

THINR: Investing in GLP-1

The GLP-1 weight loss drug revolution

According to a 2022 study released by the Lancet, more than one billion people in the world, or one-eighth of the global population are living with obesity. At a global level, the number of obese adults is more than twice what it was 34 years ago and currently stands at 43% of all adults, according to the WHO.¹ Morgan Stanley posits that the negative health outcomes and associated drain on productivity are responsible for trimming 3.6% off the U.S. gross domestic product (GDP).²

GLP-1 (glucagon-like peptide 1) drugs have been proven to be effective in promoting weight loss. GLP-1 is a natural hormone released to the gut and brain in response to food. It helps regulate blood sugar by stimulating insulin-producing cells in the pancreas when blood sugar levels rise too high. GLP-1 drugs have been approved since 2005, as a treatment for type-2 diabetes. But today's drugs now last long enough to reach the pancreas. As a result of that breakthrough, new drugs have been found to promote reductions in body weight by 10-20% and curb the appetite, resulting in the reduction of consumption volumes by 50%.

¹ WHO, "One in eight people now living with obesity," March 1, 2024, <https://www.who.int/news/item/01-03-2024-one-in-eight-people-are-now-living-with-obesity>

² Nic Sochovsky and Helena Miles, Morgan Stanley, "GLP-1: The Weight Speculation," December 2023, https://www.morganstanley.com/im/publication/insights/articles/article_geoglp1_us.pdf?1714161368409



A recent landmark trial on cardiovascular outcomes saw that patients taking Semaglutide GLP-1 drugs Wegovy and Ozempic for more than three years, had a 20% lower risk of cardiovascular events versus placebo.³ As a result of those studies, the drugs were recently approved by the FDA as the first treatment to reduce the risk of heart problems in obese or overweight adults.⁴ Anecdotally, patients also report a reduction or cessation of other bad habits like alcohol, drugs, and smoking. There is now research on GLP-1 drugs for treating physical addiction. There appear to be other therapeutic benefits as well.⁵

While the latest GLP-1 drugs are not without side effects like nausea, they are being hailed as “miracle drugs.” This is because they are extremely effective in promoting weight loss and represent a major advancement for public health.

This breakthrough status also carries with it the potential to disrupt other companies in health care

and has broad-ranging implications for many other industries. Some analysts estimate that GLP-1 drugs could reduce calorie intake by 15% to 20%.⁶

GLP-1 drugs are a disruptive economic force, with Goldman Sachs estimating the market for GLP-1 drugs will grow to \$100 billion by 2030, and potentially higher if insurance companies cover these drugs, given their promise to treat a wide range of issues and improve health outcomes. These new anti-obesity drugs could see a patient population as high as 70 million, resulting in an increase in U.S. GDP levels by as much as 1% in the coming years.⁷

History of diet drugs

Despite the promise of today's GLP-1 drug therapies, weight loss drugs have had a long and problematic history. In 1933, Dinorphenol (DNP), used in the

³ Michael Zoler, PhD, “Semaglutide Cuts Cardiovascular Events in Landmark Trial,” Medscape, August 8, 2023, <https://www.medscape.com/viewarticle/995270?form=fpf>

⁴ U.S. Food and Drug Administration, March 8, 2024, <https://www.fda.gov/news-events/press-announcements/fda-approves-first-treatment-reduce-risk-serious-heart-problems-specifically-adults-obesity-or>

⁵ Nic Sochovsky and Helena Miles, Morgan Stanley, “GLP-1: The Weight Speculation,” December 2023, https://www.morganstanley.com/im/publication/insights/articles/article_geoglp1_us.pdf?1714161368409

⁶ Nic Sochovsky and Helena Miles, Morgan Stanley, “GLP-1: The Weight Speculation,” December 2023, https://www.morganstanley.com/im/publication/insights/articles/article_geoglp1_us.pdf?1714161368409

⁷ Goldman Sachs Global Macro Research, “Weighting the GLP-1 Market,” April 12, 2024 and “Obesity drugs are among health breakthroughs forecast to boost GDP,” March 7, 2024.

The rise ... and fall of weight-loss drugs



Note: This does not constitute an exhaustive list of all weight-loss drug-related developments.

Source: National Institutes of Health; FDA; Li MF, Cheung BM, “Rise and fall of anti-obesity drugs”; NY Times; various news source.

manufacturing of munitions and pesticides, was prescribed for weight loss, only to be banned for sale by the FDA by 1938. Amphetamines (Benzedrine) and Methamphetamine were initially approved for treating obesity but were later banned for that purpose due to their addictive qualities. And then there was the fen-phen weight loss drug combination in the 1990's, which was ultimately withdrawn from the market in 1997 because it was linked to severe heart defects.

Should investors be concerned about GLP-1 drug safety? In the case of fen-phen, it only took a few years to recognize it caused serious heart defects. Similarly, rimonabant's serious psychiatric effects were discovered reasonably quickly. GLP-1 drugs have been used to treat diabetic patients for over a decade. Exanatide, the first drug for type-2 diabetes to target the GLP-1 receptor was approved by the FDA in 2005. After almost a decade of widespread use, the incidence of adverse reactions is relatively low and safety concerns are minimal. Indeed, the largest trial of GLP-1 patients, the SELECT trial that involved 18,000 participants released in November of 2023, saw many positive health outcomes.⁸

GLP-1 101: How do these drugs work?

GLP-1 was discovered by a medical physiologist at the University of Copenhagen, named Jens Juul Holst. Even though this class of drugs has been available for a decade, the current generation of GLP-1 medications has higher efficacy in treating obesity than past generations of the drug and other weight-loss medications.

GLP-1 agonists work by mimicking the action of glucagon-like peptides which are naturally released by the intestines after eating food.

GLP-1 agonists:⁹

- **Triggers insulin release from the pancreas:** Insulin is an essential hormone that allows the body to use food to create energy. It lowers the amount of glucose (sugar) in the blood. If you do not have enough insulin, blood sugar increases, leading to diabetes.
- **Blocks glucagon secretion:** Glucagon is a hormone the body uses to raise your blood sugar levels when necessary. GLP-1 prevents more glucose from going into the bloodstream.
- **Slows stomach emptying:** Slower digestion means that the body releases less glucose (sugar) from the food you eat into the bloodstream.
- **Increase satiety (how full you feel after eating):** GLP-1 affects areas of the brain that controls hunger and satiety.

Additional ongoing studies have found that GLP-1 has multiple biological effects beyond diabetes and weight loss. It also exerts a positive therapeutic effect on the human brain, pancreas, heart, gastrointestinal tract, and liver as illustrated in the image on the next page.¹⁰

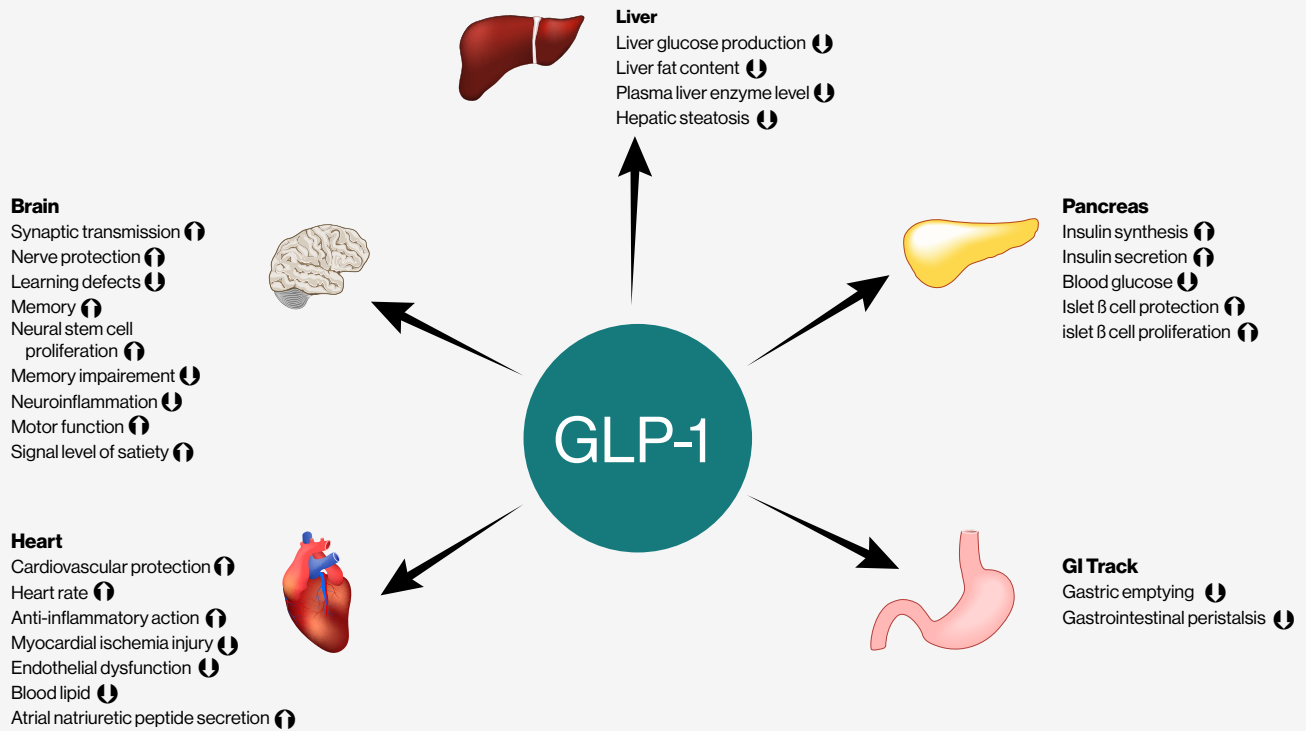
The semaglutide and tirzepatide classes are the second-generation GLP-1 receptor agonists driving the diet drug revolution. Semaglutide, the second generation of GLP-1s approved in 2021 that includes Ozempic – the trade name for the treatment of

⁸ A. Michael Lincoff, M.D., Kirstine Brown-Frandsen, M.D. Helen M. Colhoun, M.D, et al, "Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes," New England Journal of Medicine, November 11, 2023, <https://www.nejm.org/doi/full/10.1056/NEJMoa2307563>

⁹ Cleveland Clinic, GLP-1 Agonists, <https://my.clevelandclinic.org/health/treatments/13901-glp-1-agonists>

¹⁰ Xin Zhao, Minghe Wang, et al, "GLP-1 Receptor Agonists: Beyond Their Pancreatic Effects," Frontiers in Endocrinology, 2021, <https://www.frontiersin.org/journals/endocrinology/articles/10.3389/fendo.2021.721135>

GLP-1 has multiple biological effects beyond diabetes and weight loss



Today's generation of GLP-1 drugs

Approval year	GLP-1 agonist	Marketer	Frequency of dose	Approval indication
2023	Zepbound (tirzepatide)	Eli Lilly	Weekly injection	Obesity/weight management
2022	Mounjaro (tirzepatide)	Eli Lilly	Weekly injection	Type-2 diabetes
2021	Wegovy (semaglutide)	Novo Nordisk	Weekly injection	Obesity/weight management
2020	Rybelsus (semaglutide)	Novo Nordisk	Weekly oral	Type-2 diabetes
2017	Ozempic (semaglutide)	Novo Nordisk	Weekly injection	Type-2 diabetes, cardiovascular
2014	Trulicity (dulaglutide)	Eli Lilly	Weekly injection	Type-2 diabetes
2012	Bydureon Bcise (exenatide)	AstraZeneca	Weekly injection	Type-2 diabetes
2010	Victoza (liraglutide)	Novo Nordisk	Daily injection	Type-2 diabetes, cardiovascular
2005	Byetta (exenatide)	AstraZeneca	Twice daily injection	Type-2 diabetes

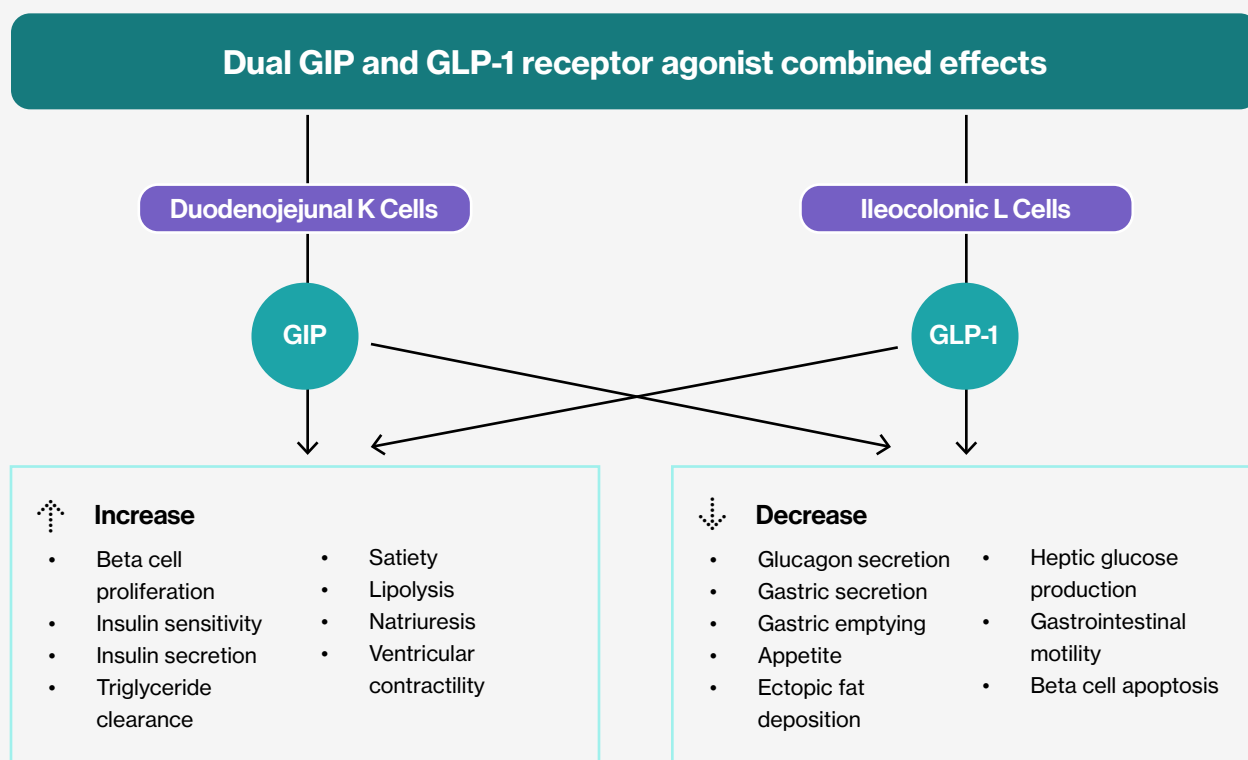
There are currently several GLP-1 agonist drugs on the market that are generally taken by injection on a daily or weekly basis.



The introduction of second-generation GLP-1s crossing the 10% weight-loss threshold and the dual agonist drugs crossing the 20% threshold got the world’s attention.

diabetes – and Wegovy – the trade name for the treatment of obesity – saw results as much as 14.9% total body weight loss.

The comparable figure for tirzepatide, which is a dual agonist combining GLP-1 and glucose-dependent insulinotropic polypeptide (GIP) that the FDA approved in November 2023, is around 22.5% weight loss or around 52 pounds. The introduction of second-generation GLP-1s crossing the 10% weight-loss threshold and the dual agonist drugs crossing the 20% threshold got the world’s attention.



The mechanism of action of GLP-1 agonists and GIP agonists.

The example depicted above is that of a dual GLP-1 agonist and GIP agonist, tirzepatide (**Mounjaro and Zepbound**), the two GLP-1 agonist and GIP agonist combos approved. Ozempic, Rybelsus, Wegovy, and the remaining are exclusively GLP-1 agonists. (Updated from Fisman & Tanenbaum, 2021, Cardiovascular Diabetology).

Source: Visual Alpha

New generation of dual GIP and GLP-1 receptor agonists

Glucagon-like peptide-1 (GLP-1) and glucose-dependent insulintropic polypeptide (GIP) are peptide hormones or incretins released by the gut in response to nutrients. This hormone pathway is a self-regulating feedback system connecting the gut with the brain, the pancreas, and the liver.

Will GLP-1's alone solve the obesity crisis?

Researchers now face the question of whether patients will have to take these medications for life to maintain their weight. A subset of clinical trial participants who ceased taking semaglutide and stopped the study's lifestyle interventions regained about two-thirds of their lost weight after one year. Because these drugs reduce muscle mass, an exercise program is recommended for their use.

While GLP-1 drugs are a remarkable weight loss cure for many patients, it is not the answer for everyone. Other treatments such as lifestyle changes may be more appropriate for other patients. But in many cases, GLP-1 treatments are a viable alternative to bariatric surgery. Indeed, the reduction in volume for bariatric surgery is around 20-30% since the advent of GLP-1 medications.¹¹

Some patients may be contraindicated for GLP drugs, such as those with a history of medullary thyroid cancer, multiple endocrine neoplasia type 2, and pancreatitis, as well as those who are pregnant or breastfeeding.

The current generation of GLP-1 drugs causes side effects that some patients do not tolerate. They range from mild side effects, such as fatigue, nausea, and vomiting, to more serious side effects such as gastroparesis, intestinal obstruction, and gallbladder disease.

Finally, not all patients who are candidates for these drugs are willing to take them. Not everyone wants to deal with an injectable drug and prick themselves with a needle every week. Patients may be more amenable to a pill version of semaglutide, and the FDA is currently evaluating such a medication with analogous efficacy, orforglipron. As mentioned, patients who take GLP-1s for weight loss will also most likely need to take them for the rest of their lives, which only some people are willing to do.

Pricing and insurance reimbursement amid supply constraints

One major economic headwind related to GLP-1 drugs is constrained supply leading to higher costs with limited insurance reimbursement. A monthly package of GLP-1 costs between \$900 and \$1,350 before insurance and other rebates. Both Novo Nordisk and Eli Lilly have savings programs that aim to reduce out-of-pocket expenses regardless of insurance coverage.

All private/employer-sponsored insurers in Massachusetts currently cover anti-obesity medications, but at the national level, however, only around 50% of employers provide some coverage.¹²

A study from researchers at Yale University, King's College Hospital in London, and Doctors Without Borders suggests that these drugs could be

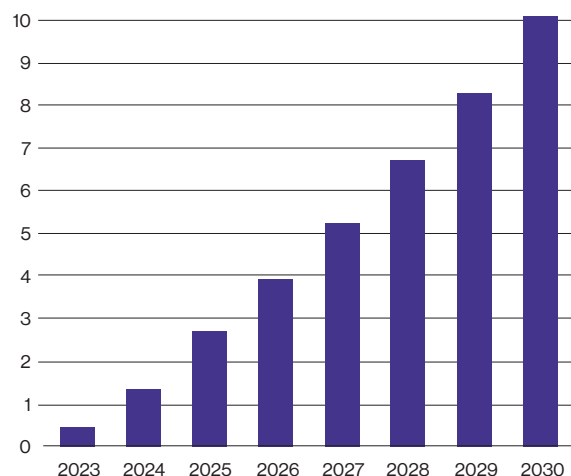
¹¹ Cedars Sinai Medscape, "Do New Weight Loss Meds Mean the End of Bariatric Surgery?," <https://www.cedars-sinai.org/newsroom/medscape-do-new-weight-loss-meds-mean-the-end-of-bariatric-surgery/>

manufactured for less than \$5 per month.¹³ Studies like these raise questions about the high price tag for GLP-1 drugs and the need for pricing reforms. However, another survey released by Evercore ISI found that more than half of people currently taking a GLP-1 said they are paying a monthly price of \$50 or less out of pocket.¹⁴

As depicted below, the top two drug manufacturers, Novo Nordisk and Eli Lilly, are ramping up manufacturing spend in a struggle to meet accelerating demand.

Manufacturing spend on GLP-1 drugs is expected to increase significantly ahead, driven by Eli Lilly and Novo Nordisk

Estimated GLP-1 obesity manufacturing spend by Eli Lilly and Novo Nordisk, \$B



Source: Company data

Goldman Sachs believes that production shortfalls could constrain the size of the GLP-1 market in the medium to near term. Nonetheless, Goldman assumes that the U.S. patient population will grow from around 2 million people today to 15 million in 2030, addressing 14% of the US adult population with obesity – which would increase the size of the GLP-1 market from \$10 billion today to \$100 billion by 2030.¹⁵

That number could rise with more insurance coverage for these drugs. Private coverage should increase to 80% by the end of the decade, due to rising demand, coupled with demonstrated health benefits associated with weight loss.¹⁶ And lower price points, enabled by increased manufacturing capacity, should also aid in the expansion of private coverage.

For insurers, obesity is an economic burden as well as a health risk. Insurance companies must weigh the benefits of coverage relative to the financial cost.

On the public insurance side, limited Medicare reimbursement is already starting to happen. The FDA's recent approval of Wegovy for the prevention of heart disease led to Medicare coverage of the drug for this indication. Additional studies for the treatment of sleep apnea, liver disease, and other diseases could have similarly promising outcomes, which could increase the odds of more Medicare coverage, expanding the U.S. GLP-1 patient population far beyond Goldman's 15 million patients estimate.

¹² Goldman Sachs Global Macro Research, "Weighting the GLP-1 Market," April 12, 2024 and "Obesity drugs are among health breakthroughs forecast to boost GDP," March 7, 2024

¹³ Melissa J. Barber, Dzintars Gotham, Helen Bygrave, MBBS, et al, "Estimated Sustainable Cost-Based Prices for Diabetes Medicines", JAMA Network Open. March 27, 2024, https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2816824?utm_source=For_The_Media&utm_medium=referral&utm_campaign=ftm_links&utm_term=032724

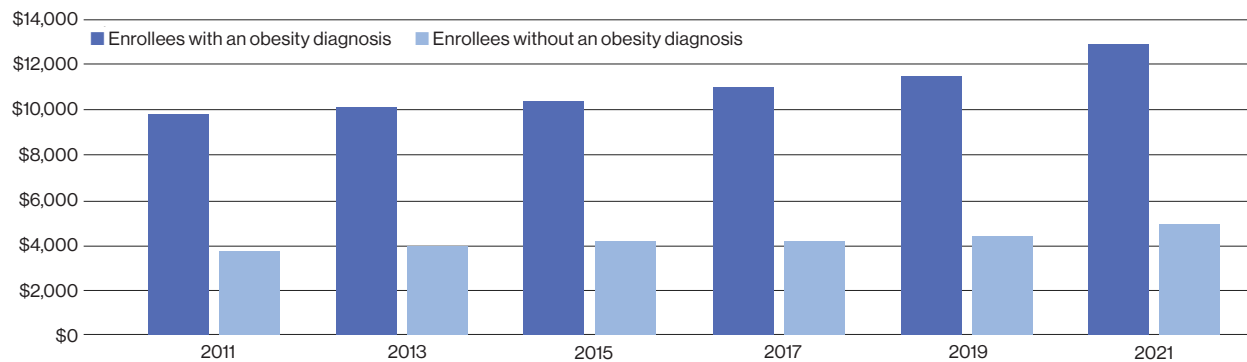
¹⁴ Annika Kim Constantino, "Here's how much people are willing to spend on weight loss drugs, according to a new survey," CNBC, March 23, 2024, <https://www.cnbc.com/2024/03/23/weight-loss-drug-cost-how-much-people-are-willing-to-spend.html>

¹⁵ Goldman Sachs Global Macro Research, "Weighting the GLP-1 Market," April 12, 2024 and "Obesity drugs are among health breakthroughs forecast to boost GDP," March 7, 2024.

¹⁶ JP Morgan, "The increase in appetite for obesity drugs," November 29, 2023, <https://www.jpmorgan.com/insights/global-research/current-events/obesity-drugs>

Obesity is an economic burden and health risk

Average annual health spending for enrollees in US employer insurance plans with or without an obesity diagnosis, 2011-21



Source: KFF analysis of Merative MarketScan Commercial Database

Medicare insurance coverage for even less than half the obese population at today's pricing would be a staggering sum, almost as much as the entire government spends on Medicare today. Expanding Medicare coverage for GLP-1s to include people with obesity is enormously expensive but it may happen anyway given the compelling non-financial reasons to approve coverage.

At these rates of growth, GLP-1 drugs hold implications for the broader economy. Goldman Sachs's senior global economist Joseph Briggs projects that the widespread adoption of GLP-1 drugs, and the associated improvement in health

outcomes and productivity increases, could have a meaningfully positive impact on economic growth.

Poor health imposes a significant economic cost on society, primarily by limiting labor force participation. Taken together, poor health lowers the level of US GDP by 10%.

According to Goldman Sachs, the widespread use of these new weight-loss drugs in the US could boost GDP by 1% in the coming years by lowering obesity-related complications and boosting workplace efficiency.¹⁷



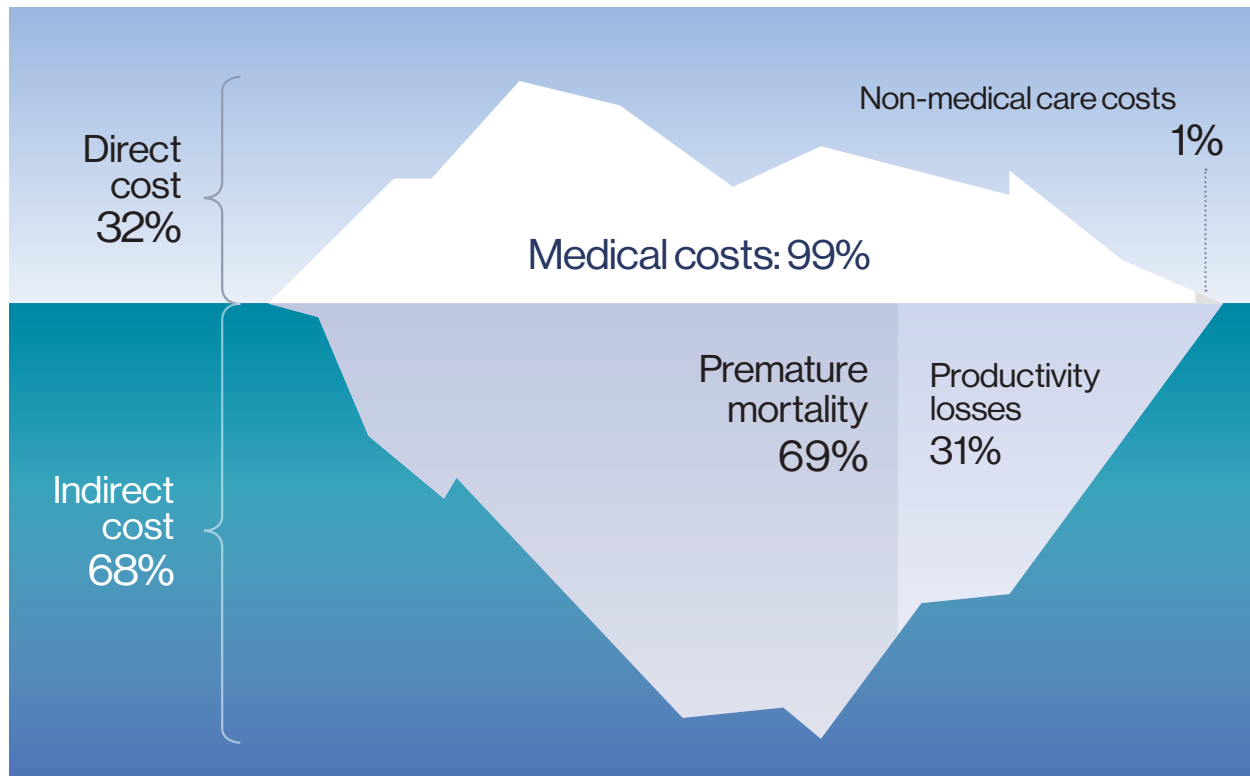
If 40% of all Americans with obesity took these drugs at current prices—roughly \$15,000 per year per person—[the bill] would total over \$1 trillion annually... That is almost as much as the government spends on the entire Medicare program... So, it's a staggering figure.

Goldman Sachs¹⁸

¹⁷ Reuters, "Weight-loss drugs could boost US GDP by 1% in coming years, Goldman says", February 22, 2024, <https://www.reuters.com/business/healthcare-pharmaceuticals/weight-loss-drugs-could-boost-us-gdp-by-1-coming-years-goldman-says-2024-02-22/>

¹⁸ Goldman Sachs Global Macro Research, "Weighting the GLP-1 Market," April 12, 2024 and "Obesity drugs are among health breakthroughs forecast to boost GDP," March 7, 2024

Economic costs of overweight and obesity



Source: World Obesity Federation and RTI International "The Economic Impact of Overweight & Obesity in 2020 and 2060", 2022

GLP-1 drug pipeline

While the current GLP-1 landscape is currently dominated by two drug manufacturing companies, Novo Nordisk and Eli Lilly, there are many other promising drugs in the GLP-1 pipeline.

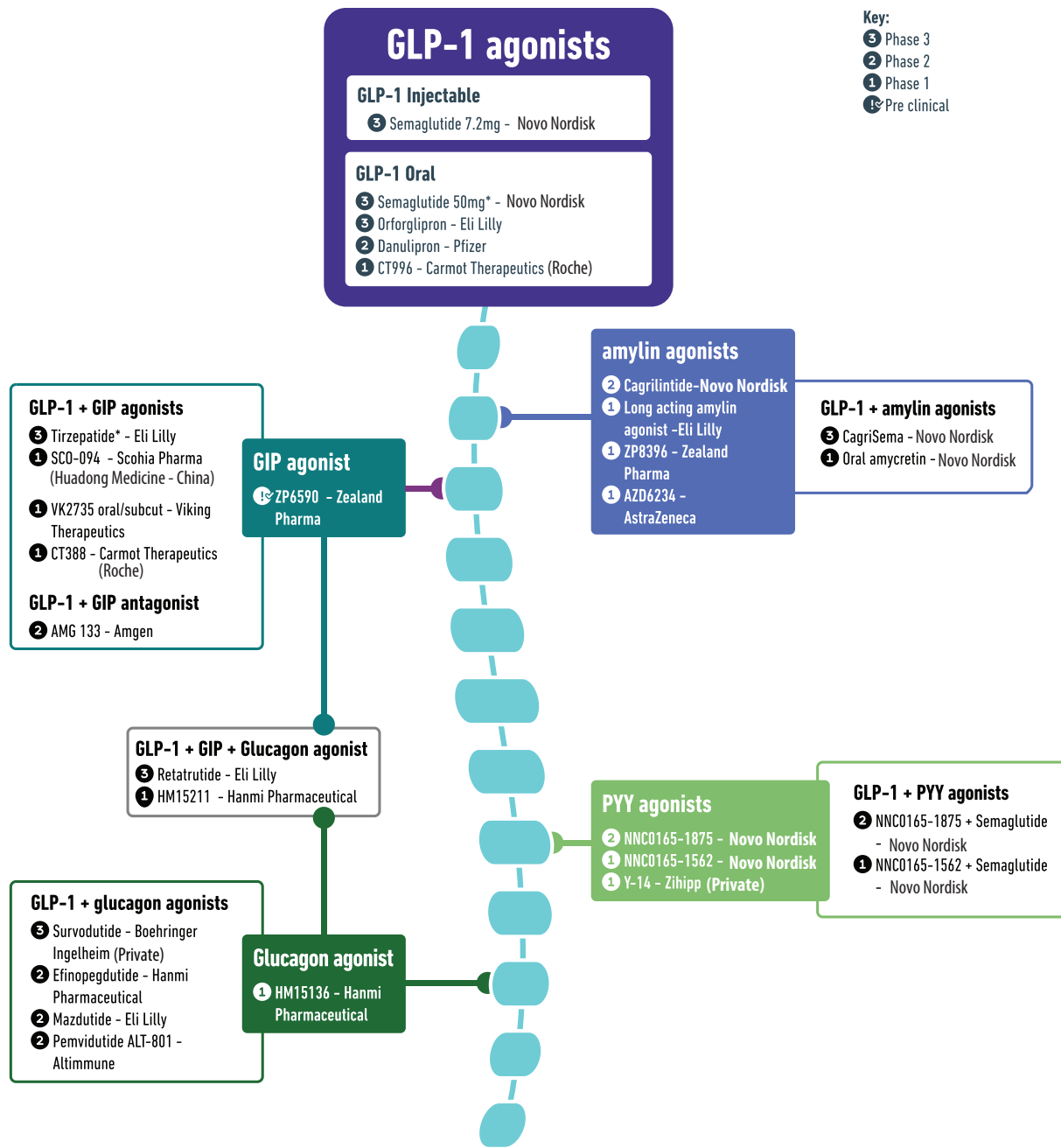
Tirzepatide is the first dual agonist which has been approved for chronic weight management, but numerous other dual and/or triple agonists like cagrisema (Novo Nordisk), retatrutide (Eli Lilly), mazdutide (Eli Lilly/Innovent Biologics) and survodutide (Boehringer Ingelheim/Zealand Pharmaceuticals) are also in phase 3 trials as

potential treatments for obesity and its metabolic complications. Early data suggests this next generation of drugs may generate even more weight loss than tirzepatide. Additionally, oral GLP-1 drugs that will provide an alternative option to injection are also under development.¹⁹

GLP-1: Market opportunity and disruption

Two companies, Novo Nordisk and Eli Lilly, accounted for 98% of the revenues derived from the GLP-1 market in 2023, generating \$37.3 billion of

¹⁹ Melson, E., Ashraf, U., Papamargaritis, D. et al, « What is the pipeline for future medications for obesity? », International Journal of Obesity, February 1, 2024, <https://doi.org/10.1038/s41366-024-01473-y>



Source: International Journal of Obesity

Phase 3 GLP-1 drug candidates

Drug candidate in Phase 3	Company	Mechanism of action	Indication	Expected launch year for first indication
Icosema	Novo Nordisk	GLP-1 receptor agonists & insulin analog	Type 2 diabetes	2024
Mazdutide (LY3305677) (IBI-362)	Eli Lilly & Innovent Biologics	GLP-1 receptor agonist & glucagon receptor agonist	Type 2 diabetes; obesity/weight loss management	2024
Orforglipron-Oral (LY3502970, OWL833)	Eli Lilly & Chugai Pharmaceutical	Oral GLP-1 receptor agonist	Type 2 diabetes; obesity/weight loss management	2025
Cagrisema (Cagrilintide plus semaglutide)	Novo Nordisk	GLP-1 receptor agonist (semaglutide) & amylin analog (Cagrilintide)	Type 2 diabetes; obesity/weight loss management, cardiovascular benefit	2025
Retatrutide	Eli Lilly	GLP-1 receptor agonist glucagon receptor agonist & GIP agonist	Type 2 diabetes; obesity/weight loss management, cardiovascular benefit	2026
Survodutide (BI-456906)	Boehringer Ingelheim & Zealand Pharma	GLP-1 receptor agonists & glucagon receptor agonist	Obesity/weight management, in Phase 2 for type 2 diabetes & non-alcoholic steatohepatitis (NASH)	2027
TG103	CSPC Pharma	Novel GLP-1/Fc fusion protein	Type 2 diabetes; Alzheimer's disease; non-alcoholic steatohepatitis (NASH); obesity/weight management	2025

Source: Visible Alpha BioPharma (March 22, 2024)

Early stage GLP-1 pipeline

Drug candidate	Clinical phase	Company	Mechanism of action	Indication
PF-06882961 (Danuglipron)	Phase 2	Pfizer	GLP-1 receptor agonist & glucagon receptor agonist; GIP receptor agonist	Type 2 diabetes; non-alcoholic steatohepatitis (NASH)
AMG-133 (Maridebart cafraglutide)	Phase 2	Amgen	GLP-1 receptor agonists; GIP receptor agonists	Type 2 diabetes; obesity/weight management
GSR-1290	Phase 2	Structure Therapeutics	GLP-1 receptor agonist	Type 2 diabetes; obesity/weight management
LY2944876	Phase 2	Eli Lilly	GLP-1 receptor agonists; Glucagon receptor agonist - xyntomodulin analog	Type 2 diabetes
Amycretin	Phase 2	Novo Nordisk	GLP-1 receptor agonists; Amylin receptor agonists	Obesity/weight management
ALT-801 (Pemvidutide)	Phase 2	Altimune	GLP-1 receptor agonists; Glucagon receptor agonists	Obesity/weight management, non-acholic steatohepatitis (NASH)
VK-2735	Phase 2	Viking Therapeutics	GLP-1 receptor agonists; GIP receptor agonists	Obesity/weight management, non-acholic steatohepatitis (NASH)
MK-6024 (Efinopegdutide)	Phase 2	Merck	GLP-1 receptor agonists; Glucagon receptor agonists	Non-alcoholic fatty liver disease (NAFLD); non-alcoholic steatohepatitis (NASH)
Oxyntomodulin	Phase 2	OPKO Health	GLP-1 receptor agonists; Glucagon receptor agonists - xyntomodulin analog	Type 2 diabetes; obesity/weight management
HS-20094	Phase 2	Hansoh Pharmaceutical	GLP-1 receptor agonist; GIP agonist	Type 2 diabetes; obesity/weight management; non-alcoholic; steatohepatitis (NASH)
AZD9550	Phases 1/2	AstraZeneca	Oral GLP-1 receptor agonist	Type 2 diabetes; obesity/weight management; non-alcoholic; steatohepatitis (NASH)
SemaDapa FDC	Phase 1	Novo Nordisk	GLP-1 receptor agonists & dapagliflozin, a SGLT2 inhibitor	Type 2 diabetes
NN9541	Phase 1	Novo Nordisk	GLP-1 receptor agonists; GIP receptor agonists	Type 2 diabetes
TERN-601 - Oral	Phase 1	Terns Pharmaceuticals	Oral GLP-1 receptor agonists	Obesity/weight management

Source: Visible Alpha BioPharma (March 22, 2024)

the \$37.9 billion of GLP-1 revenues. Novo Nordisk, who markets Ozempic, Rybelsus, Wegovy, Saxenda, and Victoza, generated \$24.9 billion in GLP-1 drug revenues last year. Eli Lilly, with Mounjaro, Zepbound, and Trulicity, generated \$12.4 billion in GLP-1 drug revenues in 2023.²⁰

Novo Nordisk and Eli Lilly also have promising drugs in the pipeline that should build on their market dominance, however other competing pipeline programs with novel mechanisms of action could turn out to be superior in terms of efficacy, safety, and patient convenience. That could disrupt Novo and Lilly's dominant position, advocating for a diversified investment approach.

In line with Goldman Sachs research, JP Morgan Research also expects the GLP-1 market to exceed \$100 billion by 2030. While demand could continue to outstrip supply for the next several years, they expect production issues to be resolved over the longer term with more production coming online and more convenient oral options becoming available.²¹

In a country with 40% of the population living with obesity, GLP-1 agonists offer effective weight loss drugs that could lead to higher productivity, gains in longevity, and potentially lower medical costs elsewhere in the healthcare system. Columbia Threadneedle Investments estimates the weight-loss industry could become a \$1.7 trillion annual market if 100 million Americans take these drugs at current pricing levels.²²



The results of the SELECT trial of nearly 18,000 participants make the drug class a life-and-death matter and not just “weight loss drugs.”

J.P. Morgan Asset Management

Furthermore, there is an enormous patient pool suffering from conditions that GLP-1 drugs may address in addition to obesity, such as cardiovascular disease, sleep apnea, diabetes, chronic kidney disease, arthritis, heart failure, and even Alzheimer's.

In November 2023, data from the largest clinical trial of GLP-1's to date, the SELECT trial of nearly 18,000 non-diabetic participants showed evidence of reduced heart attacks, strokes, and deaths due to cardiovascular disease; and 73% of patients did not progress to diabetes. Subjects also saw a 19% reduction in all causes of morbidity. These results make the drug class a life-and-death matter, not just “weight loss drugs.”²³

Another important takeaway from the SELECT trial is that the meaningful benefits from GLP-1s were

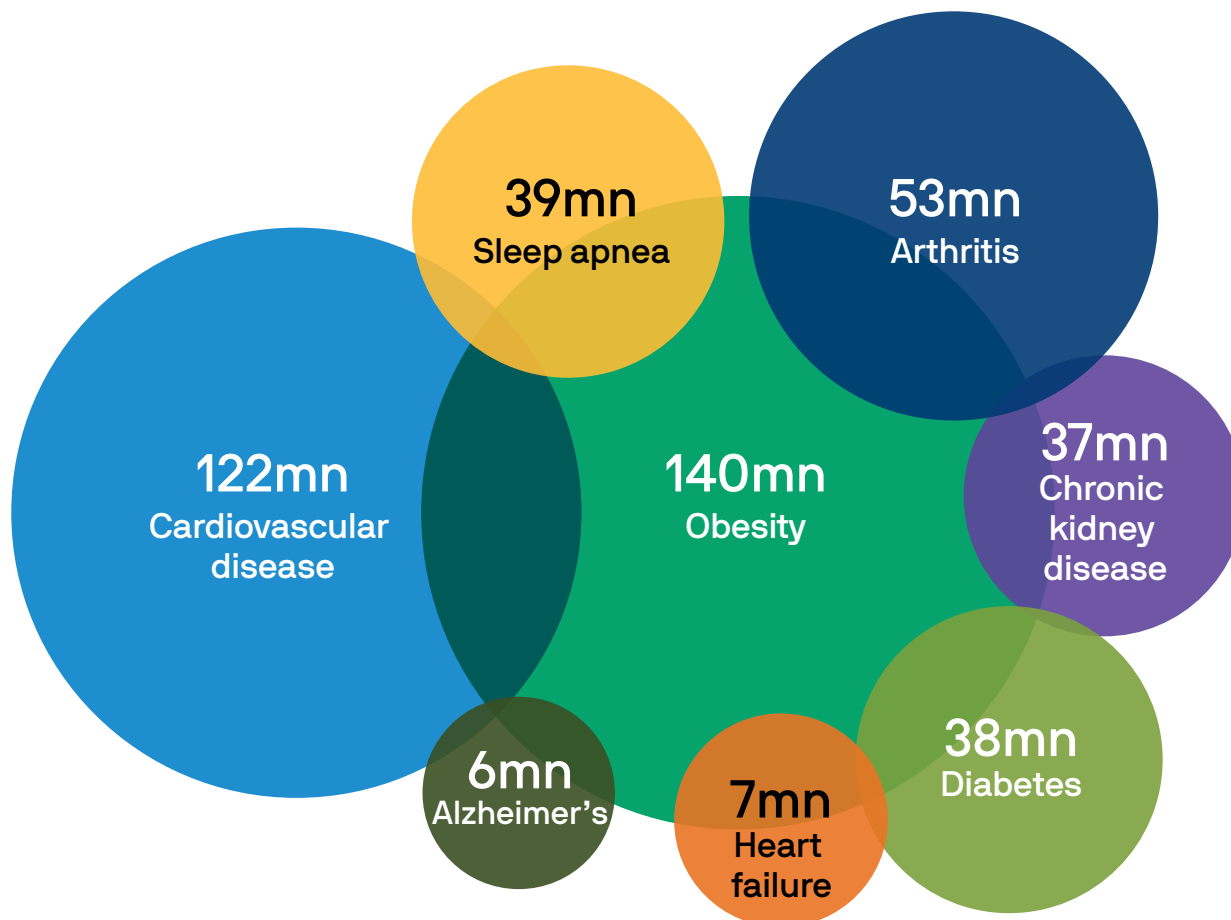
²⁰ Visible Alpha Biopharma, March 22, 2024.

²¹ J.P. Morgan, “The increase in appetite for obesity drugs,” November 29, 2023, <https://www.jpmorgan.com/insights/global-research/current-events/obesity-drugs>

²² Cork Gaines, Allie Kelly, “How Ozempic could change the economy as we know it,” Business Insider, March 22, 2024, <https://www.businessinsider.com/semaglutide-wegovy-ozempic-weight-loss-healthcare-airlines-economy-productivity-2023-11>

²³ Holly Morris, Janet King, “GLP-1's: More than just obesity drugs,” J.P. Morgan Asset Management, February 23, 2024, <https://am.jpmorgan.com/us/en/asset-management/institutional/insights/portfolio-insights/equity/glp-1s-more-than-just-obesity-drugs/#:~:text=Data%20from%20the%20largest%20clinical,the%20control%20group.>

Chronic diseases that may respond to GLP-1 drugs



Source: Alzheimer's Association, American Diabetes Association, American Heart Association, Centers for Disease Control and Prevention, Journal of Cardiac Failure, National Council on Aging, National Institute of Diabetes & Digestive & Kidney Diseases, World Obesity Federation, as of January 2024

achieved with only a 9% loss of body weight, on average. The GLP-1 drugs commercially available now, and new iterations currently in trials, offer even more significant average weight loss. Losing as much as 20% of body weight could translate to even better clinical outcomes.

Sector and industry disruption – from health care to airlines

The GLP-1 diet drug revolution is expected to disrupt many sectors and industries. Within healthcare, GLP-1 will transform how obesity is viewed and

managed. In addition to weight management, GLP-1 drugs will aid in the management of cardiovascular disease and shape the treatment of other weight-related illnesses like type-2 diabetes and kidney disease.

In Pharma, biotechs will also likely angle for a slice of the pie, researching medications that work in tandem with GLP-1s. Contract development manufacturing organizations (CDMO), and drug suppliers and distributors will likely benefit as well.

On the medical device side, the market for insulin pumps and continuous glucose monitors (CGMs) could be negatively impacted. Kidney dialysis centers could see less business. Similarly, better cardiac outcomes could avoid the need for cardiac devices such as implantable defibrillators.

Among insurers, life insurance companies that cover mortality risk stand to benefit from longer life spans for the insured population, allowing life insurers to earn more premium income and higher investment income on reserves, as mortality claims are deferred.

Expanded usage of GLP-1 drugs is also expected to impact the food and beverage industry, reducing consumption and impacting the types of food and beverages consumed. Using data from alternative data provider Numerator, J.P. Morgan Research has found that current GLP-1 users purchased around 8% less food – including snacks, soft drinks, and high-carb products – for at-home consumption over the last 12 months compared with the average consumer.²⁴ Some analysts estimate that GLP-1 drugs could reduce calorie intake by 15% to 20%. Extrapolating this figure and projecting that 25 million to 50 million Americans may be taking the drug by 2030, the nation's calorie intake could be reduced 1% to 3%.²⁵

Anecdotes from patients taking GLP-1 drugs indicate that the drug helps curb certain addictive behaviors like smoking cigarettes or drinking alcohol, so this could be bad news for beer and tobacco companies.²⁶

On the flip side, will a thinner, healthier population spend more on lifestyle and fitness? Healthier product options and fitness and athletic brands could be key beneficiaries of this trend as consumers change their spending habits and shape.

Finally, GLP-1 drugs could also help other businesses indirectly like airlines, which could save 27.6 million gallons of fuel per year, at a cost of \$80 million, if the average passenger weighed 10 less pounds.²⁷

Index approach

The **VettaFi Weight Loss Drug & Treatment Index (THINR)** consists of 70% of drug developers/manufacturers and 30% of enablers.

Drug developers/manufacturers are pharmaceutical and/or biotech companies with either a branded GLP-1 agonist product or a product in the GLP-1 drug development pipeline in FDA clinical trials.

Enablers are companies involved with the outsourced development and manufacturing of GLP-1 agonist drugs, also known as contract development and manufacturing organizations (CDMOs), companies conducting measurement and analysis of GLP-1 agonist drugs, and companies involved in the distribution or administration of GLP-1 agonist drugs, including the coordination of prescriptions and drug-delivery mechanisms such as injection pens.

²⁴ JP Morgan, "The increase in appetite for obesity drugs," November 29, 2023, <https://www.jpmorgan.com/insights/global-research/current-events/obesity-drugs>

²⁵ Nic Sochovsky and Helena Miles, Morgan Stanley, "GLP-1: The Weight Speculation," December 2023, https://www.morganstanley.com/im/publication/insights/articles/article_geoglp1_us.pdf?1714161368409

²⁶ Matthew Fox, "The disruptive effect of weight loss drugs like Ozempic could have surprising impacts on the stock market. Here are potential winners and losers." September 24, 2023, <https://markets.businessinsider.com/news/stocks/ozempic-wegovy-glp1-weight-loss-drugs-stock-market-winners-losers-2023-9>

²⁷ Cork Gaines, Allie Kelly, "How Ozempic could change the economy as we know it," Business Insider, March 22, 2024, <https://www.businessinsider.com/semaglutide-wegovy-ozempic-weight-loss-healthcare-airlines-economy-productivity-2023-11>

To qualify for inclusion in the index, companies must be members of the VettaFi S-Network Developed World Equity 5000 Index or the VettaFi Developed World Index and meet a minimum market capitalization requirement of \$500 million USD. Constituents are float-adjusted market cap weighted within their segment allocation as follows:

Drug manufacturer segment – 70% weight allocation

Constituent maximum caps

- Companies at commercial or phase 3 stage: constituents are capped at 15%
- Companies at phase 2 or lower stage: constituents are capped at 5%

Enabler segment – 30% weight allocation

Constituent maximum caps

- Constituents capped at 5%

Additionally, the sum of all constituent weights greater than 5% must be less than or equal to 45% of the total index. Capped weights are redistributed within their segment. The index is rebalanced quarterly.

Bracketested results from 4-30-2024 appear in the chart below. A basket of GLP-1 drug manufacturers and enablers has significantly outpaced the overall market on a year-to-date basis.

Currently, there are 21 holdings in the VettaFi Weight Loss Drug and Treatment Index (THINR), with the top 10 holdings appearing below. The index portfolio currently holds 14 drug manufacturers and 7 enablers.

VettaFi Weight Loss Drug & Treatment Index (THINR)



Index returns

	Quarter 1				Quarter 2				Quarter 3				Quarter 3				Year
	J	F	M	Q1	A	M	J	Q2	J	A	S	Q3	O	N	D	Q4	
2024	5.69%	9.57%	4.65%	21.18%	-2.51%			-2.51%									18.14%
2023	1.72%	0.29%	4.87%	6.99%	3.72%	-0.90%	1.33%	4.16%	0.44%	6.38%	-3.05%	3.59%	-6.26%	8.90%	3.62%	5.78%	22.11%
2022	-9.67%	-1.71%	6.53%	-5.42%	-5.00%	1.93%	-3.44%	-6.50%	3.34%	-7.56%	-6.51%	-10.69%	6.59%	8.99%	0.64%	16.93%	-7.65%
2021							2.59%	2.59%	3.51%	6.06%	-2.44%	7.10%	4.20%	-2.69%	5.40%	6.87%	17.42%

Source: VettaFi Indexes

Holdings summary

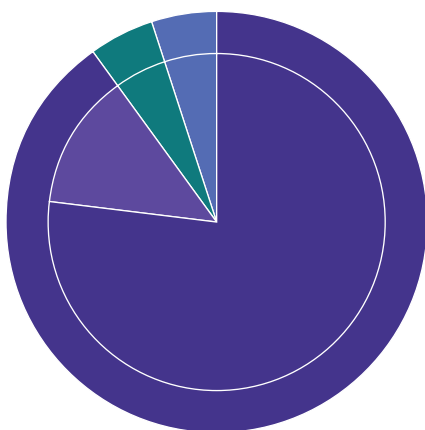
	THINRT Index
Equity holdings	21.00
Effective number of holdings	13.00
Effective holdings ratio	0.62
Weight in top 10 names	70.97

Effective number of holdings is a measure of portfolio concentration that ranges between 1 (weight of the portfolio concentrated in a single stock) and the total number of constituents of the portfolio. Everything else being equal, a low effective number of holdings can be interpreted as a high concentration of the portfolio.

Top 10 holdings (%)

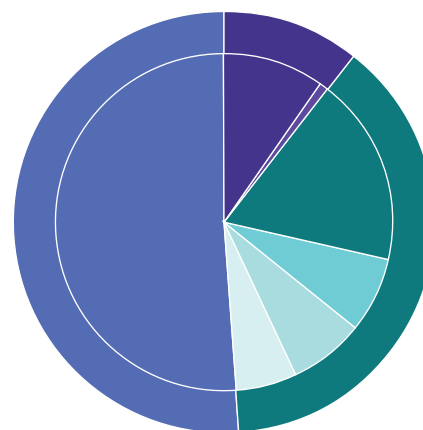
Novo Nordisk A/S Class B	14.62
Eli Lilly and Company	14.62
AstraZeneca PLC	5.92
Merck & Co., Inc	5.48
West Pharmaceutical Services, Inc.	5.16
Catalent Inc	5.14
Amgen Inc	5.13
Viking Therapeutics, Inc.	4.98
Thermo Fisher Scientific Inc.	4.97
FUJIFILM Holdings Corp	4.92

Sector and geographical allocation charts



Sector/industry group	THINRT Index
Healthcare	90.21%
Biopharma	77.07%
Healthcare Equipment & Services	13.14%
Materials	4.87%
Chemicals	4.87%
Technology	4.92%
Tech Hardware & Equipment	4.92%

Shaded area indicates top industries



Region/country	THINRT Index
Asia	10.75%
Japan	9.79%
South Korea	0.97%
Europe	38.30%
Denmark	17.98%
Germany	7.13%
Switzerland	7.28%
United Kingdom	5.92%
North America	50.94%
United States	50.94%

The index portfolio is predominantly large-cap, with some mid-cap exposure

Market cap	THINRT Index
Large Cap	80.43%
Mid Cap	19.03%
Small Cap	0.54%

Conclusion

- **Obesity is a growing global problem:** One-eighth of the global population is living with obesity. Beyond the mental and physical toll obesity poses at the individual level, it has a negative macroeconomic impact on the global economy due to negative health impacts and lost productivity.
- **GLP-1 is spurring a diet drug revolution:** GLP-1 drugs are proving to be a breakthrough treatment for weight loss, promoting reductions in body weight by 10-20% and reducing consumption volumes by as much as 50%.
- **GLP-1 drugs may have therapeutic indications beyond diabetes and weight loss:** In a recent landmark study, GLP-1 drugs were found to reduce the incidence of cardio events and stroke by 20% in non-diabetic patients. But beyond cardiovascular disease, research is being conducted to explore its effectiveness as a treatment for many other medical conditions as well.
- **GLP-1 drugs are a disruptive economic force:** GLP-1 drugs are expected to disrupt not just health care, but many other sectors and industries. GLP-1 drugs are a disruptive economic force. Investment research firms estimate the market for GLP-1 drugs will grow to \$100 billion by 2030. By promoting healthier living and boosting productivity, these new drugs hold the potential to increase U.S. GDP levels by as much as 1% in the coming years.

To learn more about VettaFi Indexing click [here](#)

About VettaFi

VettaFi is a provider of indexing, data & analytics, industry-leading conferences, and digital distribution services to ETF issuers and fund managers. It operates the ETFdb, Advisor Perspectives, and ETF Trends websites and the LOGICLY portfolio analytics platform – engaging millions of investors annually – empowering and educating the modern financial advisor and institutional investor. VettaFi owns and administers the EQM Indexes Series. For more information, please visit: www.vettafi.com.

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