

The pharmaceutical revolution in weight-loss drugs will continue



By Amish Patel,
Head of Equity Research
Charles Stanley

With almost 40% of people worldwide categorised as obese, as well as providing a revolution in healthcare, weight-loss drugs could have significant implications across many other industries too.

Obesity is an increasingly common problem because many people find it difficult to eat healthy and to do enough physical activity. According to The World Obesity Federation, nearly 40% of the global population is overweight or obese, and this is forecast to increase to 51%, or more than four billion (bn) people, by 2035. This would push up the global cost of obesity to more than \$4 trillion a year – comparable to the impact of the Covid-19 pandemic in 2020.

This makes solutions that reduce the prevalence of excess weight an effective means of cutting costs in healthcare systems, especially considering the more than 200 other diseases and complications which can result from obesity, including diabetes, heart disease, and arthritis. Despite the scale and scope of this challenge, only about 2% of all affected people are receiving professional medical treatment.

New blockbuster diabetes and weight-loss drugs are proving highly effective at helping people shed the extra pounds. The new class of drugs promise body-weight reductions of as much as 20%

and may cut users' risk of heart attack or stroke too. They work by mimicking a hormone produced in the gut, called GLP-1, which regulates blood sugar and signals the brain when a person is full. These drugs require a prescription from a doctor and are administered by injection, typically once a week.

Rival to Novo's dominance will emerge

Novo Nordisk currently dominates the market with the brands Ozempic and Wegovy. Ozempic is an established diabetes treatment that can result in weight loss, while Wegovy is a new weight-management medication for obesity. The main rival is Eli-Lilly with Zepbound (US) or Tirzepatide (UK) – its rebranded diabetes drug Mounjaro that is now approved on both sides of the Atlantic as a treatment for obesity.

At one point during the summer of 2023, Novo Nordisk became Europe's biggest company by stock-market value, buoyed by excitement about its ground-breaking medicines that tackle unmet medical needs in obesity. The company's

GLP-1 treatment is called semaglutide – the active ingredient in both Ozempic and Wegovy. In clinical trials, this has demonstrated significant weight loss of 17-18% and notable outcomes on the heart and kidneys too. Overweight or obese patients taking the drug show a 20% reduction in strokes and heart attacks. Novo Nordisk is the global market leader with 54% share of the GLP-1 market and the company anticipates a "significant" step up in Wegovy sales in the US in 2024.

Morgan Stanley believes the global obesity market could grow to \$77bn by 2030, from just \$2.4bn in 2022, as these breakthrough treatments and new drugs in the pipeline are made available to a global audience.

The race for new products is on

This is unlikely to remain a two-horse race. Competition is heating up and the aim of these second movers is to create a next wave of products that have fewer side effects and that are more easily produced and less costly to make than the once-weekly injectable treatments currently on the market. At \$1,000 a month, these are prohibitively expensive for those people footing the bill themselves, either because they are uninsured or because treatment for obesity as a standalone condition is not covered by their health plan.

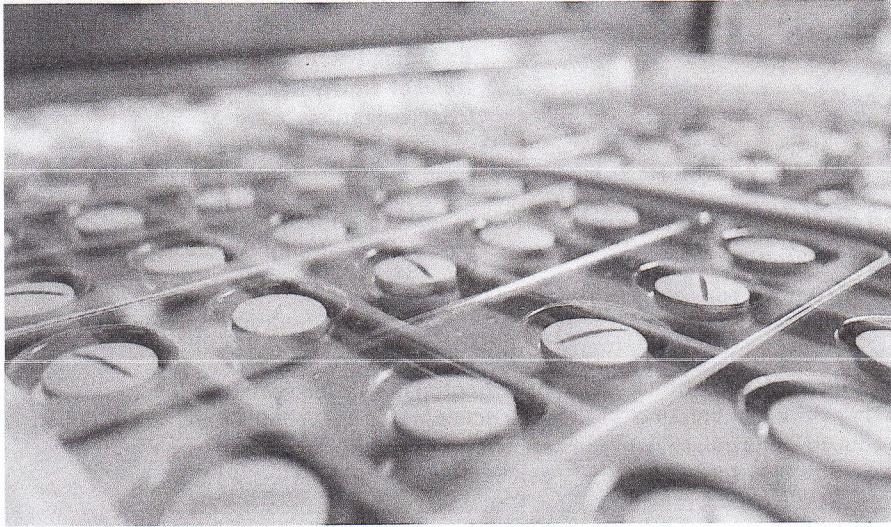
The holy grail is a once-daily pill. This would be easier to manufacture, potentially alleviating supply constraints, and also more convenient for users. While there is still a long way to go and there will be inevitable setbacks along the way, the hope is that in the not-so-distant future there will be an obesity drug accessible to a much broader pool of users around the world, including those in low and middle income countries.

Pfizer wants in on the action with



...nearly 40% of the global population is overweight or obese, and this is forecast to increase to 51%, or more than four billion (bn) people, by 2035.





s experimental obesity pill called anuglipron. The company still plans to release data on a once-a-day pill in the first half of 2024, which will “inform the path forward”. But tests of a twice-daily version were recently stopped due to high rates of adverse side effects.

AstraZeneca is another new entrant. The Anglo-Swedish pharmaceutical giant, best known for its cancer drugs and Covid-19 vaccine, is paying up to \$2bn to license a diabetes and weight-loss pill from China's Eccogene. The experimental drug, named ECC5004, is only at the start of multi-stage clinical trials. Early testing suggests it is easily absorbed and doesn't stay in the stomach for long, which could reduce side effects such as nausea, diarrhoea, vomiting, and abdominal pain. Ultimately, AstraZeneca aims to reach people in both developed and emerging markets with the once-daily pill.

Similarly, Roche recently agreed to buy obesity-drug developer Carmot Therapeutics for up to \$3.1bn. The deal will give the Swiss pharma company exclusive rights to several assets based on the GLP-1 treatment for obesity in patients with and without diabetes. Carmot's lead asset, called CT-388, is in the second phase of what is likely to be a three-stage clinical trial. This experimental drug is administered as a once-weekly injection, like the current market leaders. But it is also working on an oral pill to be taken once a day.

Implications of lower food consumption

These obesity drugs are already affecting people's relationship with food. Their

users are losing weight by eating less and consuming 20-30% fewer calories, according to a Morgan Stanley study. But weight-loss drugs don't seem to suppress appetite for all foods in a uniform way. People eat more fruit and vegetables and weight-loss management foods while on the drugs, but they consume less confections, baked goods, sugary drinks, alcohol, and salty snacks.

Similarly, JP Morgan found that people on weight-loss drugs purchase 8% less food – including snacks, soft drinks, and high-carbohydrate products – for at-home consumption and it estimates that food intake could decrease by 3% in North America by 2030. Of course, there are still a lot of unknowns and whether these changes in eating behaviour will stick when people stop taking the drugs remains to be seen.

The potential threat posed to the packaged food and beverages industries has spooked investors and companies are paying close attention. The prospect of people snacking less and eating fewer high-sugar and high-fat foods as these drugs become more widely available raises questions for some major household names, from PepsiCo and McDonald's to Hershey and Heineken.

Also, any major transition in medical-treatment strategies to a more preventative and weight-centric approach could be disruptive for a host of medical-device makers in years to come.

There will certainly be some winners here too. The chief executive of Walmart's US operations says people who are taking obesity drugs are buying a bit less food

and slightly fewer calories at its stores, although they are still spending more overall. This hints at a shift towards healthier options, which are often more expensive, and this could be a tailwind for those operating in this space already, such as nutritional snack company Simply Good Foods, US salad restaurant Sweetgreen, and protein shake maker BellRing Brands.

The full extent of the impact on other industries is yet to be seen and we will continue to monitor the obesity-drugs trend closely. But we believe the main players in the consumer staples space, especially where junk food and fizzy drinks are only part of a much larger business, will find ways to adjust. Some have started to pivot already.

KitKat maker Nestle has not seen any impact from these drugs on its sales so far, but the Swiss company is now developing ‘companion products’ to help weight-loss drug users ensure they get enough nutrition and to minimise the loss of lean muscle mass. Globally, Nestle's biggest businesses are coffee and pet care, while frozen food, confectionary, and ice cream make up 15% of sales.

Similarly, spirits maker Diageo has been launching alcohol-free versions of its most popular drinks including Guinness beer, Captain Morgan Spiced Gold rum, and both Tanqueray and Gordon's gin. Unilever, the maker of Ben & Jerry's ice cream and Hellmann's mayonnaise, is leveraging the power of digital technologies and AI to speed up the formulation of new products and to explore the connection between diet and health.



This is a major opportunity for a pharmaceutical sector that has seen valuations depressed since the end of the Covid-19 pandemic.

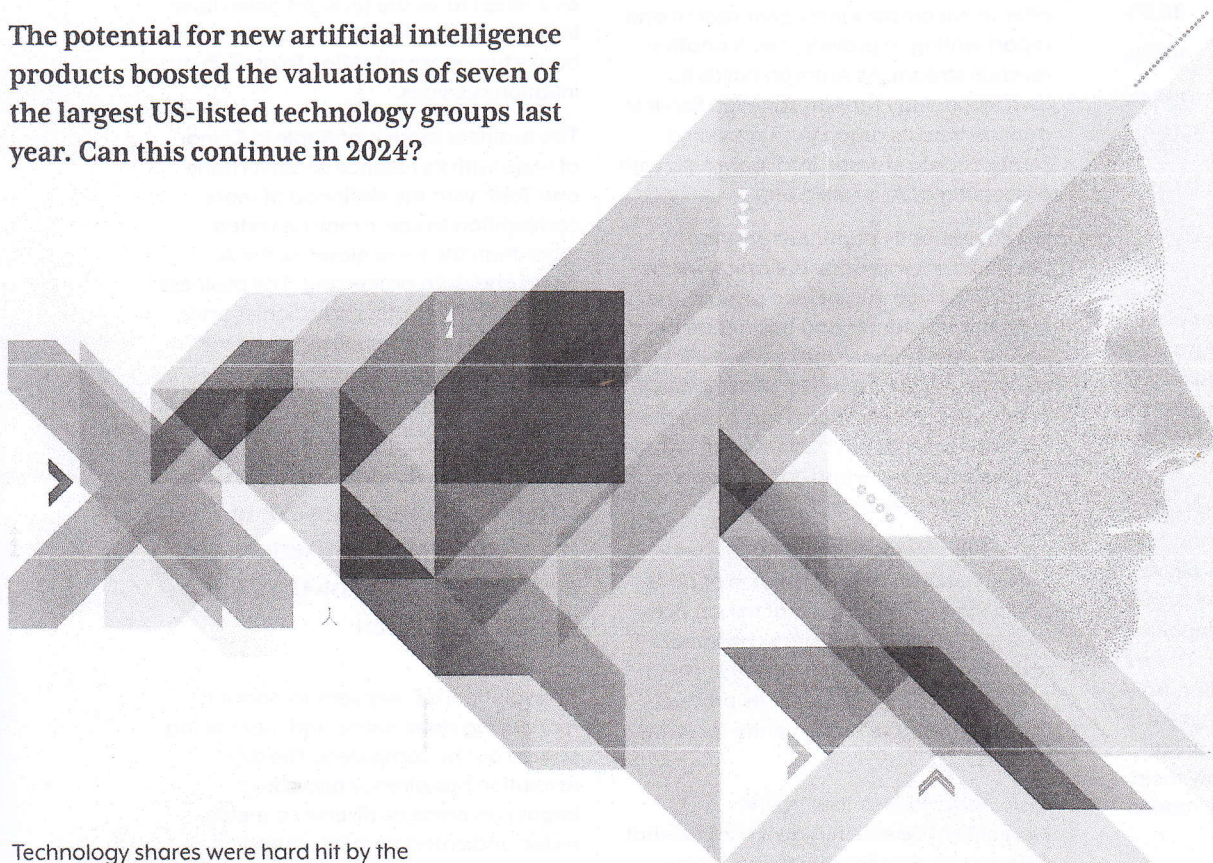
The next few years is likely to see significant adoption of these revolutionary weight-loss products globally. This is a major opportunity for a pharmaceutical sector that has seen valuations depressed since the end of the Covid-19 pandemic.

The 'Magnificent Seven' are not riding off into the sunset yet



By John Redwood
Chief Global Strategist,
Charles Stanley

The potential for new artificial intelligence products boosted the valuations of seven of the largest US-listed technology groups last year. Can this continue in 2024?



Technology shares were hard hit by the bear market of 2022. Many investors had taken some profits from their holdings of the faster-growing technology darlings of lockdown as circumstances changed. These lower valuations occurred as interest rates rose. Commentators argued that higher interest rates would slow growth and make the future earnings of these glamour stocks less valuable.

At the end of 2022, we argued that equities should do better in 2023, with the digital space offering plenty of opportunity. This was based on the fact we expected the world would continue to build more elaborate social media, data handling, automated factories, downloaded entertainment, online retailing, artificial intelligence, electronic learning – and many other areas subject to the digital transformation.

In February last year, Chat GPT made its big announcement that it will provide enhanced search or artificial intelligence

(AI) as a service. We wrote enthusiastically that this would be stardust on the shares of companies able to exploit this new advance.

The big technology companies are now in a race to develop new and enhanced services based on these developments. Computers can now analyse large data sets and use the conclusions to exercise some decision-making ability under the control of software that uses data storage and retrieval systems that are based in the cloud. We were soon hearing of the companies that markets expected to benefit from these technological advances. Out went references to the FANG stocks of lockdown fame (Facebook, Amazon, Netflix and Google) – and in came references to the 'Magnificent Seven'.

Market participants focused on Apple, Amazon, Alphabet, Microsoft, Nvidia and Meta Platforms – which are all looking at the new opportunities of the digital revolution. Tesla was also included in this new set of market darlings as the business is developing new electric cars fitted with significantly more control technology.

All these equities soared in 2023. The companies are seven of the top nine companies in the MSCI World Index and dominate the S&P 500 and Nasdaq indices in the US. All the top nine companies in this equity index are American, with Broadcom, another technology company, and Morgan Chase making up the nine.

The Magnificent Seven share price gains in 2023

Apple	48.2%
Microsoft	56.8%
Alphabet	58.3%
Amazon	80.9%
Tesla	101.7%
Meta Platforms	194.1%
Nvidia	238.9%

Source: Bloomberg

Can the Magnificent Seven deliver more?

There have been various worries about how sustainable this is. It is most unusual for one country, however large and important, to be so ahead. It is even more unusual for one cluster of industries to be so dominant.

In previous decades large oil and energy companies, large banks and financial businesses, large industrial businesses and big pharmaceutical companies have often been represented in the top ten names in the MSCI World Index. There has usually been some representation from Japan or Europe. Bears of the current trend have been doubting the ability of the technology giants to grow their revenues and profits in the way market valuations imply.

Culls of other sectors have been pointing to the favourable impact higher interest rates should have on banks and some financial businesses, on how the higher energy prices should bolster energy company returns, on how Covid-19 and the obesity wave should boost pharmaceutical earnings, and how industrial activities in advanced countries might benefit from the big move to reshoring. So far, these arguments have not been persuasive enough to change the top rankings in the MSCI World Index. Indeed, 2023 saw the Magnificent Seven become even more dominant.

Rising demand for digital technology

The bull case has rested on the way the main technology giants have gained a stronghold over consumers and business customers. Microsoft is the preferred software supplier of so many firms and homes. As it enhances its AI offering so it

will be able to provide more and charge more to the many businesses where it has become the co-pilot sitting alongside employees at their desks.

As Google sees challenges to its position in searches sustained by advertising revenue, it too is looking to enhance its offer to encompass intelligent search and report writing to provide it with another revenue stream. As Amazon builds its own technology for Amazon Web Services it can extend its range from providing plenty of data storage into more help with processing as AI is rolled out.

Nvidia retains its dominant position in the smart microprocessors which will be needed in huge numbers to provide the capacity individuals and businesses need in their smartphones and other devices. It is difficult to see a future without these companies or their successors being more and more involved in business activity and consumer service – and finding ways to remunerate their shareholders.

Apple has retained considerable sway over consumers in the provision of pads and phones, and in some of the services that these devices can offer consumers. It has difficult issues in its relationship with China, both as a market for its products and as a manufacturing centre for what it offers.

Tesla has attached itself to the Magnificent Seven, though it is somewhat different. Its success to date has come from providing upmarket electric cars to a segment of the car market where the traditional suppliers have not been quick enough off the mark to deliver sufficient attractive product. It is true Tesla is also working on a lot of additional car technology to make their vehicles more automated. It will also face more competition as prices come down and the marketplace widens.

Meta Platforms is getting into AI as an adjunct to its social media positioning, as it is very dependent on advertising on its media platforms. These three are not so bound into the AI business enhancing revolution as the other four.

Another good year?

It seems unlikely the technology sector can have another year as good as 2023 as we enter 2024. There will be some strong competition between the three leaders of the AI revolution – Amazon, Microsoft

and Alphabet. There will be additional free services and discount offers as they expand their range and grip on businesses and consumers alike to increase their dependence on internet-based technology. There will be some good profits performance in some other sectors as interest rates are brought down later in 2024, and as governments and central banks turn more attention to growth as inflation subsides.

The business models of Apple in China, of Meta with its reliance on advertising and Tesla with the likelihood of more competition to come may be tested more than the three giants of the AI world and data processing. The business models of many other companies and sectors will also be challenged by the

In 2024, many portfolios will still want some exposure to the all-pervasive presence and continuing growth of the digital revolution.

AI revolution, as they seek to adapt to more being done online and more being carried out by computers. The digital revolution has already had a huge impact on areas as diverse as media, music and entertainment, shopping, communications and office working. There is much more to come. Analysts need to ask the AI question of most major companies to see how they can use it without losing crucial business opportunities.

In 2024, many portfolios will still want some exposure to the all-pervasive presence and continuing growth of the digital revolution. The steady increase in business sharing by the majors and in the build-up of their cloud-computing capacity, AI and general service revenues underwrites a lot of the share price performance.

Investors, however, may need to become more discerning over which companies will have what it takes to develop those opportunities in a profitable enough way. The equity-market ratings now expect quite a lot after their 2023 recovery. Any failure to translate this new business opportunity into good corporate cashflow could worry markets significantly.