New weight loss drugs: Biotech's mission to end obesity

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Worldwide adult obesity has more than doubled since 1990, and, even more shockingly, adolescent obesity has quadrupled, becoming an ever-growing health threat. The latest figures from the World Health Organization (WHO) estimate that, in 2022, more than 2.5 billion adults in the world were overweight, with 890 million of those being officially obese. Meanwhile, in 2024, 35 million children under the age of five were thought to be overweight, and more than 390 million children and adolescents aged between five and 19 years old were considered overweight – 160 million of whom officially had obesity.

Obesity can be defined as abnormal or excessive fat accumulation that presents a risk to health, with a body mass index (BMI) of over 30 being the official indicator of whether an individual is obese or not.

Statistics from WHO show that at least 2.8 million people die each year as a result of being overweight or obese. This is because obesity is essentially a precursor to disease, potentially leading to type 2 diabetes, heart disease, and even some cancers.

Generally, the advice for overweight and obese people is to eat a healthy diet and do regular exercise, but the truth is that it is not quite as simple as that. Hunger is controlled by powerful hormones and chemicals in the brain, and involves areas of the brain responsible for cravings and rewards. In many individuals with obesity, the hormones, and even the brain's reward system, are dysfunctional, altering eating behavior and causing a strong physiological desire to eat more.

Fortunately, this is where weight loss drugs come in; they can deal with the hormones related to obesity directly, which, in turn, can change behavior by regulating appetite and reducing cravings. With this in mind, obesity is now finally being treated as the root cause of disease, with a flurry of biotech companies racing to develop new weight loss drugs that are more and more effective in reducing obesity, as well as producing fewer side effects for the people taking them.

Dr. Kathryn Stecco, Medical Monitor at Novotech (CRO), told Labiotech that, as physicians and researchers learn more about the complex factors that promote obesity, it opens up opportunities to develop drugs that can target different pathways, either alone or in combinations.

Now, in a rapidly evolving treatment landscape, Stecco said the race is on to target new genetic, epigenetic, hormonal, metabolic, and cellular pathways that regulate adipose tissue growth, energy balance, and metabolic health. "These approaches aim to improve tolerability, efficacy, and patient adherence, address comorbidities, while moving beyond traditional weight-loss paradigms."

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GLP-1 agonists: A breakthrough for obesity

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Designed to mimic the glucagon-like peptide-1 (GLP-1) hormone receptor that is released in the gut in response to eating, GLP-1 agonists had originally been developed as a treatment for diabetes – but when one of the side effects of these medications was found to be weight loss

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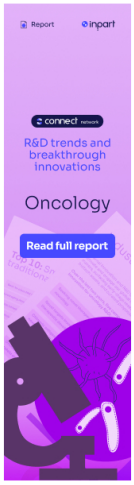

diabetes – but when one of the side effects of those medications was found to be weight loss, companies saw the promise and began to develop them as anti-obesity drugs as well.

This is thanks to the fact that GLP-1 agonists, also known as incretin-based therapies, have several effects on individuals with obesity, including slowing down stomach emptying, reducing appetite by acting on the brain, and boosting the release of insulin, helping to regulate blood sugar levels.

When Novo Nordisk's GLP-1 drug Wegovy was approved by the U.S. Food and Drug Administration (FDA) for the treatment of obesity in 2021 – after it had already been approved under the brand name Ozempic for type 2 diabetes in 2017 – it was viewed by experts, clinicians and patients as a breakthrough for weight loss treatment. This was the first drug approved for the indication that used the active ingredient semaglutide.

It also happened to be the first new weight loss drug to be approved since Saxenda in 2014, and is much more effective in allowing people to lose weight. In clinical trials, Wegovy was shown to reduce body weight in individuals with BMIs of 27 or greater by 15% over a period of 68 weeks and, on average, people lost around an eighth of that weight in the first month.

Wegovy is also given as a once-weekly injection at a dose of 2.4 milligrams – an improvement on earlier formulations like Saxenda, which needed to be given on a daily basis, causing a significant burden to patients.

The sheer success of Wegovy saw Novo Nordisk bring in 58.2 billion kroner ($8.8 billion) in sales of the drug in 2024. It also became Europe's most valuable company for a while, before being unseated by German software developer SAP SE in March 2025. In fact, at the beginning of September 2023, the Danish giant's stock market value exceeded Denmark's entire economic output, to the extent that Denmark's economy ministry actually doubled its growth forecast for 2023 to 1.2%.

Despite its popularity and efficacy, however, it turned out that Wegovy was only a stepping stone to bigger conquests within the obesity field for Novo and other pharma and biotech giants.

inpart New technologies related to weight loss drugs

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The hunt for superior efficacy: Next-generation incretin-based therapies are already in the pipeline

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Indeed, the obesity field is advancing at an incredible pace, particularly when it comes to the development of incretin-based therapies like GLP-1 agonists.

According to Stecco, the recent success of single and dual gut hormone receptor agonists has already spurred the emergence of triple and quadruple gut hormone receptor agonists, as well as the combination of gut hormone receptor agonists with complementary peptide hormones.

In a field with so many competitors, efficacy reigns supreme, and time is of the essence. So, which companies are currently leading the race for next-generation incretin-based therapies?

Novo Nordisk vs Eli Lilly: Who will emerge victorious in the big pharma obesity battle?

Eli Lilly upped the ante in the obesity race in 2023 when the FDA approved its injectable dual glucose-dependent insulinotropic polypeptide (GIP)/GLP-1 receptor Zepbound. Containing the active ingredient tirzepatide, the drug had initially been approved the previous year under the brand name Mounjaro for type 2 diabetes.

This brought the pharma giant into direct competition with Novo, with the two companies now undisputed leaders in the obesity market. In fact, their weight loss drugs became so popular that they actually experienced prolonged shortages, forcing both companies to heavily invest in scaling up drug production.

The "efficacy race" between the two companies has heated up of late, with Eli Lilly recently gaining a significant edge when it comes to comparative data between Zepbound and Wegovy. At the end of last year, Eli Lilly announced topline results from a phase 3b trial that showed that, on average, Zepbound led to a superior weight loss of 20.2% compared to 13.7% with Wegovy. This is likely due to Zepbound's dual effects on both GLP-1 and GIP (whereas Wegovy only targets GLP-1).

Nevertheless, Novo – which decided to bet on a new chief executive officer (CEO) earlier this month to regain its weight loss drug edge over Eli Lilly – is now focusing on developing its own dual therapy, called amycretin, which targets both GLP-1 and amylin, another type of hormone that plays a role in regulating blood sugar, appetite, and satiety. In January, Novo announced that the candidate elicited up to 22% weight loss in a phase 1b/2a trial.

In the never-ending battle, Novo also recently took a bet on a "triple G" obesity drug by entering into a licensing agreement worth up to $2 billion with United Laboratories. This gives Novo access to United's triple hormone receptor agonist, which targets GLP-1, GIP, and glucagon receptors.

According to BioSpace, analysts believe that this deal is to "take aim at Lilly's retatrutide," which is also a triple G agonist that was shown in 2023 to result in an average weight loss of 24.2% at 48 weeks in a phase 2 study, and is now in late-stage trials. Triple G agonists are thought to be able to elicit higher levels of weight loss than single or dual agonists due to the fact that they act on multiple hormone receptors.

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Furthermore, the two giants also happen to be competing to bring the first oral weight loss pill to the market. It is a close race, but Novo inched one step closer to being the first to cross the finishing line when the FDA accepted its New Drug Application (NDA) for an oral formulation of Wegovy at the start of this month, with the FDA's verdict expected in the fourth quarter of 2025. The NDA acceptance was based on results from a phase 3 study demonstrating that daily oral Wegovy could match the weekly injectable in lowering bodyweight.

Meanwhile, in April, Eli Lilly announced that its oral GLP-1 treatment orforglipron significantly lowered blood glucose levels in patients with type 2 diabetes, achieving what BMO Capital Markets described as "injectable-like efficacy." A few days after the late-stage win, Eli Lilly's CEO, David Ricks, told Fox Business that, while the study was primarily in diabetes, the company's first drug application for orforglipron will be for chronic weight management later this year.

Oral weight loss pills could help increase the market size even further due to their convenience compared to injections. As Martin Holst Lange, Novo's executive vice president of development, said in a company press release back in 2023, "the choice between a daily tablet or weekly injection for obesity has the potential to offer patients and healthcare providers the opportunity to choose which suits individual treatment preferences."

Another advantage of oral drugs is that they are easier to manufacture than injections, which come in the form of single-use pens. This could alleviate potential supply shortages like those experienced by Novo and Eli Lilly. Pills are also generally cheaper than injections, but it is unclear if this will be the case with obesity drugs.

Considering injectable weight loss drugs caused such a frenzy, giving people the option of a pill that can provide the same efficacy will likely result in even higher demand from consumers. We will have to wait and see if this will be the case, as Novo looks set to receive approval to bring the first oral weight loss pill to the market.

Other big players also gain ground in the incretin-based weight loss field

Elsewhere in the pharma industry, Roche's acquisition of Carmot Therapeutics in 2023 brought the Swiss giant into the obesity race, providing it with a trio of clinical candidates for obesity and diabetes. Two of these candidates, CT-388 and CT-996, have recently produced positive phase 1 results.

In May 2024, Roche reported phase 1b results showing that a once-weekly injection of CT-388 – a dual GLP-1/GIP receptor agonist – over 24 weeks achieved a clinically meaningful and statistically significant mean placebo-adjusted weight loss of 18.8%, with all patients on the drug losing at least 5% of their body weight. The candidate is now being tested in phase 2b trials in people who are overweight or have obesity with and without type 2 diabetes. Meanwhile, CT-996, a once-daily oral small molecule GLP-1 receptor agonist, achieved positive phase 1 results in July 2024, in which participants with obesity lost 7.3% of their body weight after just four weeks of treatment.

AstraZeneca also announced positive early data for its lead weight loss candidate in November 2024 at The Obesity Society's ObesityWeek 2024 meeting, showing that it resulted in 5.8% weight loss after four weeks of treatment in type 2 diabetes patients. The company licensed the drug, an oral GLP-1 receptor blocker called AZD5004, from Shanghai-based Ecogene in 2023. The candidate is currently being evaluated in two phase 2b studies in obesity and type 2 diabetes, with readouts expected at the end of 2025 and early 2026, respectively.

Viking Therapeutics also captured attention at ObesityWeek 2024, presenting compelling phase 1 data on its oral GLP-1/GIP dual agonist, VK2735. Over 28 days, relative to placebo, the 100mg dose of the candidate cut 6.8% of participants' body weight. According to Fierce Biotech, William Blair analysts said they had been hoping for weight loss in the range of 5% to 6% for the highest dose, which would have been in line with the 5% seen by Novo's amycretin. Therefore, the 6.8% weight loss achieved by VK2735 meant Viking's candidate appeared to have "outmaneuvered" amycretin.

Biopharma giant Amgen is also seeing positive results for its most advanced obesity asset MariTide, a monoclonal antibody linked to a pair of peptides designed to boost GLP-1 receptor activity while tamping down on the receptor for GIP. In November 2024, the company announced that MariTide had achieved average weight loss of up to 20% over 52 weeks in people who were overweight or had obesity, but without type 2 diabetes. According to Amgen, its candidate is the first obesity treatment with monthly or less frequent dosing to demonstrate safe and effective weight loss in a phase 2 study. Amgen is now testing the drug in a phase 3 program.

Beyond GLP-1 agonists: Which other types of new weight loss drugs are in the pipeline?

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Amylin analogs: The latest obesity trend competing against GLP-1 drugs

Along with dual or triple incretin-based receptor agonists, amylin analogs are the latest trend in weight loss medication. Compared to GLP-1 therapies, these drugs could lead to an improved quality of weight reduction, resulting in lower loss of lean mass relative to fat. They could also be used in combination with other drugs, such as incretin-based therapies, to enhance weight loss even further.

Naturally, Novo and Eli Lilly are developing their own amylin analog therapies. As mentioned previously, Novo is focused on advancing amycretin, targeting both GLP-1 and amylin, and is also developing a drug called CagriSema, which combines semaglutide and a new drug called cagrilintide, a dual amylin and calcitonin receptor agonist that is designed to enhance semaglutide's effects. However, Novo's initial vision of achieving 25% plus weight loss with its new drug took a big hit earlier this year. Its stock fell in March when the company announced results from a second phase 3 trial showing that patients taking CagriSema only achieved 15.7% weight loss after taking CagriSema for 68 weeks.

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Eli Lilly, meanwhile, is a little further behind in the development of its most advanced amylin agonist, a weekly therapy called eloralintide currently being tested in a phase 2 trial in combination with tirzepatide in non-diabetic obese people. The readout for this study is expected in mid-2025. The pharma giant is also running two other clinical trials testing the combination, including another mid-stage study in obese and overweight type 2 diabetes patients with an initial completion date in June 2026, and a phase 1 trial in nondiabetic patients scheduled to be completed in October 2025.

Roche also recently got involved in amylin agonists after it entered into a collaboration and licensing agreement with Zealand Pharma to co-develop and co-commercialize Zealand's long-acting candidate, petrelintide, which showed promising efficacy and safety data in a phase 1b trial, in which the drug achieved an average weight reduction of 8.6% at 16 weeks. The Roche-Zealand deal will concentrate on developing petrelintide as a monotherapy and as a fixed-dose combination with Roche's CT-388.

In addition to the aforementioned frontrunners of the amylin drug weight loss field, AbbVie, AstraZeneca, and startup Metsera are also testing amylin drugs.

Glyscend Therapeutics announces positive topline phase 2a results for diabetes and obesity drug

Glyscend Therapeutics, meanwhile, is looking to develop a new generation of orally administered first-in-class gut-targeted polymer therapies and is progressing GLY-200 through the clinic for the treatment of type 2 diabetes and obesity.

"Our lead compound, GLY-200, is designed to alter duodenal signaling by crosslinking to native intestinal mucin in a pH-dependent manner, enhancing its natural barrier properties. This enhanced mucus barrier results in a pharmacologic 'duodenal exclusion' that may non-invasively and safely reproduce many of the beneficial effects of metabolic surgery, while avoiding the complications associated with invasive surgeries and procedures," explained Glyscend's co-founder Ashish Nimgaonkar.

In developing this treatment, the company wanted to address the need for non-invasive, scalable alternatives that could replicate the effectiveness of metabolic surgery, which is invasive, expensive, and can come with possible complications.

"Moreover, none of the currently available treatments are considered disease-modifying, except for metabolic surgery. It has immediate profound effects on improving blood glucose and weight loss, with longer-term reductions in macro- and microvascular complications," said Nimgaonkar.

It was recently announced that data across completed phase 1 and 2a trials demonstrated that the novel mechanism of GLY-200 offers significant and clinically relevant reductions in postprandial glucose and body weight. The candidate is now being tested in a phase 2 obesity trial, in which the first patient was dosed in June 2024.

APHD-012: Aphaia Pharma's new weight loss drug candidate shows promise

Meanwhile, Aphaia Pharma is also developing a promising oral drug candidate for weight loss, APHD-012, with a focus on why L-cells – nutrient-sensing cells in the distal part of the intestine – in patients with metabolic disease are largely deprived from contact with food, as this leads to a lack of endocrine, neuroendocrine, and neuronal stimulation, in turn promoting the progression of obesity.

"One reason is they have motility problems with their small intestines, so the passage of food is delayed, or is slowed down. They eat large quantities of food in a composition that has never been optimized, which actually means far too many proteins, far too many fats, and not enough carbohydrates, and not enough fibers on top of that," explained Steffen-Sebastian Bolz, chief scientific officer (CSO) of Aphaia Pharma.

Another reason, he said, is the fact that the food we consume today – particularly in Western countries – is highly refined; we consume industrialized food whereby the different components, such as sugar, have been separated and then put back into a processed product.

"We knew we would need to formulate something that bypasses the food bolus independent of motility to get to the distal part of the intestine where nutrient-sensing cells are (L-cells). We designed something that behaves like a fluid, because fluid just falls down...and we had to decide what we wanted to bring down there," said Bolz.

"We developed small beads containing glucose that travel down and hit L-cells with a very low interpatient variability. And more or less at exactly 1.5 hours after ingestion, you see the increase in the key metabolic hormones GLP-1, glicentin, oxyntomodulin, etc. It's very promising because we're just emulating what nature has defined over millions of years. We did not reinvent anything."

In June 2024, Aphaia Pharma announced positive results for its weight loss candidate in a phase 2 trial, which met its primary endpoint by showing that APHD-012 improved glucose tolerance in individuals with a pathological oral glucose tolerance test (OGTT) after six weeks of administration.

Tough competition: A crowded market for weight loss drugs

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As obesity becomes more prevalent in the general population, the weight loss drug market grows with it. In fact, with more and more biotech companies looking to develop new weight loss drugs, it is estimated that the global obesity therapeutic market could be worth $105 billion by around 2030.

Despite the new technologies we have already seen in the last two years or so, Dr. Stecco pointed out that there are still more therapeutic strategies emerging in the weight loss field, such as novel molecular approaches like non-peptide formulations and innovative delivery

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systems, muscle-preserving therapies aiming to mitigate the muscle loss that occurs when you lose weight in general, and expanded therapeutic targets to address obesity-related comorbidities such as achieving remission of obstructive sleep apnea, improvement liver fibrosis, reducing kidney disease risk.

"Obesity is a real disease with both near- and long-term clinical and psychosocial consequences to the individual," said Nimgaonkar. "We therefore believe strongly that these patients should have access to effective therapies that are easy to administer and affordable."

As the money continues to pour in for weight loss medications – a good example of which is Verdiva Bio's $411 million series A fundraising to advance its next-gen obesity drugs – it does seem like patients will soon be spoiled for choice when it comes to weight loss drug selection.

Ultimately, the race is on to develop a drug with superior efficacy and safety to the currently approved crop of medications, as companies attempt to unseat Novo Nordisk and Eli Lilly from their thrones to make room in a market that is set to be incredibly crowded.

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