focus



One of the big market stories of 2023 has been the sudden rise of GLP-1 weight loss and diabetes drugs. Healthcare is not normally a sector we associate with high volatility: that has changed this year. Hype around the potentially massive opportunity for GLP-1 drugs has seen the stock prices of their developers, Novo Nordisk and Eli Lilly, soar. Conversely, the stock prices of many other healthcare companies have plunged, with investors questioning how many patients they may lose to GLP-1 treatments in the future. For now the market has declared GLP-1s the winner, but like any exciting new technology, the market can be prone to overexcitement. There remain significant uncertainties around how these drugs will be used in the future and the impact they will have.





What are GLP-1s and how do they work?

A glucagon-like peptide 1 (GLP-1) is a hormone produced in the gut. GLP-1s work on the insulin-producing cells of the pancreas to produce insulin when blood sugar rises too high. Insulin helps cells store this sugar and brings the body's sugar levels to normal. Simply put, taking GLP-1 drugs diminishes appetite and increases feelings of fullness after eating. This often leads to a reduction in the number of calories eaten at each meal and, over time, the recipient, in most cases, loses weight.

Reduces glucagon secretion in the liver

Increases insulin secretion in the pancreas

Increases insulin secretion in the pancreas

Source: Novo Nordisk company presentation

This is not new science

The genesis of GLP-1s started with Type 2 Diabetes (T2D). T2D is caused by high blood sugar levels. Insulin has long been used as the primary treatment for T2D.

Over the decades, the medical field has been looking at alternative ways to treat T2D. In 1990, a researcher noticed that a lizard was able to keep its blood sugar levels stable even when fasting. This discovery formed part of the first GLP-1 approval for T2D in 2005 (AstraZeneca's Byetta) and the first GLP-1 targeted at weight loss (Novo Nordisk's Saxenda) was approved in 2014.

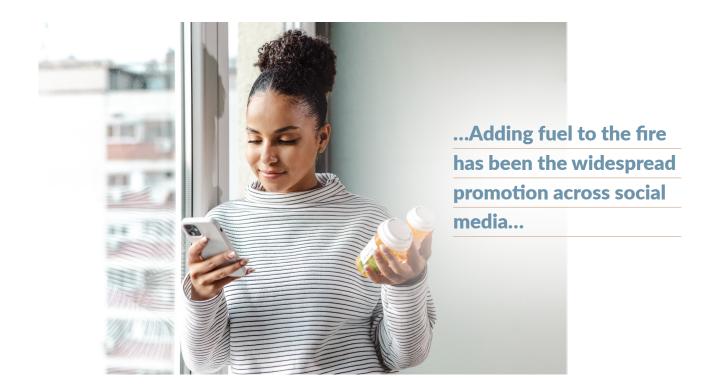
GLP-1S HAVE BEEN AROUND FOR SOME TIME



Source: ResMed, US Agency for Healthcare Research and Quality $\label{eq:control} % \begin{center} \begin{cent$

So why all the hype now?

Though GLP-1s were initially developed as a treatment for T2D, after further research scientists discovered they impact other systems within the human body.



Novo Nordisk noticed animals treated with GLP-1s reduced their food intake. The company pushed forward with studies into obesity. From its first drug, Saxenda, patients lost about 5% of their body weight — helpful, but not game changing.

More recently, substantial improvements in efficacy has seen growing use. GLP-1s have demonstrated significant reduction in weight of around 10–20% and a reduction in associated adverse cardiovascular events.

Adding fuel to the fire has been the widespread promotion across social media and use among celebrities, including former basketball star Charles Barkley, CEO of Tesla and SpaceX (amongst other things) Elon Musk, and ex-British PM Boris Johnson to name a few. Sales have taken off.

SALES GROWTH HAS BEEN VERY STRONG FOR NOVO NORDISK AND ELI LILLY



Source: Novo Nordisk and Eli Lilly company reports, Visible Alpha

GLP-1 PRODUCT OVERVIEW

Product	Manufacturer	First US approval	Weight loss on label?	Headline weight loss
Saxenda	Novo Nordisk	Nov-14	No	<10%
Trulicity	Eli Lilly	Sep-14	No	~5%
Ozempic	Novo Nordisk	Dec-17	No	~7%
Wegovy	Novo Nordisk	Jun-21	Yes	~17%
Mounjaro	Eli Lilly	May-22	No, but expected	~22%

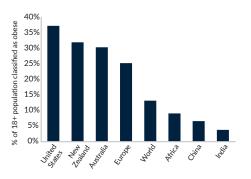
Source: Eli Lilly, Novo Nordisk

Markets have responded to the hype

Normally, most view the healthcare sector as defensive for investors. This year it has been anything but, with some big up and down share price movements.

The potential market for GLP-1 drugs is huge. Over one billion people globally are obese, including about 650 million adults, of which only around 2% are medically treated. A further 540 million or so people have diabetes, of which only 15% are in 'good control' of their condition.

OBESITY IS A BIG PROBLEM



Source: Our World in Data

The share prices of Eli Lilly and Novo Nordisk. the makers of GLP-1 drugs, have surged up +55% and +44% year to date, adding about US\$295 billion in aggregate market capitalisation.

In contrast, a broad range of obesity 'beneficiaries' have seen share price falls, including (1) CPAP (Continuous Positive Airway Pressure) manufacturers, with fears this therapy for Obstructive Sleep Apnea (OSA) may be displaced, (2) fast-food chains, and (3) bariatric surgery providers, to name a few.

An example close to home is Australian Healthcare Company, ResMed, who provides sleep apnea therapy products. ResMed's share price has dropped -30% since the end of July, even though expectations for the company's profits over the next few years are unchanged. The stock has dropped on the fear of how GLP-1s might impact the business far into the future.

Sign of things to come or market getting ahead of itself?

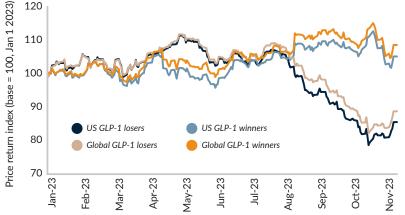
In a recent interview, the CEO of US retail giant, Walmart, noted for those consumers taking weight loss drugs, 'we definitely do see a slight change compared to the total population, we do see a slight pullback in overall basket. Just less units, slightly less calories'. In contrast, at Pepsi's recent Q3 result, its CFO noted it hadn't yet seen any impacts.

While sales of GLP-1 drugs have surged recently, it remains early days. Could they cure one of the world's largest social and health problems? Maybe. It will be a number of years before the market gains clarity on the full implications. Today, there are still significant uncertainties and limitations around their use, including:

Success for GLP-1 drugs in the real world has been significantly lower than in trials (including due to lack of exercise, which was part of the trial), with a large majority of patients discontinuing use within one to two years. The result is that the weight returns.

GLP-1s are expensive (US\$800-\$1500 per month) and not covered by insurance for obesityrelated claims (they are covered for diabetes). In the US, federally funded programmes are currently prohibited from covering obesity drugs.





Source: Bloomberg



Without assistance, the ongoing cost is unaffordable for the majority of the population. For context, US\$1.7 trillion annually would be needed to treat the entire US obese population (using current pricing, although pricing will likely decline). We don't yet know if further trial results and the subsequent cost-benefit analysis will push insurers towards being more inclined to reimburse these drugs.

GLP-1s have been around for over 15 years and are known to have a wide range of side effects. Today's drugs are more potent, so we are yet to see the full implications.

Other key questions are: what will the impact be of future studies? How will this product be sold in time (prescription or over the counter)? At what price point? Will it be a mass market product or not? And what are the longer-term health impacts?

Markets can be prone to overexcitement, especially when it relates to a headline grabbing new technology. Is that the case this time around? We'll only know for sure in time, but right now markets are pricing GLP-1s as the big winners despite all the long-term uncertainties related to these drugs. GLP-1s are likely to be a big part of the conversation around the healthcare sector in the years ahead. But key to successful investing will be trying to stay grounded and avoiding the hype along the way.

If at any time you want to discuss investment options and opportunities, your Forsyth Barr Investment Adviser is available to provide you advice and assistance.



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