

Beyond Fundamentals: A New Frontier in the Treatment of Diabetes & Obesity

Polen Capital Portfolio Managers Dan Davidowitz and Steve Atkins unpack the investment and public health opportunities they see in the emerging class of GLP-1 drugs.



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Q: Let's start with the term "diabesity," which combines the words diabetes and obesity. Do you view this as a misleading term for investors?

A: We think conflating diabetes and obesity is a bit disingenuous. These conditions interact together. Obesity can lead to diabetes, but not always. We think it's important for investors to understand what the companies operating in this space are doing for the diabetic population and, separately, what they are doing to address obesity issues.

Q. How large is this market opportunity?

The diabetes market, estimated at roughly \$70 billion to \$80 billion, enjoys strong reimbursement and is well-vetted from a clinical standpoint.¹ Obesity market drug sales, on the other hand, prior to GLP-1s coming on the scene, represented a substantially smaller market of under \$1 billion here in the U.S., according to our research.

Q: There seems to be a cultural belief that obesity is linked to an individual's behavior and how they take care of themselves. This idea persists even though new research underscores the importance of biological factors. What do you make of this?

A: Yes, there's a widespread belief that obesity is rooted in an individual's chosen behaviors due in part to overeating, but that's not usually the whole story, as other factors can cause obesity. The industry has yet to devise a viable approach to help obese people with real medical needs and high risks lose weight effectively with minimal side effects.

While the GLP-1s are a relatively new class of drugs, they have been used for diabetes for more than ten years. We now see an opportunity where these drugs, well-studied in the diabetic market, appear to be effective at weight loss with minimal side effects. Data also shows that reducing body weight from obese levels can minimize rates of heart attack, stroke, sudden cardiac death, and progression to diabetes. So, these drugs are effective and open a whole new market today.

Here at Polen, we're focusing on whether companies will be reimbursed for these types of drugs. Our research suggests that we will indeed start to see meaningful reimbursement here.

Q: One challenge we're seeing is the hefty price tag on these drugs. A typical list price for Ozempic (Novo's GLP-1) or Mounjaro (Lilly's GLP-1) is over one thousand dollars a month.² Given this pricing, we are seeing some pushback from payers. What is your outlook on this?

A: It's understandable that some payers may be reticent to pay these expensive prices as they seek good value for their money.

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Beyond the immediate health benefit, they also want to see reduced medical care costs down the road. Insurance companies are concerned about profit margins, and although the data suggests these drugs should help alleviate chronic conditions down the road, they're not convinced of seeing a reduced cost of care over time.

This situation requires some out-of-the-box thinking. Novo recently proposed a pay-for-success type program, where instead of being paid up-front for their drugs, insurers are paid over time as a patient's body mass index (BMI) lowers to designated thresholds. This smooths the insurance company's payment as the cost burden is spread over time, and they know the patient is already seeing some health benefits from the drug.

We'll have to see how this plays out, but we do observe that these drugs, based on large, well-controlled studies, reduce the chances of serious future chronic disease. And that's very different from what we've ever seen in obesity before. For example, Novo Nordisk published the results of a large clinical trial of nearly 20,000 patients in the summer of 2023, indicating a clear cardiovascular benefit from GLP-1s, in addition to weight loss.³ Beyond that, there is a general awareness of the many comorbidities related to obesity. This is a population already at high risk for cardiovascular diseases, diabetes, and cancer. Obesity is also associated with smaller issues like sleep apnea.

The data from that trial signaled to us that it would be extremely difficult for payers not to reimburse. Even with conservative assumptions, we expect this could be the largest class of drugs ever created, with Novo Nordisk and Eli Lilly basically sharing a global duopoly. It's exciting from an investment standpoint and, more importantly, from a public health perspective.

Q: Novo has publicly stated that they estimate the obese population globally at roughly one billion.⁴ The market opportunity seems substantial, but it may not be a linear path to growth due to some of the challenges we've discussed. Do you expect to see fits and starts in terms of opening up the market?

A: Absolutely. Even if every payer does pay, and every physician with an obese patient prescribes, we know that just scaling up production and supply is already somewhat constrained. Novo and Lilly must increase their production facilities to satisfy demand. Patients also need to be well-vetted, as doctors must ensure the right patients are getting access to these drugs. The best-case scenario is that these drugs are used when they need to be used. A patient's behavior should be modified as they lose weight to guarantee a sustainable outcome, even if they decide to stop taking the drug. That's going to take time.

Additionally, a better dosage profile should emerge. Right now, there are limited doses available for each of these drugs. Over time, we'll likely see a more laddered approach that will start to titrate

patients down over time. Perhaps we'll see a low-maintenance dose for a while as people are getting those behavioral changes locked in, and then eventually, they might come off the drug entirely.

It's still very early days. If we're right about how big the opportunity really is, there's still a long runway of growth.

Q: What do you think the future competitive dynamics in this space will be?

With pharmaceuticals, you don't usually have a market to yourself for very long. Eventually, someone else comes around, as we see to some extent today. Nonetheless, we think it could be quite hard to catch the leaders.

Once patients are on a drug and reach a well-controlled status, they tend to stick with that drug. They tend not to switch, even when a new drug comes to market. Moreover, based on the clinical data that we've seen thus far, the competitors' products don't look any better than what Novo and Lilly currently offer or what they might have in their pipelines in the next two or three years.

Among the next drugs to market will likely be oral GLP-1s in pill form versus today's auto-injectables. Some in the market believe that once a pill is available, people won't want to auto-inject anymore. Historically, that hasn't been true. These are not giant needles that are highly painful. They are easy to self-administer with a very thin needle, and don't really hurt. On that front, we're inclined to think the persistence of the current offerings from Novo and Lilly is likely to be maintained.

Q: In 2023, we saw several other companies, in and outside of healthcare, whose stock prices were affected by the narrative around GLP-1 drugs. How do you view these "knock-on" effects?

A. There will almost certainly be knock-on effects, all of which we can't yet identify. For example, some believe that as uptake increases and patients lose weight, the demand for blood glucose monitors, bariatric surgery, or even soda and candy will be reduced.

There is some truth in that argument, but we think it has been over-dramatized in the short term. These scenarios will take quite some time to play out. Is it possible that with broad access to these drugs, we may see fewer bariatric surgeries? Yes, it's possible. Intuitive Surgical performs bariatric surgery, but it's only a portion of their business. So, we saw Intuitive Surgical stock get hit hard, but in our view, it probably didn't make sense.⁵

Let's consider continuous glucose monitors for diabetes, which actually work better with the drugs. Monitoring your glucose and insulin levels in combination with the GLP-1 has a better result than either one separately. So, we must examine each situation individually. We think that the level of stock market carnage we saw in 2023 for some companies was disconnected from the facts.

Sources

¹ IQVIA, CDC, Morgan Stanley Research.

² Lilly, Prescribing Information Links, "How much should I expect to pay for Mounjaro?" accessed February 21, 2024, <https://www.lillypricing.info.com/mounjaro>.

NovoCare, Diabetes, "Find out the cost for Ozempic®" accessed February 21, 2024, <https://novocare.com/diabetes/products/ozempic/explaining-list-price.html>.

³ Novo Nordisk, Company announcement, August 8, 2023, "Novo Nordisk A/S: Semaglutide 2.4 mg reduces the risk of major adverse cardiovascular events by 20% in adults with overweight or obesity in the SELECT trial," accessed February 21, 2024, <https://www.novonordisk.com/news-and-media/news-and-ir-materials/news-details.html?id=166301>.

⁴ "Novo Nordisk – a focused healthcare company, Investor event in connect with AHA Philadelphia," 11 November 2023, presentation materials, page 8.

⁵ Allison Gatlin, "Intuitive Surgical Crumbles As Weight-Loss Drugs Weigh on Bariatric Surgery," Investor's Business Daily, July 21, 2023, accessed February 21, 2024, <https://www.investors.com/news/technology/isrg-stock-intuitive-surgical-earnings-q2-2023>.

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