Drug Development: Peter Charlish

Change coming to the weight loss sector

Ever since Novo Nordisk A/S's Saxenda (liraglutide) became the first glucagon-like peptide-1 (GLP-1) receptor agonist to be approved for chronic weight management in September 2014, the anti-obesity sector has shown steady growth. According to IQVIA Inc, the provider of analytics and clinical research services to the life sciences industry, the global obesity medicines market reached $66 billion in list price sales value in 2025, and is forecast to rise to $92 billion this year, before reaching between $105 billion and $200 billion by 2027 and beyond.

Currently Novo Nordisk's Wegovy/Ozempic (semaglutide) and Eli Lilly & Co's Zepbound/Mounjaro (tirzepatide) dominate the GLP-1 sector, but the competition is about to heat up. A number of factors are driving this trend. The first of these is the appearance of GLP-1 drugs that can be given by mouth. Novo Nordisk actually led the way in this respect: in February 2026 it introduced Ozempic tablets in the US, although so far only for the management of type 2 diabetes. Ozempic tablets must be taken first thing in the morning on an empty stomach, with no food or drink for 30 minutes.

Then in April 2026, the US Food and Drug Administration approved Lilly's Foundayo (orforglipron), for the treatment of adults with obesity, and for certain adults with overweight who also have weight-related medical problems. Foundayo is a once-daily small molecule orally active GLP-1 receptor agonist that can be taken any time of the day without restrictions on food and water intake. And in August 2026, the UK became the first European country to approve Foundayo for weight management and type 2 diabetes. Orforglipron was discovered by Chugai Pharmaceutical Co, and licensed to Lilly in 2018.

Importantly, there is a crucial distinction to be made between the tablet formulation of Ozempic, on the one hand, and Foundayo, on the other. Semaglutide is a peptide, and as such it is vulnerable to digestion in the stomach if given by mouth, thus reducing its effectiveness. Foundayo is a non-peptide GLP-1 agonist, and does not suffer from this limitation. What influence this consideration will have on the market share of each product, if and when oral semaglutide is approved for the management of weight loss, remains to be seen.

Multiple receptors

Another factor likely to challenge the current situation is the growing interest in agents that target multiple receptor sites. The first of these, of course, was Lilly's tirzepatide, which activates both GLP-1 and GIP (glucose-dependent insulinotropic polypeptide) receptors. An analysis of data from *clinicaltrials.gov*, the online database of medical research studies run by the US government, shows that, of the approximately 30 products in advanced clinical trials for weight management, five are dual GLP-1/GIP receptor agonists, two are GLP-1/amylin dual agonists, and two are GLP-1/GIP/glucagon triple agonists. What is also noticeable is that over half of these products are being developed by Chinese companies.

Probably the most significant of these drugs acting on multiple receptors is Lilly's retatrutide, a once-weekly injectable triple agonist targeting GLP-1, GIP and glucagon receptors. In May this year, Lilly announced positive topline results from TRIUMPH-1, a Phase 3 clinical trial evaluating the efficacy and safety of retatrutide. This was an 80-week randomised double-blind placebo-controlled master trial comparing retatrutide's efficacy and safety with placebo in adults with obesity or overweight. The trial also included two basket trials (a type of clinical study that tests a single drug or treatment across several different diseases) for knee osteoarthritis pain and for moderate-to-severe obstructive sleep apnoea, both potential indications for weight control.

The trial showed that once-weekly retatrutide achieved significant weight loss at 80 weeks, along with improvements in cardiometabolic health markers and obesity-related complications. Weight loss efficacy was dose-dependent, with mean weight reductions of 19.0% with the 4 mg dose, 25.9% with the 9 mg dose, and 28.3% with a dose of 12 mg, compared to 2.2% for placebo. 45.3% of participants on 12 mg lost 30% or more of their body weight, a level historically only seen with bariatric surgery. Cardiometabolic markers improved, including waist circumference, non-HDL cholesterol, triglycerides, systolic blood pressure, and high-sensitivity C-reactive protein, and functional improvements. Functional improvements included reductions in knee osteoarthritis pain scores and apnoea-hypopnoea index scores for patients with sleep apnoea. Adverse events were typical of the incretin/agonist class, primarily gastrointestinal

Hormonal control of appetite and body weight

Both hunger and body weight are regulated by a delicate balance of hormones that communicate with the brain. For example, ghrelin is formed in the stomach and stimulates appetite, while hormones like GLP-1, cholecystokinin and leptin suppress it.

From a therapeutic point of view, several of these hormones are important. GLP-1 and GIP are both members of a group of gut hormones known as incretins. They promote insulin release from the pancreas when blood sugar is high, stop the liver from synthesising extra sugar, delay gastric emptying and communicate with the brain to promote satiety.

Pancreatic hormones glucagon and amylin help control energy intake and suppress appetite. Amylin acts directly on the brain to promote a feeling of fullness while slowing gastric emptying. Glucagon signals the liver to reduce further food intake and works in concert with other metabolic signals.

issues like nausea, diarrhoea, vomiting, and constipation. Discontinuations due to adverse events ranged from 4.1% to 11.3% across active doses compared with 4.9% for placebo.

Another GLP-1/GIP/glucagon triple receptor agonist in advanced clinical trials is UBT251, a long-acting synthetic peptide being developed by Novo Nordisk. The company acquired global rights to UBT251 from the United Bio-Technology (Hengqin) Co of China in March last year in a deal worth up to $2 billion, obtaining exclusive worldwide rights to develop, manufacture and commercialise the drug, excluding in mainland China, Hong Kong, Macau and Taiwan. At its R&D investor event in New Orleans, US, in June 2026, Novo Nordisk discussed the findings from a Phase 2 study comparing the efficacy and safety of UBT251 with placebo in a Chinese population. UBT251 achieved up to 19.7% weight loss, and more than 48% of participants achieved weight loss of at least 20%. The company said that UBT251 appeared to have a safe and well-tolerated profile, with final readout of data expected in 2027.

For its part, United Bio-Technology is planning a Phase 3 study to evaluate the efficacy and safety of UBT251 injection in overweight/obese patients. The study will be carried out at the Peking University People's Hospital in Beijing. Completion of the 600-subject study is expected towards the end of next year.

Dual agonists

Meanwhile Novo Nordisk is not putting all its eggs in one basket. It is conducting clinical trials of two products that are dual GLP-1/amylin agonists. The first is amycretin (NNC0487-0111), a dual agonist medication that acts on both GLP-1 and amylin receptors via a single molecule. In a Phase 1b/2a trial, the safety profile of amycretin was similar to that of other incretin-based therapies, with most adverse events of a gastro-intestinal nature. The company is planning the AMAZE programme of Phase 3 studies of subcutaneous and oral amycretin in conditions like obesity, obstructive sleep apnoea, and knee osteoarthritis.

The other GLP-1/amylin dual agonist under investigation by the Danish company is zenagamtide. In a Phase 2 trial comparing subcutaneous zenagamtide with placebo, the drug achieved a weight loss of up to 14.6%, the company has said. As with similar experimental medicines, it appeared to be well tolerated.

Lastly, mention should be made of CagriSema, a once-weekly subcutaneous treatment being developed by Novo Nordisk for adults with overweight or obesity as part of the REDEFINE programme. CagriSema is a fixed-dose combination of semaglutide and the long-acting amylin analogue, cagrilintide. In December 2025, Novo Nordisk submitted a New Drug Application to the US Food and Drug Administration for CagriSema's weight management potential: a decision is expected in the 2026 fourth quarter.

Several companies are taking the route of dual GLP-1/GIP agonism (like Lilly's tirzepatide). These include Viking Therapeutics Inc of the US and Fujian Shengdi Pharmaceutical Co, a wholly-owned subsidiary of Jiangsu Hengrui Pharma based in Fujian, China. Viking's candidate, VK2735, is being developed in both oral and subcutaneous formulations for the potential treatment of various metabolic disorders including obesity. In the Phase 2 VENTURE trial of subcutaneous VK2735 for obesity there was a statistically significant weight loss in patients after 13 weeks, with up to 14.7% reduction from baseline. VK2735 demonstrated encouraging safety and tolerability.

Fujian Shengdi Pharmaceutical's candidate, ribupatide (HRS9531), is being developed globally (except for Greater China) by Kailera Therapeutics Inc as KAI-9531. In 2025, the two companies announced positive top-line data from a Phase 3 clinical trial of subcutaneous ribupatide in the treatment of obesity. The trial met both its primary endpoints, showing superior weight loss and a higher percentage of participants achieving significant weight reduction compared with placebo.

Other dual GLP-1/GIP agonists in advanced development include Guangdong Raynovent Biotech Co's RAY1225 and Hangzhou Zhongmei Huadong Pharmaceutical Co's HDM1005.

Bucking the trend, Amgen Inc is at an advanced stage of development with MariTide (maridebart cafraglutide), an antibody-peptide conjugate that activates the GLP-1 receptor and antagonises the GIP receptor. MariTide is currently the subject of a number of trials related to obesity. MARITIME-1 is a Phase 3 study of MariTide for chronic weight management in adults living with obesity or overweight, without type 2 diabetes; MARITIME-2 is a Phase 3 study for chronic weight management in adults living with obesity or overweight, together with type 2 diabetes; while several other trials are underway in patients with overweight and other conditions such as cardiovascular disease or obstructive sleep apnoea. Amgen says MariTide's long-acting design allows for a monthly dosing schedule and continued use with as few as four or six doses annually.

Finally, two other products that are in late development and act via receptors other than GLP-1 should be mentioned. The first is Innovent Biologics Inc's IBI362, which acts via both GLP-1 and glucagon receptors. It is the subject of several trials in China of overweight individuals and related conditions. The other is Regeneron Pharmaceuticals Inc's mibavademab, which targets leptin receptors. It is being studied to determine whether combining tirzepatide with mibavademab will result in more weight loss in adult participants than tirzepatide alone.

Chinese companies

Returning to the *clinicaltrials.gov* data referred to earlier, there appear to be around a dozen additional companies, mainly Chinese, developing pure GLP-1 agonists. Some of these have already received marketing approval in China, such as Hangzhou Sciwind Biosciences Co's ecnoglutide. China's National Medical Products Administration (NMPA) approved ecnoglutide injection in March 2026 for chronic weight management in Chinese adults with overweight or obesity. The company says ecnoglutide selectively activates the cAMP signalling pathway and minimises β-arrestin recruitment, which distinguishes it from conventional non-biased GLP-1 receptor agonists. This mechanism delivers potent and sustained weight loss with no obvious plateau phase, Sciwind says, and supports improvement in metabolism and reduced chronic disease risk alongside weight reduction. Furthermore, because ecnoglutide is composed entirely of natural amino acids it is simpler to

manufacture than some other GLP-1 agonists.

Generally speaking, each of the GLP-1 agonists under investigation has something which differentiates it from the first generation of GLP-1 agonists, such as oral availability or extended duration of action. Gan & Lee Pharmaceuticals, for example, which is headquartered in Beijing, recently reported that its independently developed biweekly GLP-1 agonist, bofanglutide, met its primary endpoints in both the pivotal GRADUAL Phase 3 weight management trial in China and a pivotal Phase 2 study in the US. Gan & Lee has commercial agreements relating to bofanglutide with a number of non-Chinese companies such as Lupin Ltd of India and JW Pharmaceutical Corp of Korea.

At least one Chinese company, Hangzhou Zhongmei Huadong Pharmaceutical, a major Sino-foreign joint venture pharmaceutical company, is developing a semaglutide biosimilar product.

One further factor that may influence the future direction of the weight control sector is the quality of the weight loss achievable with incretin therapy. Specifically, while GLP-1 agonists and similar products are effective at reducing body fat, they can also reduce muscle mass, which is not desirable. The Korean company Hanmi Pharmaceutical Co is developing HM17321, a potential first-in-class treatment which the company claims promotes weight loss while simultaneously preserving lean body mass. It has just entered an exclusive licensing agreement with Genentech Inc, part of the Roche Group, for the development, manufacture and commercialisation of HM17321 outside South Korea.

Investigational products mentioned in this article

Product	Developer	Mechanism
amycretin	Novo Nordisk	GLP-1/amylin dual agonist
bofanglutide	Gan & Lee	GLP-1 agonist
CagriSema	Novo Nordisk	GLP-1/amylin dual agonist
Ecnoglutide	Hangzhou Sciwind	GLP-1 agonist
HDM1005	Hangzhou Zhongmei Huadong	GLP-1/GIP dual agonist
HM17321	Hanmi/Genentech	CRF2 agonist
IBI362	Innovent	GLP-1/glucagon dual agonist
MariTide	Amgen	GLP-1 agonist/GIP antagonist
mibavademab	Regeneron	Leptin agonist
orforglipron	Chugai/Lilly	GLP-1 agonist
RAY1225	Guangdong Raynovent	GLP-1/GIP dual agonist
retatrutide	Lilly	GLP-1/GIP/glucagon triple agonist
Ribupatide	Fujian Shengdi/Kailera	GLP-1/GIP dual agonist
UBT251	Novo Nordisk	GLP-1/GIP/glucagon triple agonist
VK2735	Viking Therapeutics	GLP-1/GIP dual agonist
zenagamtide	Novo Nordisk	GLP-1/amylin dual agonist

HM17321 is a long-acting corticotropin-releasing factor 2 (CRF2) receptor-selective urocortin-2 (UCN2) analogue: urocortin itself is a human protein involved in a number of physiological responses to stress, including the modification of appetite and food intake. Hanmi says that preclinical studies have demonstrated both quantitative and qualitative improvements in weight reduction when HM17321 is used as a monotherapy and in combination with GLP-1-based treatments. In November 2025, Hanmi received clearance from the US FDA to begin a Phase 1 clinical trial of HM17321 to assess its safety, tolerability, pharmacokinetics and pharmacodynamics in healthy volunteers and people with obesity.

Under the terms of the deal with Genentech, Hanmi will receive an initial payment of $190 million, although the total deal could be worth as much as $2.3 billion when development, regulatory and commercial milestone payments are taken into account. Furthermore, Hanmi will be eligible to receive tiered royalties on future product sales. Hanmi will retain responsibility for completing the Phase 1 trial, after which Genentech will take over development starting with Phase 2 trials.

Hanmi says that, as a peptide-based therapy, HM17321 may have potential for use in fixed-dose combinations with incretin-based treatments.

Looking ahead, the appearance of new products on the market will inevitably increase price competition: lower prices could have the paradoxical effect of increasing the overall size of the market for weight management products, according to some observers. Although the US currently accounts for a large share of the global market, lower prices would aid penetration into more middle-income countries, with parts of Europe, Asia and Latin America seen as ripe for further expansion.

The final factor with potential to drive the market is the approval of new indications for GLP-1 agonists and other weight management products. Evidence has been accruing that, besides their ability to lower blood glucose and body weight, GLP-1 agonists can reduce the incidence of diabetic kidney disease, cardiovascular disease, osteoarthritis and metabolic liver disease. Substance abuse and compulsive behaviour are also reported to have improved following GLP-1 treatment for other conditions. Meanwhile Lilly has carried out the SURMOUNT-OSA trial which demonstrated a significant reduction of a number of cardiometabolic risk measures in participants with obstructive sleep apnoea and obesity following treatment with tirzepatide.

While there are a number of unknowns in this narrative, for the foreseeable future the weight management market seems firmly set on a growth trajectory.

This article was written by Peter Charlish, PhD, science editor at *MedNous* and a former editor at Informa Plc.