cause): 21.9% / 22.5% / 24.4% vs 29.9% placebo • No hepatic safety signal observed

Orforglipron's weight loss is disappointing and falls short of street expectations. Discontinuation rates however are better than expected. Orforg is likely still a viable option for needle-phobic obese patients without food effects and greater manufacturing scalability. Though weight loss data may be a harder sales pitch relative to generic semaglutide.

Novo Nordisk - Amycretin (2x50mg daily oral)

Amycretin is a novel, single-molecule co-agonist that targets two different receptors: the GLP-1 receptor and the amylin receptor. Amylin is another natural hormone that is co-secreted with insulin from the pancreas after meals and plays a role in glucose regulation and appetite control. By activating both of these pathways, Amycretin is designed to have a more potent and potentially complementary effect on weight loss compared to a GLP-1 agonist alone. Novo Nordisk recently published first-in-human data for Amycretin and is advancing both oral and subcutaneous formulations of Amycretin into Phase 3 development for weight management. Oral amycretin Phase 1 trial - The trial evaluated the single-ascending dose and multiple ascending doses for oral amycretin, up to 2x 50 mg, in 144 people with overweight or obesity, with a total treatment duration of up to 12 weeks.

key benefits	• 50 mg QD: −10.4%, 50mg twice daily: −13.1% • weight loss trajectory for participants on Amycretin was still trending downward at the 12-week conclusion of the study
Side Effects	• TEAEs in participants: 62% vs 46% with placebo • GI events ≈ 49% of AEs ; mild to moderate in severity • AE related discontinuation rate ~6%

After 12 weeks of treatment with amycretin up to 50 mg and up to 2x 50 mg, participants achieved a mean change in body weight of -10.4% and -13.1% respectively, compared to -1.2% with placebo. GI-related side effects were the most common, accounting for approximately 49% of all adverse events.

Roche (Carmot) - CT-996 (oral, small-molecule GLP-1 RA)

Roche, through its 2024 acquisition of Carmot Therapeutics, has entered the oral GLP-1 space with CT-996, an oral small-molecule GLP-1 receptor agonist.

Preliminary data from the Phase 1 trial of CT-996 in obese adults without type 2 diabetes have shown encouraging results. The trial demonstrated a mean weight loss of approximately 7.3% after only 4 weeks of treatment. For instance, in one cohort, the weight loss was -6.1% compared to a 1.2% reduction in the placebo group. The drug was well-tolerated, with adverse events primarily being mild to moderate gastrointestinal side effects. CT-996 is designed as a signal-biased GLP-1 receptor agonist, meaning it selectively activates the G protein pathway while minimizing β-arrestin recruitment, potentially leading to prolonged pharmacological activity and reduced adverse effects. Preclinical studies highlighted CT-996's potency and its ability to reduce weight and preferentially fat mass in obese cynomolgus monkeys. Roche plans to progress CT-996 into Phase 2 studies to further evaluate its efficacy and safety profile in type 2 diabetes and obesity.

Structure Therapeutics — Aleniglipron (GSBR-1290; oral small-molecule GLP-1 RA)

Phase/Trial	• Phase 2a in obesity (12 wks) + tablet PK/PD; Phase 2b ongoing
Efficacy (12 wks)	• placebo-adjusted mean WL ($p<0.0001$) • tablet study ~6.9%. 67% ≥6% WL; 33% ≥10% WL
Status	• Phase 2b ACCESS studies underway; topline by year-end 2025

There was a 5% discontinuation rate in the phase 2a obesity study and an 11% discontinuation rate in the capsule to tablet study. Adverse effects were mainly gastrointestinal but specific percentages are not available, instead being simply stated that GSBR-1290 has a generally favorable safety and tolerability profile.

Viking Therapeutics - VK2735 (oral, dual GLP-1/GIP agonist)

Viking Therapeutics is actively developing VK2735, a dual agonist of glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP) receptors, with both subcutaneous and oral formulations in its pipeline.

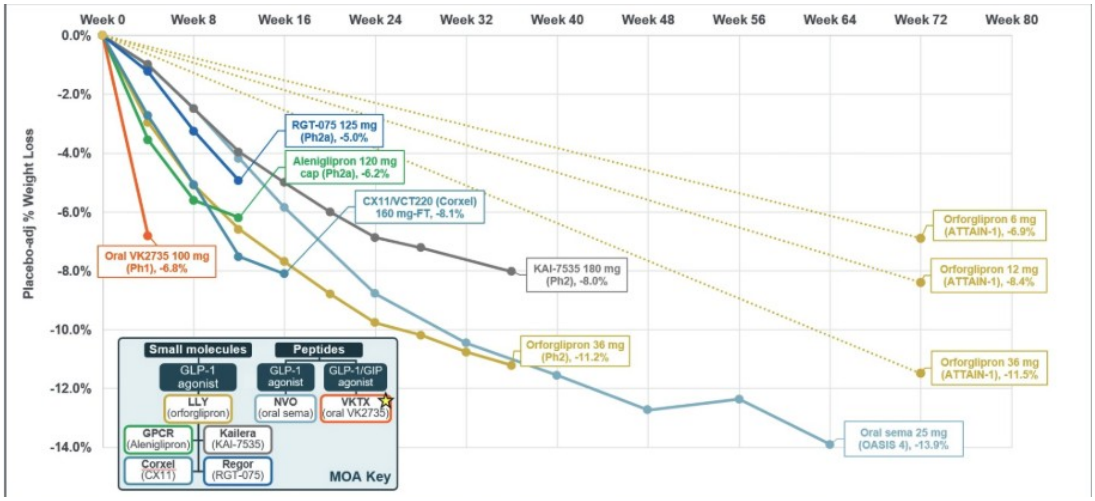
Viking's tablet formulation of VK2735 completed a 28-day multiple-ascending-dose Phase 1 trial in adults with obesity (BMI ≥ 30 kg/m²). Doses from 2.5 mg to 100 mg were titrated weekly. The 100 mg cohort achieved an 8.2% mean weight loss from baseline (-6.8% placebo-adjusted) in just four weeks, with the trajectory still trending downward at Day 28 and durability to Day 57 (-8.3% from baseline four weeks off-drug).

Average Body Weight Reduction	• Patients saw up to 8.2% mean weight reduction from baseline at the 100 mg dose after 28 days. • The placebo-adjusted mean weight loss was up to 6.8%.

Weight Loss Thresholds	• The drug was generally well-tolerated.
	• 90% of all treatment-emergent adverse events (TEAEs) were categorized as mild
	• The most common gastrointestinal events were:
	  • Mild Nausea: 32% of treated subjects (vs. 11% placebo)
	  • Vomiting: 4% of treated subjects
	  • Diarrhea: 7% of treated subjects (vs. 21% placebo)
	• No serious adverse events (SAEs) were reported during the trial
	• Discontinuations: low and similar to placebo (0-11% across cohorts; none in the 100 mg group)

VK2735 delivers the steepest early weight loss slope among oral agents (-8% in 4 weeks). If the curve remains linear, it could meet or exceed Amycretin's 12 week benchmark, while its mild GI profile and balanced discontinuation rates provide a tolerability edge over Orforglipron.

weight loss cross-trial comparison of oral incretins: placebo adjusted % Weight loss



source: piper sandler, company materials

Novel Mechanisms

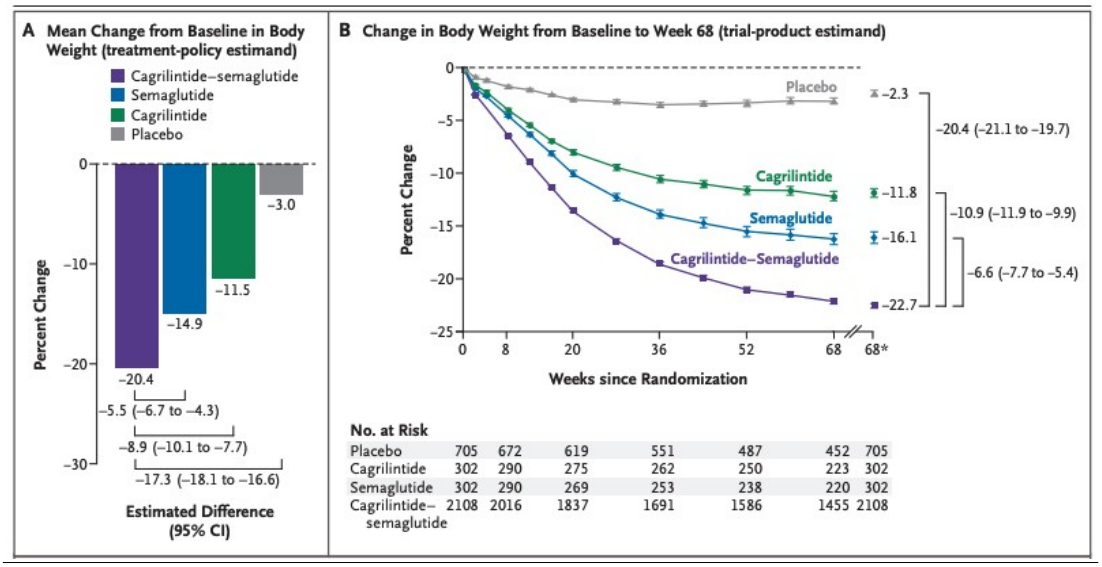
Novo Nordisk - CagriSema (once-weekly, subcutaneous)

CagriSema is a fixed-dose combination of a long-acting amylin analogue, cagrilintide 2.4 mg and semaglutide 2.4 mg. This combination is designed to provide synergistic effects on weight loss and glycemic control by targeting both amylin and GLP-1 receptors.

Key efficacy results	• -20.4 % mean Weight loss at 68 wks in REDEFINE-1 (placebo -3 %) • -12.6 % at 68 wks in REDEFINE-2 (patients with T2D) • 50.7 % of REDEFINE-1 participants moved from BMI ≥ 30 to < 30 kg/m²
Safety profile	• GI AEs in 79.6 % vs 39.9 % placebo (nausea 55 %, constipation 31 %, vomiting 26 %); mostly mild-to-moderate • Discontinuation for AEs: 6 % (REDEFINE-1) and 8.4 % (REDEFINE-2)

REDEFINE is a phase 3 clinical development program with once-weekly subcutaneous CagriSema in obesity. REDEFINE 1 and REDEFINE 2 have enrolled approximately 4,600 adults with overweight or obesity. REDEFINE 1 was a 68-week, double-blind, placebo- and active-controlled efficacy and safety phase 3 trial of once-weekly CagriSema, cagrilintide 2.4 mg and semaglutide 2.4 mg versus placebo in 3,417 adults with obesity or overweight with one or more comorbidities and without type 2 diabetes. REDEFINE 2 was a double-blind, randomized, placebo-controlled 68-week efficacy and safety phase 3 trial of once-weekly CagriSema versus placebo in 1,206 adults with type 2 diabetes and either obesity or overweight.

Change in Body Weight with Cagrilintide–Semaglutide as Compared with Semaglutide, Cagrilintide, and Placebo

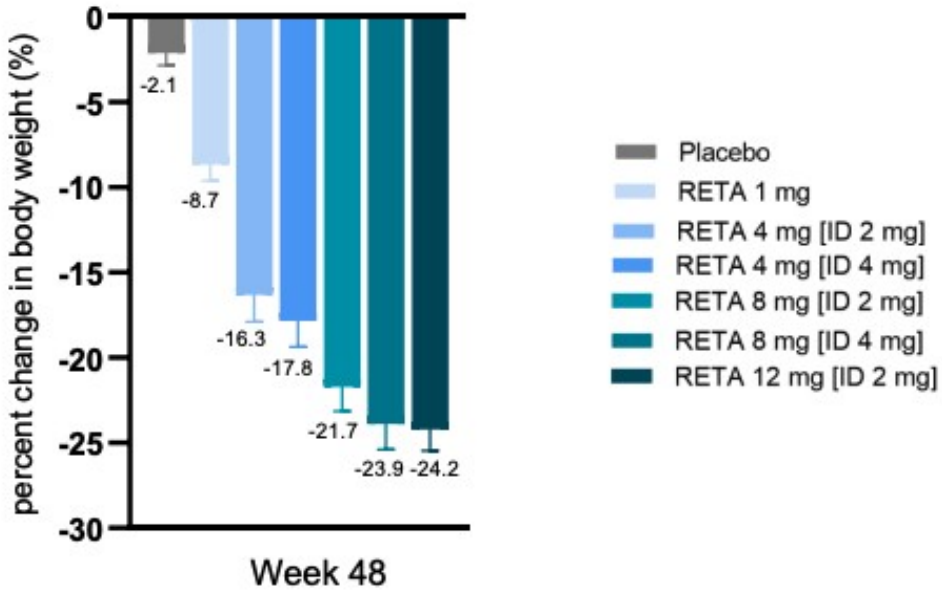


Eli lilly - Retatrutide (Once weekly, subcutaneous)

Retatrutide is a novel, once-weekly injectable triple agonist that targets the glucose-dependent insulinotropic polypeptide (GIP), glucagon-like peptide 1 (GLP-1), and glucagon receptors. Most weight loss occurred within the first 24 weeks, suggesting patients don't need to wait a year to see clear results. For weight reduction, 92% of participants on 4 mg, 100% on 8 mg, and 100% on 12 mg achieved a 5% or more reduction at 48 weeks.

Key efficacy results	• -24.2 % mean WL at 48 wks with 12 mg; -17.5 % at 24 wks • Best in class Weight loss for T2D • 100 % of participants on 8 mg or 12 mg lost ≥ 5 % of baseline weight at 48 wks; ≥ 90 % lost ≥ 10 %. • HbA1c ↓ 2.02% (T2D substudy); liver-fat ↓ 82 % in MASLD cohort
Safety profile	• TEAEs 73–94 % across doses vs 70 % placebo; almost all GI (nausea 14–60 %, diarrhea 12–38 %) • AE-related discontinuation 6–16 % (dose-dependent); serious AEs 4 % (same as placebo) • One acute pancreatitis; no thyroid-c-cell, gall-bladder or CV safety signal to date.

Percent change in weight at week 48



Amgen - AMG133 (420mg, once monthly, subcutaneous)

AMG 133 (maridebart cafraglutide) is a long-acting antibody–peptide conjugate that combines two mechanisms in a single molecule. The peptide portion is a potent GLP-1 receptor agonist; the antibody portion is an antagonist of the glucose-dependent insulinotropic polypeptide receptor (GIPR) that prolongs the molecule's half-life and may blunt the orexigenic actions of endogenous GIP. The drug is administered as a once-monthly subcutaneous injection.

Key Efficacy Results	• Achieved a mean body weight reduction of -19.9% at week 52 vs -2.6% placebo • -17% mean weight loss at 52 wks in obesity with T2D (vs -1.4% placebo) • At 52 weeks, 82.3% of participants lost ≥10% of their body weight, and 56.5% lost ≥15% • Demonstrated improvements in systolic blood pressure and glycemic control • HbA1c ↓ 2.2 percentage points in T2D cohort
Safety Profile	• GI AEs (nausea, vomiting, diarrhea, constipation) mostly mild-to-moderate • AE-related discontinuation: • Fixed high-dose groups: 12-27% • Dose-escalation groups: ≤7.8% • Most GI events occurred after first dose and resolved within days

Therapeutics Innovations in China

Drug	Company	Description	Current Phase	Mechanism
INJECTABLE/SUBCUTANEOUS				
Mazdutide	Innovent Biologics	World's first dual GCG/GLP-1 RA approved for weight loss; achieved 14% weight loss at 6mg dose in Ph3	Approved (CN)	GCG/GLP-1 dual
HRS-9531 (KAI-9531)	Hengrui Pharma	GLP-1/GIP dual agonist; achieved 22.8% weight loss in Ph2, 17.7% in Ph3; seeking China approval	Phase 3	GLP-1/GIP dual
BGM0504	BrightGene Bio	Dual GLP-1/GIP agonist; superior to semaglutide with up to 19.78% weight loss in Ph2	Phase 2	GLP-1/GIP dual
Visepegenatide (PB-119)	PegBio	Once-weekly GLP-1 RA without dose titration; completed successful Ph3 with good glycemic control	Phase 3	GLP-1 RA
Ecnoglutide (XW003)	Sciwind Bio	Long-acting cAMP-biased GLP-1 RA; achieved 13.2% weight loss at 2.4mg dose	Phase 3	GLP-1 RA
HRS-4729 (KAI-4729)	Hengrui Pharma	Triple agonist targeting GLP-1/GIP/glucagon receptors for obesity treatment	Phase 1	Triple agonist
UBT-251	United Lab/Novo	Triple agonist; 15.1% weight loss in Ph2; $1.8B deal with Novo Nordisk for global rights	Phase 2	GLP-1/GIP/Gcg
ORAL				
HRS-953	Hengrui Pharma	Oral GLP-1 RA in late-stage development for obesity and type 2 diabetes	Phase 3	GLP-1 RA
HRS-7535 (KAI-7535)	Hengrui Pharma	Oral incretin stimulating gut GLP-1; enhances insulin secretion and satiety	Phase 2	GLP-1 RA

Innovent Biologics - Mazdutide (injectable, dual GLP-1/GCG RA)

Mazdutide is an injectable, dual-receptor agonist that targets both the glucagon-like peptide-1 (GLP-1) and glucagon (GCG) receptors. Developed by Innovent Biologics, mazdutide is the first GLP-1 drug approved for weight loss in China. In a phase 3 randomized, double-blind, placebo-controlled trial (GLORY-1) involving 610 Chinese adults with overweight or obesity, mazdutide achieved an average weight reduction of 14.8% with the 6 mg dose.

Key Efficacy Results	• average weight reduction of 14.8% with the 6 mg dose, compared to 0.5% in the placebo group after 48 weeks
	• weight loss thresholds:
	  • 82.8% achieved ≥5% weight loss.
	  • 67.9% achieved ≥10% weight loss.
	  • 50.6% achieved ≥15% weight loss.

Safety profile	• Nausea: 50.5% vs 5.9%(placebo) • Diarrhea: 38.6% vs 6.3% (placebo) • Vomiting: 43.1% vs 2.9%(placebo) • discontinuations due to AEs: 0.5% vs 1% (placebo)

Hengrui Medicine - HRS9531 (injectable, dual GLP-1/GIP RA)

HRS9531 is a long-acting dual agonist for the glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP) receptors. Developed by Hengrui Pharma for China and licensed to Kailera Therapeutics for global development (as KAI-9531), it is administered as a once-weekly subcutaneous injection. In July 2025, the companies announced positive topline results from the pivotal Phase 3 trial (HRS9531-301) in Chinese adults with obesity or overweight, achieving an average weight reduction of up to 17.7%.

Key Efficacy Results	• Average weight reduction of 17.7% with the 6 mg dose, compared to approximately 1.4% in the placebo group after 48 weeks
	• Weight loss thresholds:
	  • 88.0% achieved ≥5% weight loss
	  • 44.4% achieved ≥20% weight loss

Safety Profile	• overall safety and tolerability profile was reported as favorable and consistent with the established GLP-1/GIP receptor agonist class • TEAEs were noted to be mild-to-moderate and gastrointestinal-related

BrightGene Bio - BGM0504 (injectable, dual GLP-1/GIP RA)

BGM0504 is an investigational dual agonist for the glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP) receptors, developed by BrightGene Bio and is administered as a once-weekly subcutaneous injection.

Key Efficacy Results	• Placebo-adjusted average weight reduction of 19.78% with the 15 mg dose after 24 weeks. The 10 mg dose achieved a 16.21% reduction. • reductions in cardiometabolic risk factors were observed, including waist circumference (up to -12.98 cm) and systolic blood pressure (up to -13.03 mmHg)
safety profile	• TEAEs: Primarily mild-to-moderate gastrointestinal events (nausea, vomiting) consistent with GLP-1/GIP class effects

Developments in Indian GLP-1 market

Sun Pharma - Utreglutide (GL0034) (injectable, GLP-1 RA)

Utreglutide is a novel, long-acting GLP-1 receptor agonist being developed by Sun Pharma. It is a once-weekly subcutaneous injection for the treatment of obesity and other metabolic diseases. Healthy, obese male participants (n=24; Age 18-40; BMI ≥ 28 kg/m²) were enrolled into a fixed-dose Cohort 1 (4 x 680 µg) or an increasing-dose Cohort 2 (680/900/1520/2000 µg) and assigned to treatment groups in a 3:1 ratio, receiving 4 weekly doses of either GL0034 or a placebo

Key Efficacy Results	• Average weight reduction of 4.6 kg (approximately 4.7% of body weight) after 4 weekly doses • reductions in lipid levels, including triglycerides, total cholesterol, and non-HDL cholesterol
Safety Profile	• treatment was well tolerated with no discontinuations from AEs • TEAEs included nausea, decreased appetite, and vomiting. One serious GI-related adverse event was reported, from which the patient recovered quickly with treatment.

Understanding Value Chain

Two companies dominate the GLP-1 landscape: Novo Nordisk and Eli Lilly. Novo Nordisk's portfolio includes liraglutide (Victoza® for diabetes, Saxenda® for obesity) and semaglutide (Ozempic® for diabetes, Wegovy® for obesity, and Rybelsus® as an oral tablet) – all GLP-1 analogues. Eli Lilly's offerings include dulaglutide (Trulicity®, a once-weekly GLP-1 RA for diabetes) and tirzepatide (Mounjaro® for diabetes and Zepbound® for obesity, a dual GIP/GLP-1 agonist).

Methods of GLP-1 production

Solid Phase Peptide Synthesis (SPPS) – Eli Lilly produces its peptide APIs, like tirzepatide, using hybrid chemical synthesis platform. This method first creates smaller peptide fragments through the more controlled Solid-Phase Peptide Synthesis (SPPS). These highly pure, pre-assembled fragments are then joined together in a solution, a process known as Liquid-Phase Peptide Synthesis (LPPS), often utilizing continuous manufacturing technology. The key advantage of this method is that peptide synthesis can be segregated and different partners can produce parts of the final peptide drug substance for better utilization of the supply chain. This method is chemically intensive, requiring significant volumes of solvents and reagents which makes it costly.

Fermentation based synthesis – Novo Nordisk's GLP-1 products are mainly produced through fermentation-based synthesis. It is relatively lower in cost compared to SPPS but difficult to outsource manufacturing. Novo Nordisk maintains tight in-house control over this entire, complex value chain.

Novo Nordisk leverages its deep expertise in fermentation-based API production, manufactures its GLP-1 APIs almost entirely in-house. In contrast, Eli Lilly utilizes a more outsourced manufacturing model for its chemically synthesized APIs. It relies on a network of CDMOs like WuXi AppTec & PolyPeptide Group among many other players. Eli lilly is building in house capacities as well as taking steps to diversify its Tirzepatide API supplies which are heavily dependent on China currently to European CDMOs & Divi's in India.

Ongoing capacity expansion for GLP-1 production across regions

Company	Location	Type	Details
Divi's Lab	AP/ Telangana, India	For advanced intermediates, incl. GLP-1	Long term supply agreement with a customer
Asymchem	Tianjin & Dunhua, China	GLP-1 production	Solid-phase syntheses capacity to reach 30KL by 2H25 (from 21KL as of YE24)
Granules	Switzerland	Acquisition of GLP-1 capacity	Liquid- and solid-phase peptide synthesis from early research to commercial phase
Neuland	India	GLP-1 capacity	To enhance the company's peptide synthesizer reactor capacity from 0.5KL to 6.37KL
WuXi Apptec	Changzhou & Taixing, China	GLP-1 production	Peptide capacity expansion will reach 100KL by 2025 (versus 41KL by YE24)
PolyPeptide	Malmö, Sweden	GLP-1 production	The additional production capacity will mainly serve to fulfill one of the large commercial agreements
BioDuro	Shanghai, China	Peptide synthesis scale-up laboratory	The kilogram-scale laboratory is equipped with automated solid-phase peptide synthesizers, cleavage systems and freeze-drying equipment, supporting peptide synthesis scale-up to 800 mmol
Eli Lilly	Wisconsin, US	GLP-1 manufacturing and other injectable medicines	Driven by increasing demand for GLP-1 receptor agonists; construction of the expanded facility is expected to begin next year
Asymchem	Tianjin & Dunhua, China	GLP-1 production	Solid-phase syntheses capacity exceeded 20KL by 3Q24 (from 14.25KL as of 1H24)
Eli Lilly	Limerick, Ireland	GLP-1 manufacturing/ Biologic drug product APIs	With a US1bnexpansiontobolsterbiologicdrugproductionandaseparateUS800mn investment to further grow its GLP-1 manufacturing
Corden Pharma	Europe	GLP-1 peptide manufacturing	Will build a new facility over next 3 years to bolster its ability to manufacture clinical and commercial GLP-1 peptides in Europe and the US
Novo Nordisk	Dublin, Ireland	Obesity, diabetes and rare disease drugs	Cancellation of plant expansion in Dublin
Eli Lilly	Indiana, US	Tirzepatide API Production	Increasing total investment in Indiana manufacturing site from $3.7 bn to $9 bn due to strong demand of Mounjaro and Zepbound

fill finish

Fill–Finish refers to the final step of the manufacturing process that entails sterilization and standardization of medical containers and addition of drugs to the containers before sealing them. Both LLY and NVO were capacity-constrained, which limited the volume of sellable GLP-1 doses and caused shortages and are undergoing massive capex plans to expand capacity, including fill and finish pen device capacity, which represents the most significant bottleneck in the supply chain.

Novo Nordisk is investing $4.1 billion in a new 1.4-million-square-foot facility in Clayton, North Carolina, dedicated to filling injection pens for Ozempic and Wegovy. This massive fill-finish plant—with completion phased between 2027 and 2029—will match the combined floor space of Novo's three existing U.S. sites. The company is also ramping in-house pen filling in Europe. Additionally, parent company Novo Holdings completed its $16.5 billion acquisition of CDMO Catalent in December 2024, immediately selling three strategic fill-finish sites (Anagni, Italy; Bloomington, Indiana; Brussels, Belgium) to Novo Nordisk for $11 billion. These sites will begin contributing to GLP-1 pen capacity from 2026 onward.

Eli Lilly has raised its Lebanon, Indiana investment to $9 billion (up from an initial $3.7 billion) to scale tirzepatide API production, with operations starting late 2026 and full ramp by 2028. In April 2024, Lilly acquired Nexus Pharmaceuticals' Pleasant Prairie, Wisconsin injectable facility and is investing an additional $3 billion to expand it, with production expected to begin by 2027. Lilly has also partnered with contract manufacturers—including Resilience in the U.S. and BSP Pharmaceuticals in Italy—to add pen-filling and finishing capacity for Mounjaro and Zepbound.

Key Players in GLP-1 Fill Finish

Company Name	positioning in Fill finish
Catalent (Novo Holdings)	Acquired by Novo Holdings for $16.5B (Dec 2024) with 3 fill-finish sites (Belgium, Indiana, Italy) sold to Novo Nordisk for $11B; Belgium facility targeting 100-150M vials/year, Indiana 70M vials/year, with $500M invested in GLP-1 capacity.
Lonza	CHF 500M investment in new Stein, Switzerland commercial fill-finish facility (operational 2026) providing integrated end-to-end solutions; adding high-containment ADC lines by 2027.
Thermo Fisher Scientific	Global leader in scientific services including pharma services. Patheon brand provides comprehensive drug development and manufacturing services.
Simtra BioPharma (formerly Baxter BPS)	$250M+ investment in Bloomington expanding with 150,000 sq ft facility housing 2 high-speed syringe lines, 1 vial line with 3 lyophilizers (GMP-ready 2026); doubling capacity specifically for GLP-1 drugs and ADCs.
BSP Pharmaceuticals	Italian CDMO specializing in sterile injectable manufacturing. Provides conjugation and fill-finish services for complex biologics including GLP-1s.
OneSource Specialty Pharma	specializing in drug-device combinations with deep expertise in cartridge and fill-finish; expanding cartridge capacity from 40 million to 200 million units and upgrading sterile injectable infrastructure via $100 million capex
Fujifilm Diosynth Biotechnologies	Global CDMO with extensive biologics manufacturing capabilities including fill-finish services. Part of Fujifilm's Life Sciences division.
Gland Pharma	fill-finish CDMO for peptides and aggressively scaling its integrated pen/cartridge capacity from ~40 million to 140 million units annually by 2026
Recipharm	Swedish CDMO with rapid expansion including new fill-finish facilities in India (1B units capacity) and Morocco

Onesource speciality

OneSource Specialty Pharma is an India-based CDMO spanning biologics, complex injectables, soft-gel capsules, and drug-device combos. Five USFDA-audited Bengaluru plants can output over 100 m sterile doses, 2.4 bn capsules, and assemble autoinjectors and pens. The company is investing $100 million to expand production fivefold (increasing cartridge filling from ~40 million to 200+ million doses annually) to support day-one generic launches post-2026. Management expects GLP-1 generics to contribute over 10% of revenue in the first full year of launch and is targeting a 15–20% share of the global generic GLP-1 market by FY2028.

gland pharma

Gland Pharma makes sterile injectables for global markets with USFDA and EMA cleared sites in India and Europe. It sells via B2B development and CDMO work and via own-file launches, and it added EU capacity through the Cenexi deal. Formats include vials, prefilled syringes, cartridges, bags, and lyophilized drugs across oncology, anti-infectives, ophthalmics, and hormones. It has entered GLP-1 with a liraglutide launch and has two GLP-1 supply contracts. Cartridge output is rising from 40 million units by adding 100 million more by CY2026, with new lines for pens and cartridges. It targets GLP-1 fill-finish in cartridges and pens for partners in regulated markets.

Autoinjectors & Drug Devices

Autoinjectors deliver pre-measured doses through spring-loaded needles that activate with a button press, eliminating manual injection steps. These devices reduce dosing errors and improve compliance for weekly GLP-1 therapy. With the patent expiry of semaglutide in emerging markets; GLP-1 volumes will see substantial growth which will drive massive demand for pen and autoinjectors.

Key Players in GLP-1 Autoinjectors

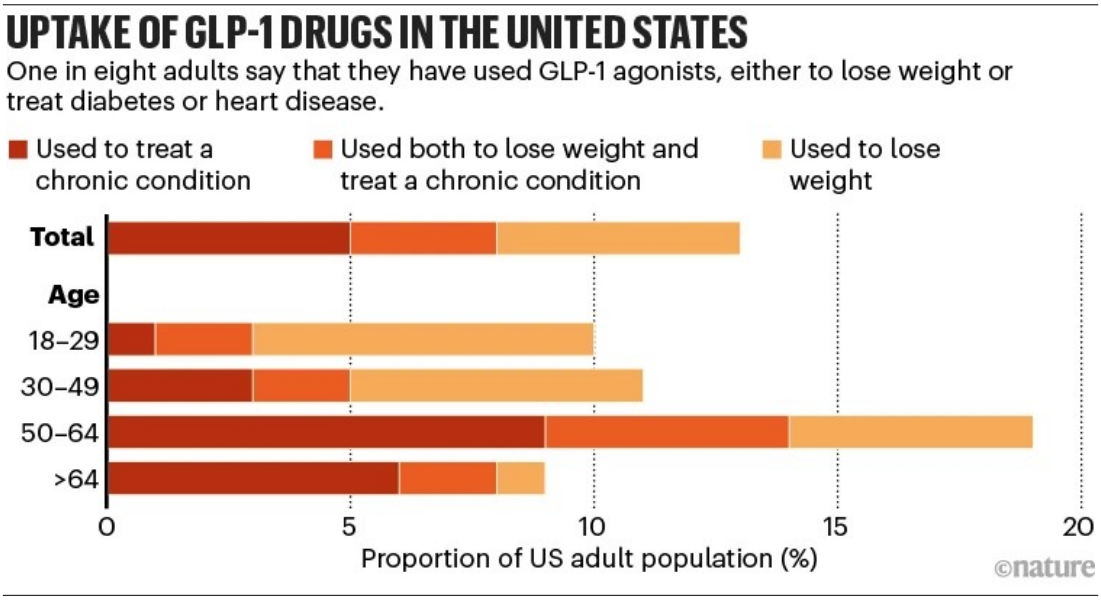
company	positioning
shaily engineering	Leading manufacturer of pen injectors for GLP-1 therapies; capacity expanding from 40 to 100 million pens by FY28, and 34-35 million pen commercial supply (including semaglutide) targeted in H1 CY26
Ypsomed	Signed long-term Novo Nordisk deal for YpsoMate 1 mL autoinjectors (deliveries from 2025); Changzhou facility opened in June 2025 with capacity for up to 100 million devices annually.
Stevanato Group	One-stop provider: glass cartridges + pen injectors + autoinjectors; Aidaptus® auto-injector w/Owen Mumford; Alina® multi-use pen in-house; pre-installed manufacturing capacity for both
BD (Becton Dickinson)	Major pen injector and prefillable syringe supplier; strong autoinjector portfolio (BD Physioject, BD Libertas); key supplier for insulin/GLP-1 delivery systems.

shaily engineering

Shaily Engineering Plastics is a leading Indian manufacturer of value-added, precision-molded plastic products, supplying global majors across healthcare, consumer, and industrial sectors, with over 75% of FY25 revenues from exports and long-standing relationships with clients like Sanofi, Aurobindo, IKEA, and GE Appliances. Shaily has invested heavily in its healthcare vertical, now comprising advanced drug delivery and injectable device platforms. The company is rapidly scaling as a contract manufacturer for GLP-1 therapies, including commercial launches of pen injectors for semaglutide and upcoming supplies for tirzepatide and dulaglutide devices, supported by seven pen platforms developed in-house and through its UK subsidiary. Shaily has signed eight contracts for pen and auto-injector platforms—particularly for semaglutide and related drugs— with first commercial supplies in FY26, and is expanding pen manufacturing capacity from ~40 million to 80–90 million pens a year, targeting both generic and innovator pharma in regulated and growth markets such as Canada and Brazil.

second order effects

Global prescriptions of GLP-1 agonist therapies grew at a remarkable rate of roughly 38 percent annually between 2022 and 2024 and sales are forecast to reach $100 billion by 2030. Because GLP-1s change eating behaviour, reduce caloric intake and reshape users' bodies and self-perceptions, GLP-1s have far-reaching second-order effects across industries. Today, as many as one in eight adults in the U.S. has already taken GLP-1 drugs. This growth trajectory is set to continue – driven by media coverage, celebrity endorsements and social media. It is creating a ripple effect among a variety of industries, including beauty & aesthetics, restaurants, packaged snacks, sugary drinks, alcohol, grocery retail, apparel sizing, fitness chains among many others.

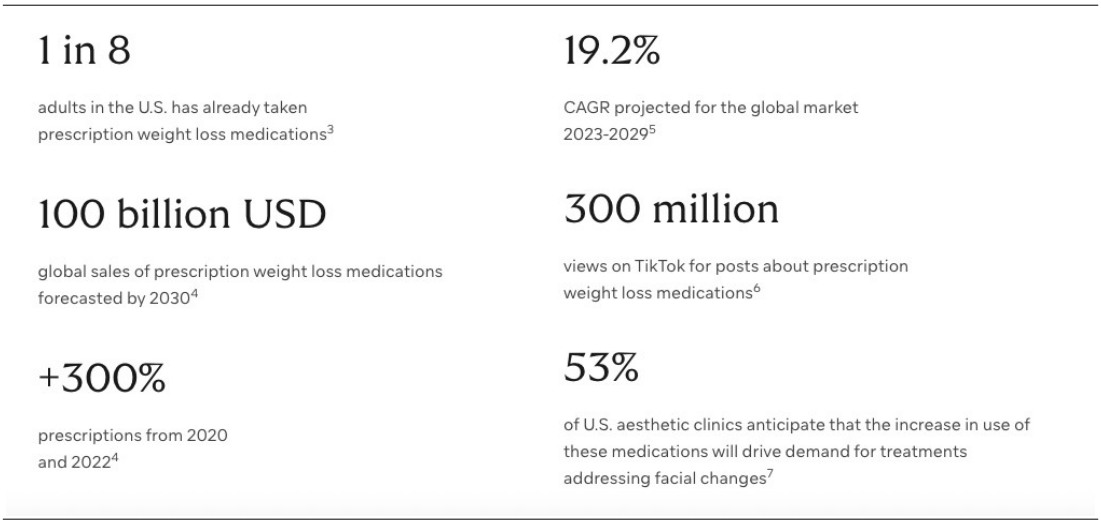


Category	Second Order Effect
Food & Beverage Consumption	Reduction in overall caloric intake and grocery spending; decline in demand for high-calorie foods, soft drinks, juice and alcohol; greater interest in nutrient-dense, smaller portions and functional foods
High-Protein & Functional Foods	Shift towards high-protein bars, shakes and nutritional supplements; growth of meal replacement drinks, macronutrient blends, and GLP-1 nutrition products
Frozen Foods & Grocery	GLP-1 users purchase more frozen fruits and vegetables and seek high-protein frozen meals; interest in portion-controlled and healthy frozen foods

Apparel & Fashion	Shifts in clothing sizes: more demand for smaller sizes, activewear and athleisure; potential decline in plus-size and big & tall lines; retailers must adjust inventory and size curves
Fitness & Exercise	Rising demand for resistance training, gym memberships, and digital fitness programs tailored for GLP-1 users; gyms and wellness platforms offering programs to prevent muscle loss
Aesthetics & Skin tightening	Rapid weight loss causes skin laxity (“Ozempic face”), loss of facial volume and sagging skin; increased demand for fillers, Botox, radiofrequency microneedling, high-intensity focused ultrasound (HIFU), fractional lasers, body contouring and hair restoration treatments
Sleep Apnea & Medical Devices	Although GLP-1-induced weight loss reduces apnea severity, many patients still require CPAP machines; GLP-1 users are more likely to adhere to therapy; obesity is not the sole cause of sleep apnea
Bariatric Surgery & MedTech	GLP-1 drugs reduce the need for bariatric surgery, leading to lower procedure volumes and impacting companies providing surgical instruments and hospitals
Mental Health & Psychosocial Effects	GLP-1 drugs quiet “food noise” and improve self-efficacy but may trigger mood changes, depression, anxiety, or altered pleasure responses; weight loss can exacerbate body image concerns and disordered eating; half of users discontinue due to side effects
Travel & Leisure	High cost of GLP-1 drugs may reduce discretionary spending on travel and entertainment initially, but improved self-confidence could later increase demand for active vacations and wellness tourism
Dialysis & Renal Care	Improved glycemic control from GLP-1 slows progression to end-stage renal disease, moderating dialysis patient growth
Retail Pharmacy & Tele-health	Spike in direct-to-consumer demand for GLP-1 prescriptions and refill logistics

Aesthetic Industry

GLP-1s are changing patients' appearances and creating new demand for aesthetic products and services. Rapid weight reduction induced by GLP-1 drugs often leads to aesthetic challenges, including facial volume loss, skin laxity, body contour irregularities and an overall appearance of premature aging which is driving the growth for Botox, fillers & cosmetic surgeries such as abdominoplasty, breast reduction/augmentation and gluteal lifts. Aesthetic providers report that most GLP-1 patients are seeking treatment for two or more skin concerns, including skin laxity and skin quality. McKinsey found that nearly two-thirds receiving an aesthetic procedure following GLP-1 use are new to the market, meaning the total addressable market (TAM) for these services is expanding significantly.



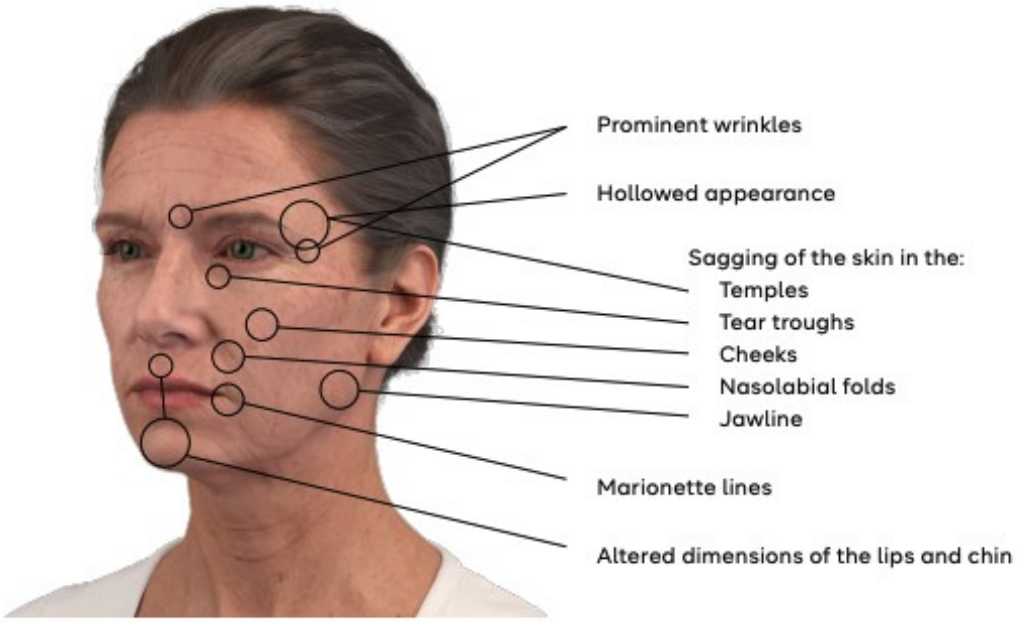
source: Galderma

ozempic face

One of the most striking effects of rapid weight loss due to GLP-1 agonists like Semaglutide is the significant reduction in facial fat, particularly in the subcutaneous layers, commonly referred to as "Semaglutide face." The face loses its natural volume, leading to a hollow or gaunt appearance, especially around the midface, temples, and periorbital areas. This can create an imbalance in facial harmony, as the fat pads that normally provide youthful contour support begin to diminish. The loss of these fat pads exacerbates sagging skin, particularly along the jawline and around the mouth, leading to jowling and a less-defined facial structure. This volume loss often results in patients appearing

older than their biological age, creating a psychological impact that can be disconcerting, especially for those who have worked hard to achieve their weight loss goals.

How GLP1s Affect the Face



Potential treatments for Ozempic face include:

Dermal fillers: A minimally invasive treatment are dermal fillers, which are injected underneath the skin to fill the volume loss of facial wrinkles and lines.

RF microneedling: RF microneedling utilizes a series of tiny needles and RF waves to create small damages in the skin to stimulate the growth of new collagen and elastin resulting in rejuvenated skin. RF microneedling has also been shown to tighten the skin and reduce skin laxity, which is a major characteristic of “Ozempic face”.

Energy-Based Devices: A popular noninvasive treatment modality includes lasers and energy-based devices proven to have skin-tightening effects. This treatment can revive the skin’s barrier by stimulating collagen and elastin production resulting in significant neck and facial tightness. Examples include fully ablative laser resurfacing devices, parallel beam ultrasound technology, and fractional energy devices.

Company spotlight

AbbVie Inc

As the parent company of Allergan Aesthetics, AbbVie is a dominant force in the facial injectable market. Its portfolio includes the JUVÉDERM® collection, the top-selling line of HA fillers in the U.S., with products like VOLUMA® XC specifically designed to correct age-related volume loss in the cheeks and augment the chin. The company also offers HArmonyCa™, an innovative hybrid filler that combines HA for an immediate lift with calcium hydroxylapatite (CaHA) to stimulate long-term collagen production.

Management's commentary on GLP-1s & impact on aesthetics business:

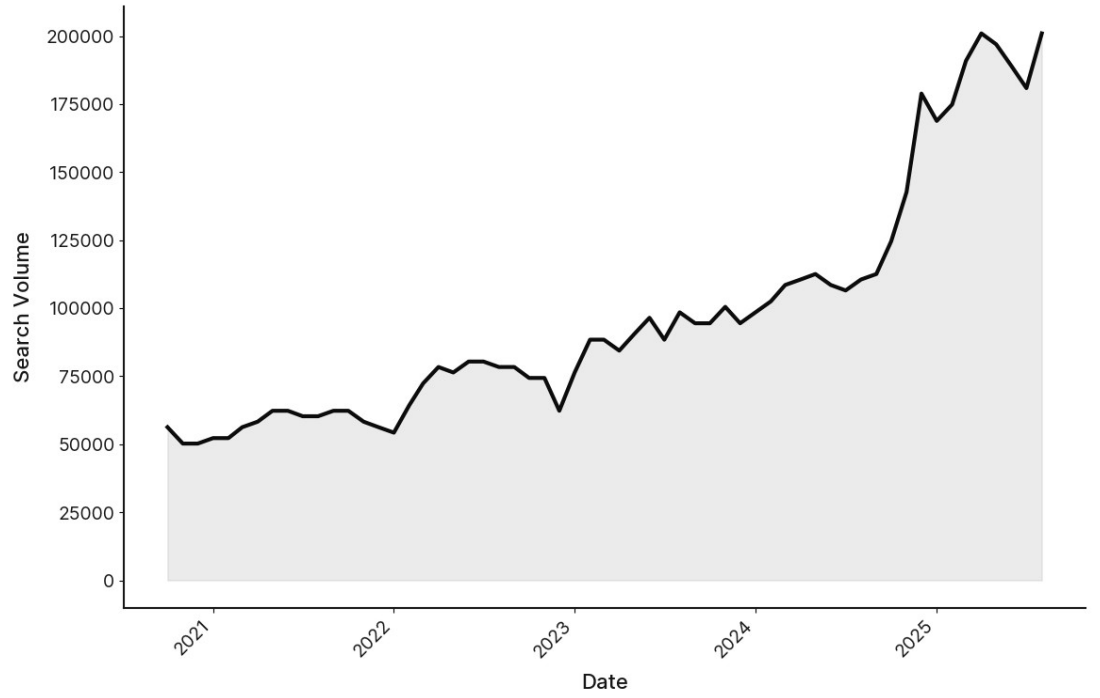
I'll answer your first question around the obesity market and the aesthetics opportunity. And you're exactly right, it continues to be both a headwind and a tailwind, a headwind in terms of share of wallet as these consumers are making decisions on what they're going to spend for. We see that more for the higher-priced products like fillers, and then also a tailwind as this gets a new group of consumers or patients interested in aesthetics, and many of our aesthetic providers are administering these products. And so they see this as an opportunity for lead generation and bringing new patients into the category.

So we do see it as both a tailwind -- a headwind in the short term, but a tailwind in the long term. And the question is not if injectables work, we know that these products work well in these patients. It's really about how we can partner with our customers to build it and integrate it into their treatment practice. And that's what we're doing with our customers now and helping them position Botox and Juvederm and our product line for these new patients that are entering their practice.

Galderma

A leading pure-play dermatology company, Galderma offers a comprehensive portfolio of injectables. This includes the Restylane® family of HA fillers, which address everything from under-eye hollows to facial wrinkles, and Sculptra®, a premier biostimulator. Sculptra is made from poly-L-lactic acid (PLLA), which works deep within the dermis to help gradually replace lost collagen, restoring facial volume and improving skin structure over time.

Growing Search Trend for Sculptra



Galderma ran a U.S. phase-IV trial on GLP-1-linked facial volume loss. Three-month interim data show better mid-face shape and contour, fewer cheek lines, higher skin radiance and thickness from Sculptra, and improved hydration from Restylane, leaving 85-89% of patients feeling fresher and more balanced.

source: company

Body Contouring & Skin Tightening

Skin laxity is another major aesthetic concern for patients who experience rapid weight loss with Semaglutide. The skin's ability to retract and conform to a new body shape is limited by factors such as age, genetics, and the rate of weight loss. When weight is lost quickly, the skin does not have time to adjust, leading to sagging areas that are particularly noticeable in the face, neck, arms, abdomen, and thighs. The loss of the fat that once supported the skin exacerbates this issue, resulting in folds and wrinkles that can detract from the overall benefits of weight reduction. In the face, skin laxity often manifests as drooping cheeks, deepened nasolabial folds, and neck sagging, which further accentuate the appearance of aging. Increasing use of weight loss drugs may lead to increased demand for body contouring and skin tightening procedures.

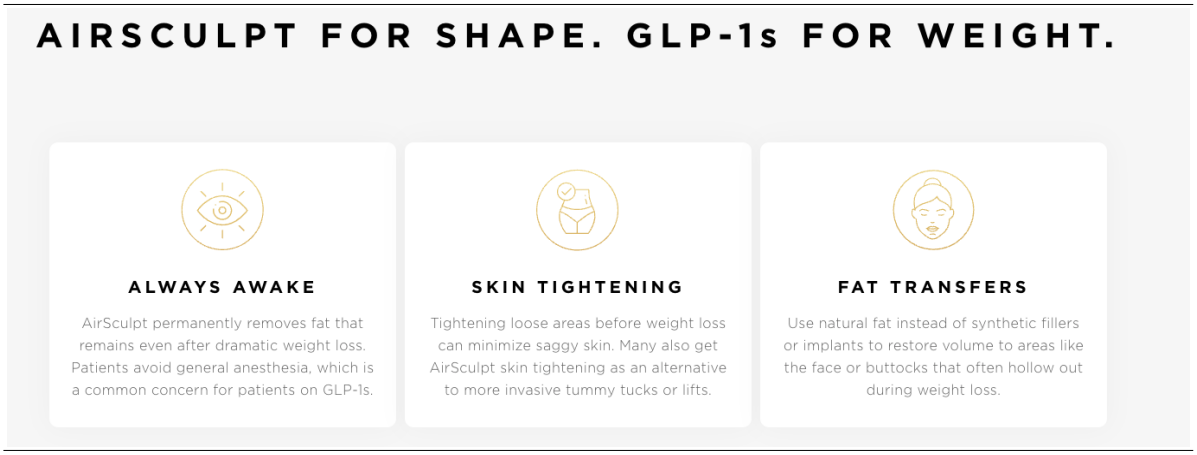
AirSculpt® Technologies, Inc.

As a specialist in this category, AirSculpt® offers a proprietary, minimally invasive body contouring procedure for permanent fat removal that is an alternative to traditional liposuction. The company also offers AirSculpt® Smooth, an FDA-cleared treatment specifically for removing cellulite dimples. To address skin laxity, its AirSculpt®+ and AirTite™ procedures utilize Renuvion® technology, which combines radiofrequency (RF) energy and helium plasma to contract collagen and tighten skin.

Management on opportunities in skin tightening services from GLP-1 drugs:

An example of this is skin tightening services, which we plan to pilot in the second quarter. This way, we tap into the complementary impact of GLP-1, which has led to an increased demand for skin tightening. We believe this can be a sizable opportunity for us to expand our customer reach and generate incremental revenues with the procedure that we already do.

So today, we offer skin tightening in all of our locations as a complement as an add-on to our fat removal services. What we're planning to do, what we are looking to pilot is doing that as a stand-alone service in our centers. This is, in many ways, our efforts to capitalize on trends we are seeing with the consumers. We continue to see skin tightening is a pretty big area of interest for consumers. Some of that we see as an outcome from GLP-1s, where customers who pin on GLP-1s tend to have -- many of them tend to have lose skin and they're looking for solutions for that.



Apyx Medical

An advanced energy technology company that manufactures the proprietary Renuvion® system (also known as J-Plasma®). This technology uses a unique combination of radiofrequency (RF) energy and helium plasma to provide controlled heat to contract soft tissue. Renuvion is the only device that is FDA-cleared for contracting subcutaneous tissue and for use after liposuction to improve the appearance of loose skin, making it a key technology for body contouring and skin tightening.

Apyx's commentary on GLP1s:

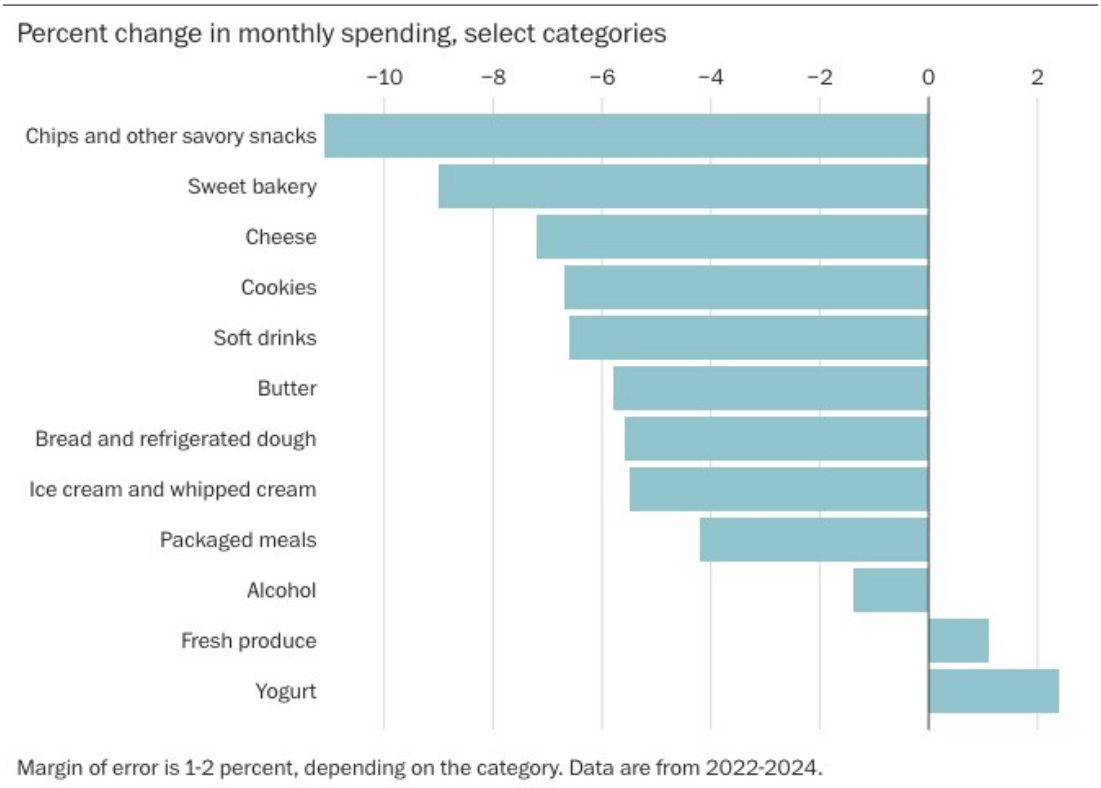
We believe the increased use of GLP-1s had an initial negative impact on the revenue for plastic and cosmetic surgeons and created uncertainty in the aesthetic space. However, we believe, that the use of these drugs will have a ripple effect which will drive people towards plastic surgery and may provide a tailwind for sales of our Renuvion products.

Rapid weight loss caused by these drugs can contribute to loose skin. To address this, the cosmetic surgery market focuses on body contouring. Body contouring is a customizable treatment for patients to target specific fat deposits, engage in the transfer of fat, and treatments to address loose or lax skin. Renuvion is the only FDA approved device for the treatment of this issue post liposuction. Additionally, Renuvion may be used to treat skin laxity without the use of liposuction, potentially increasing the total available market for our products.

Shifting Food & Beverage Consumption Patterns

GLP-1 users spend significantly less on food, with a 31% reduction in grocery spending and even sharper pullbacks on takeout (61% of users spending less) and restaurant dining (63% of users spending less). Weight loss drug users are cutting back on sugary drinks and alcohol, and incorporating more fruits and vegetables into their diets. Research from Ohio State University, assuming moderate adoption rates among overweight and obese adults, estimates a potential 3% reduction in total caloric demand in the U.S. This translates to a staggering 20 billion fewer calories consumed per day and a reduction in weekly food spending of approximately $1.2 billion.

Households with GLP-1 Users are buying fewer snacks



Source: numerator

Many nutrition players are already capitalizing on this shift by innovating products that complement GLP-1 treatments, such as probiotics to support natural GLP-1 production, supplements that promote lean muscle maintenance, and high-quality, nutrient-dense meal replacements or kits that complement the appetite-suppressing effects of GLP-1s, as well as personalized nutrition

services. Companies like Pepsi have started to reformulate products, such as adding protein and whole grains to match shifting consumer tastes.

Pepsico's commentary on Impact of GLP-1s:

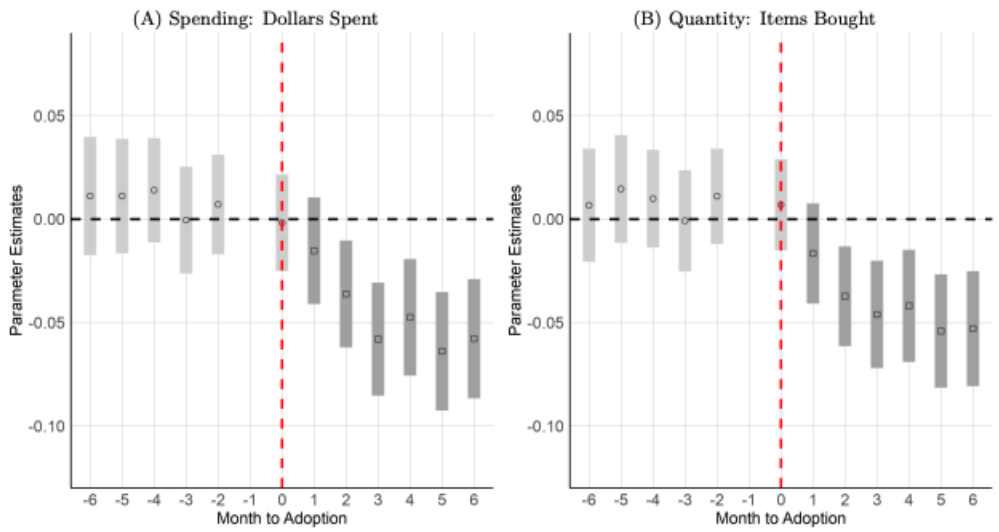
"we've been transforming the portfolio, and we'll continue to give the consumer offerings that help them in any sort of dietary preferences that they have. So whether they're in a GLP situation or they are not, we will keep providing them.

What we're seeing with GLP consumers is, again, they're driving more consumption on protein space, on fiber, on hydration. I think we're well positioned for both fiber and hydration solutions, and we will increase the availability of products in those 2 areas. I think we're a bit less well positioned in protein, and that's where we're innovating. Our teams are working on innovation for -- against protein, both on the beverage and the food business, and you will see some late this year, early next year. And that's the space that I think we can capture more incremental value.

Now the other thing we're seeing in GLP consumers is that they're keeping our brands in their repertoire, probably in a smaller portion. So they're going for -- and that's the way they are actually eating across most of their choices. They're eating less quantity. So our offerings in small portions and whether it's in multipack or some other options that we provide keeps our brands in their repertoire, and it's still relevant."

PepsiCo, Inc., Q1 2025 Earnings Call

Change in Grocery Spending and Quantity Post GLP-1 Adoption



Cornell SC Johnson College of Business

Nestle launched products targetting GLP-1 patients

Nestlé recently launched its first major U.S. brand in nearly three decades called Vital Pursuit for consumers taking GLP-1 medications and other individuals focusing on weight management.

Walmart is witnessing mid-teens growth in health & wellness segment largely due to GLP-1 sales.

> "Grocery remains a standout category with mid-single-digit growth, and we saw mid-teens growth in health and wellness due largely to GLP 1 sales, which contributed about 0.1 to the segment comp, consistent with prior quarters. "

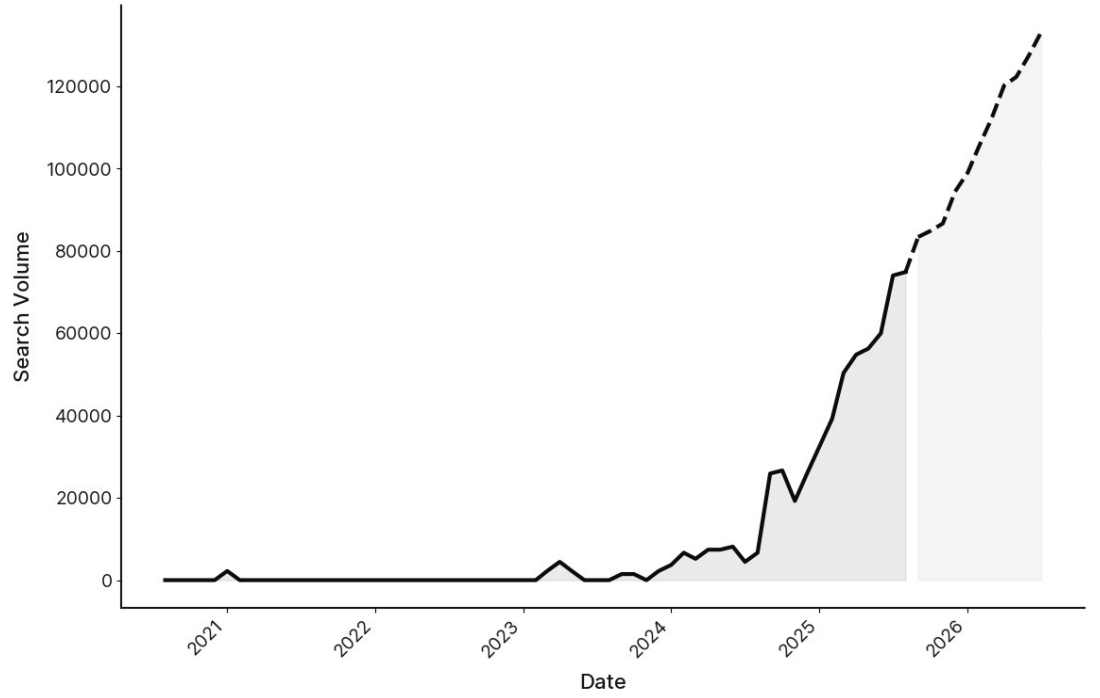
Companies are launching GLP-1 targetted calorie dense foods

GLP-1

A balanced diet is essential to your weight management journey while using GLP-1 medications like Ozempic®, Mounjaro®, or Wegovy®. Our dietitian-curated collection includes pre-portioned, calorie-conscious meals that are delicious, high in fiber, low in saturated fat, free of cholesterol, and have no added sugars.

Supplements & Protiens

Search Trend for GLP-1 Supplements



company spotlight

BellRing Brands : Premier Protein RTD shakes (30 g protein, 160 calories) already dominate the U.S. ready-to-drink segment. The company launched Premier Protein Mini-Meal shakes (150 calories, 30g protein) specifically targeting GLP-1 users, with CEO Darcy Davenport noting in the 4Q-23 call that "GLP-1 users often become heavy consumers of our shakes," using them as meal replacements as they need more protein to mitigate muscle loss and certain other side effects.

"GLP-1s. Yes. So we track it very closely, as you might expect. And I would say the headlines tracking much, so the penetration of GLP-1s based on our research is much faster and bigger than what I think the original base case that Morgan Stanley put together. And what -- I would say the one change, it benefits -- definitely benefits our products, specifically both ready-to-mix and ready-to-drink and ready-to-mix, but a little bit more on the ready-to-drink side."

BellRing Brands, Inc., Q1 2025 Earnings Call

Simply Good Foods Company

The Simply Good Foods Company develops, markets, and sells nutritional snacks and RTD drinks under Quest, Atkins, and OWYN. Products include protein bars, RTD shakes, salty snacks, and confectionery. Quest is expanding high-protein formats (Overload bars, 45g Protein Milkshakes); Atkins is adding Strong 30g RTD shakes with new packaging, site, and ads; OWYN grows plant-based RTD shakes.

Management's commentary on Impact of GLP-1s:

"We -- as you look at the demand for weight wellness solutions, is higher than ever, 60% of people actively looking to lose or maintain weight. The cultural conversation on weight has changed and increased very much driven by these new GLP-1 drugs. And our research shows that Atkins is a trusted brand in this space, help consumers on their weight loss journey. And particularly, we see GLP-1 drugs and consumers on those drugs as representing a significant opportunity, whether it be helping them when they're on the drug or helping them as an off-ramp."

The Simply Good Foods Company, Q2 2025 Earnings Call

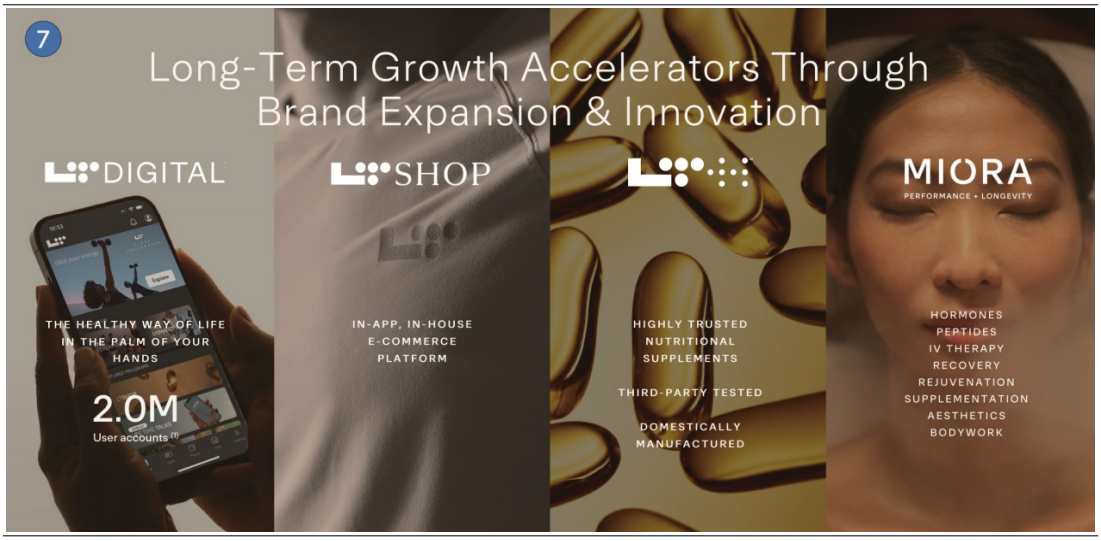
Gyms & Fitness

Rapid weight loss on GLP-1s strips fat but can also cost five to seven per cent of lean mass in the first six months, potentially lowering metabolic rate and increasing injury risk. Prescribers therefore emphasize resistance training and higher protein intake to preserve muscle, bone density and resting metabolic rate. Based on PwC's GLP-1 Trends & Impact Survey, 57% exercised the same amount or more while on medication with strength training being the most-added activity among those who increased their fitness spending. Gym operators are trying to incoporate wellness plans & personalised training programs for GLP-1 users.

Company spotlight

Life Time Group Holdings

Life Time operates 180+ athletic country clubs across the US and Canada, providing integrated health and wellness ecosystems including fitness facilities, spa services, personal training, nutrition programs, childcare, and dining venues in resort-like environments. The company has launched MIORA, an in-club longevity and performance clinic that provides members with access to medical guidance, personal trainers, and services including GLP-1 prescriptions. MIORA services include consultations, blood draws, Metabolic Code assessments, bioidentical hormones, and IV therapies tailored for metabolic challenges. Company also runs "GLP-1 & Strength" educational workshops along with memberships.

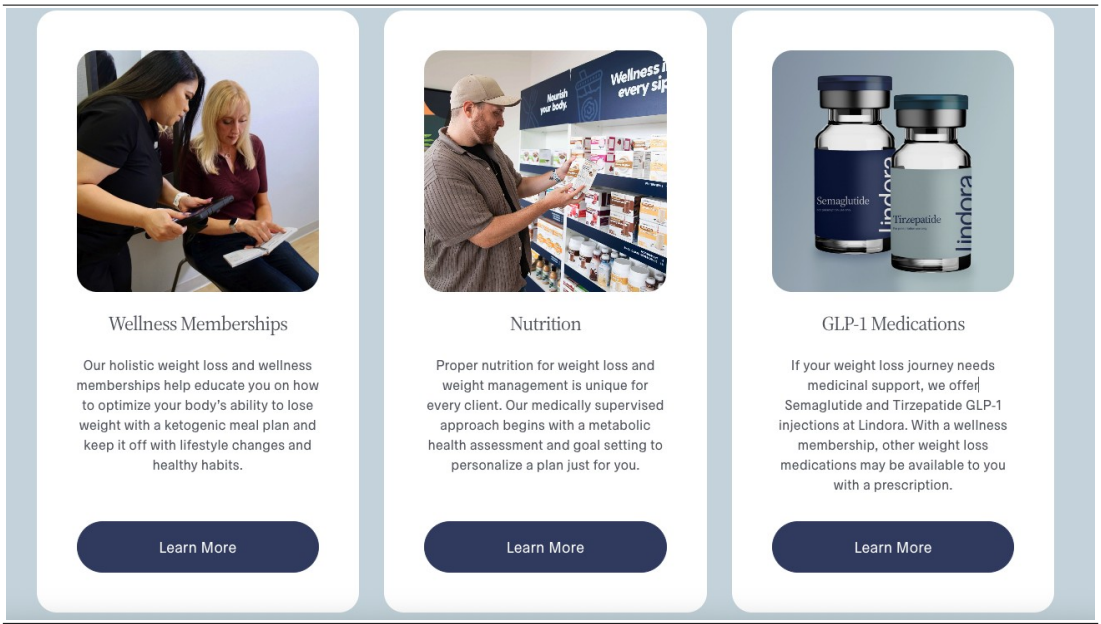


Optimize Your Health With MIORA's Personalized Medicine

Offering comprehensive blood work, GLP-1 medication, hormone optimization, and performance-based compounds & peptides.

Xponential Fitness

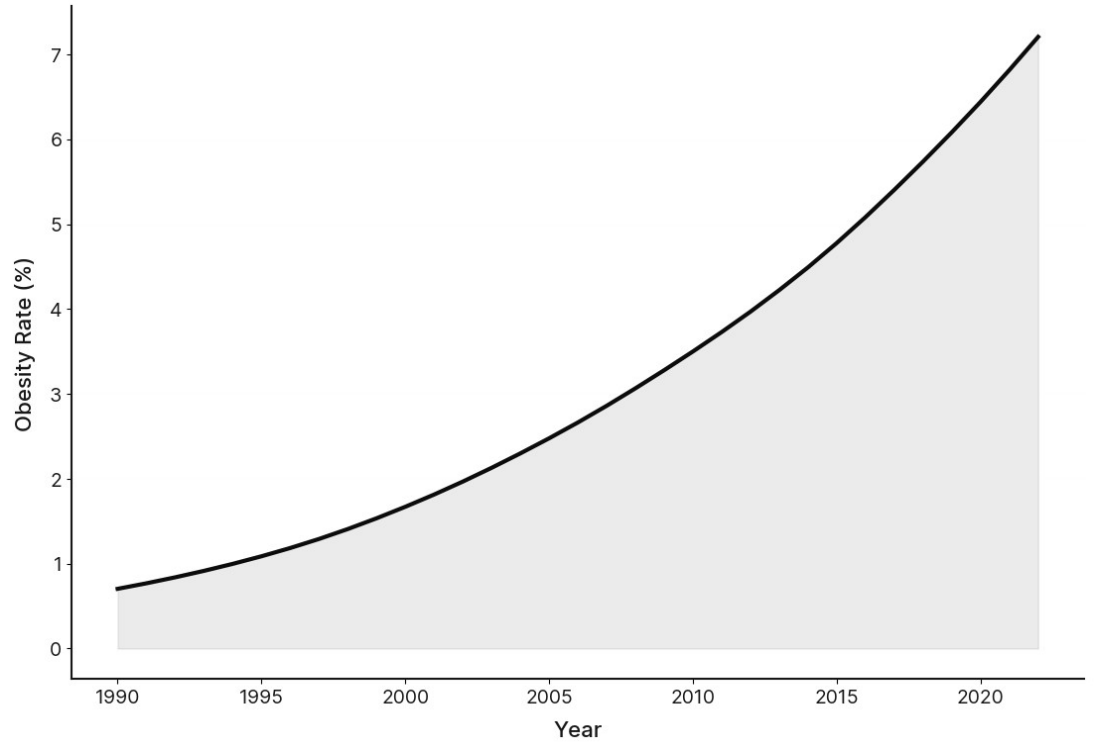
Xponential operates 3,200+ boutique fitness studios globally as the largest fitness franchisor across 8 brands including Club Pilates, CycleBar, StretchLab, YogaSix, Pure Barre, Rumble, and BFT. Xponential acquired Lindora, a 50-location medical weight loss clinic chain, for $9.5 million in 2024 to create an integrated prescribe-and-train model. Members can get GLP-1 prescriptions at Lindora then use credits at any Xponential studio (Pure Barre, Club Pilates, CycleBar) for strength and conditioning.



Indian Obesity Landspace & Generics Opportunity

Obesity rates in India are rising with obese/overweight adult population potentially growing from 180mn in 2025 to 450mn in 2050. Obesity rates for women in India increased from 1.2% in 1990 to 9.8% in 2022, and for men from 0.5% to 5.4%. According to NFHS-5, 24% of women and 23% of men in India are overweight or obese. India has more than 100m diabetic patients with an equal number in pre-diabeties. India is considered "diabetes capital" of the world.

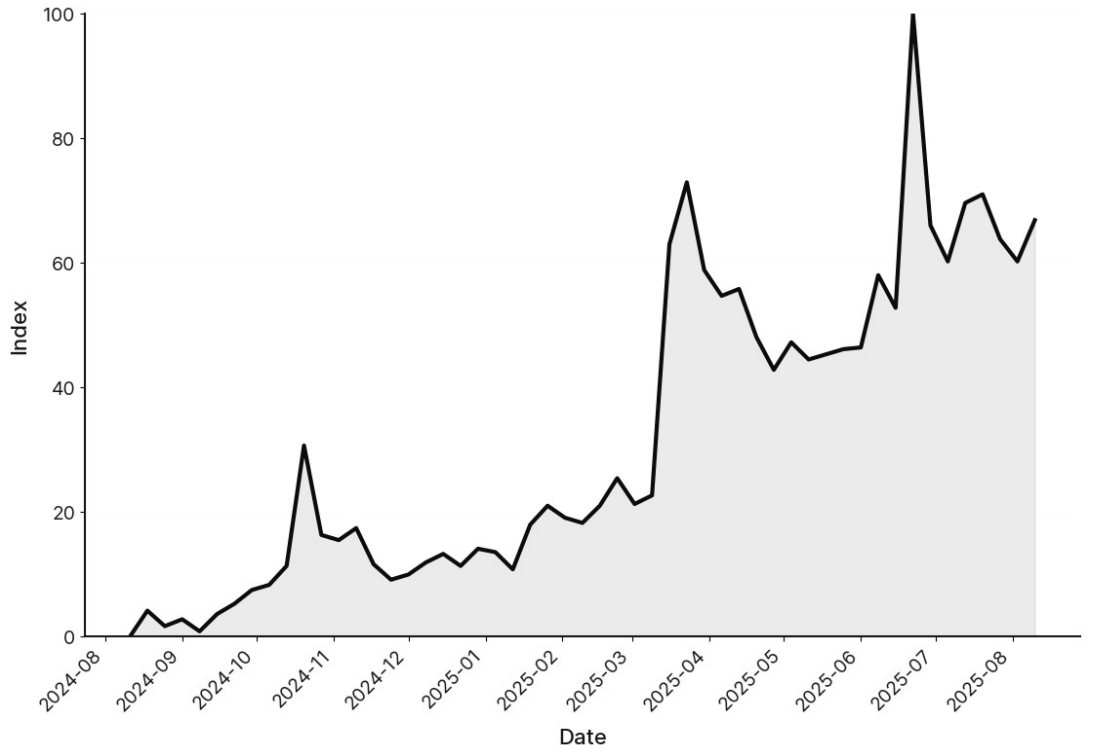
Obesity Rate in India has been rising rapidly



source- our world in data

Market for GLP-1s is still nascent in India but is growing rapidly evident by rapid growth in sales for Wegovy and Mounjaro. Mounjaro (priced at 14000-17500 per dose) has crossed Rs 100 crore in sales in India in just four months of launch, making it one of the country's fastest-growing prescription brands ever by value.

GLP-1 search terms index - India



A host of Indian companies are gearing up to launch semaglutide generics when the core patent expires in March 2026. Adoption of GLP-1s can be rapid in India, given India has over 100 million obese adults and another 180 million overweight individuals. Companies directly involved in supply chain - APIs, fill-finish, autoinjectors, manufacturers will be the obvious beneficiaries. As adoption for GLP-1s picks up, second-order effects will be visible across multiple industries like diagnostics, dairy/protein, hospitals, fast food chains, restaurants; however, these effects are likely to emerge gradually over the coming years.

patent expiry for GLP-1 drugs across markets

Company	Molecule	Brand Name	Mode of administration	First US Patent Expiry	Canada	Brazil	India
Novo	Semaglutide	Ozempic	Injectable	2031	Jan 2026	Mar 2026	Mar 2026
Novo	Semaglutide	Wegovy	Injectable	2031	Jan 2026	Mar 2026	Mar 2026
Novo	Semaglutide	Rybelsus	Oral	2031	Jan 2026	Mar 2026	Mar 2026
Eli Lilly	Tirzepatide	Mounjaro	Injectable	2036	2036	2036	2036
Eli Lilly	Tirzepatide	Zepbound	Injectable	2036	2036	2036	2036

Positioning of Indian Pharma companies in GLP-1s

company	positioning
Shaily Engineering	Leading manufacturer of pen injectors for GLP-1 therapies; capacity expanding from 40 to 100 million pens by FY28, and 34-35 million pen commercial supply (including semaglutide) targeted in H1 CY26
Gland Pharma	fill-finish CDMO for peptides and GLP-1s; launched liraglutide in Q4 FY25 and aggressively scaling its integrated pen/cartridge capacity from ~40 million to 140 million units annually by 2026
Divi's Laboratories	leading peptide API partner for global innovators, offering both solid-phase (SPPS) and liquid-phase peptide synthesis (LPPS), with recently commissioned SPPS capacity and strong backward integration into high-purity peptide fragments ; actively expanding its portfolio in GLP-1 and related analogs, working with several innovators at multiple stages
Nueland Laboratories	Over 15 years of proven expertise in peptide chemistry, including complex purification and large-scale capabilities; expanding peptide manufacturing from 0.5 KL to 6.37 KL; engaged on multiple peptide projects including late-stage/Phase-3 candidates in the CDMO pipeline
OneSource Specialty	specializing in drug-device combinations with deep expertise in cartridge and fill-finish; expanding cartridge capacity from 40 million to 200 million units and upgrading sterile injectable infrastructure via $100 million capex focused on new drug-device lines and lyophilization
Lupin	advancing its pipeline with internal and partnered development of oral and injectable Semaglutide targeting the first wave in India and select ex-India markets by FY27
Dr Reddy	Global leader preparing Day-1 semaglutide launch across 87 countries including india, canada, brazil; building a robust global pipeline of peptides including GLP-1s
Sun pharma	GL0034 (Utreglutide) Phase-1 completed showing promising weight loss results; ramping peptide manufacturing and has pen delivery partnerships to enable a Day-1 semaglutide launch in India
Glenmark pharma	First to launch liraglutide biosimilar "Lirafit™" in India, capturing over 65% share in the Indian liraglutide segment with ~70% lower therapy cost; expanding its GLP-1 and anti-diabetic injectable portfolio.
eris lifesciences	developing synthetic and recombinant semaglutide with validation underway at its EU-GMP injectables sites; scaling up fill-finish capacity with a cartridge line at Bhopal, targeting one of the first GLP-1 launches in India/ROW from March 2026
torrent pharma	gearing up for first-wave launches of both oral and injectable semaglutide in India from 2026; phase 3 trials for oral underway and injectable secured via partnership; building capabilities and IP in complex peptides
cipla	Early-mover securing early partnerships for pen delivery and targeting launch by March 2026
zydus lifesciences	targeting day-one launch of generic semaglutide in India and other emerging markets post-patent expiry