Kennedy Capital Management®

The Skinny on GLP-1s

Oprah called them “the easy way out” (and subsequently decided to use them). Weight Watchers touts the benefits. The Real Housewives gave them a pet name. Their competitive threat has upended the outlook for numerous stocks within the health care sector. As the controversy and excitement around GLP-1s—sold under brand names such as Wegovy, Ozempic, Zepbound, and others—increases, let’s explore how we arrived here and what the future may hold.

What is this stuff, anyway? A quick history and how it works.

In the early days of visualizing and isolating proteins, scientists studying a hormone called glucagon came across another hormone. While glucagon increases the level of sugar in the blood, this new hormone had the opposite effect. However, because the scientists initially thought they were looking at glucagon, the novel peptide they discovered was called glucagon-like peptide 1 (or GLP-1).

A member of the incretin class of peptide hormones, GLP-1 is produced primarily by cells in the intestine. It travels throughout the body to stimulate insulin production, decrease gut motility, and promote feelings of satiety. This slows food digestion, stops a person from eating more, and reduces daily caloric intake--a recipe for weight loss!

By the early 2000s, the action of GLP-1 and other incretin hormones was well understood and being used in short studies. Inspired by the ability of Gila monsters (a species of North American venomous lizards) to maintain stable blood sugar after infrequent and large meals, scientists began engineering variants of GLP-1 with better stability and longer action in the body.

In 2005, Exenatide (Amylin) was approved for twice-daily injection. Five years later, liraglutide (Novo Nordisk) was approved for once-daily dosing. Semaglutide, better known as Wegovy and Ozempic, lasts more than a week in the body due to intentional variations in its protein structure that slow its breakdown and allow it to stay in circulation longer.

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GLP-1s have been available for 20 years, and I'm just now hearing about them. What changed?

In a word, efficacy. From 2005 to 2021, multiple GLP-1s were approved. However, all carried some combination of dosing challenges, unpleasant side effects (such as nausea, vomiting, and diarrhea), and limited weight loss—not a formula for robust long-term use by patients.

The more recent versions of GLP-1s (Wegovy, Ozempic, Zepbound, and Mounjaro) are the game-changers. They significantly improved total weight loss while keeping the side effects consistent with previous drugs. This combination changed the risk/reward calculus for patients, with many concluding the outcomes are now worth the side effects.

How are GLP-1s impacting the stock market?

The magnitude of weight loss from GLP-1s has translated into clinically meaningful improvements in type 2 diabetes and adverse cardiovascular events (such as heart attack and stroke) in overweight adults. With these early successes, GLP-1 sponsors are studying the drugs in other conditions, such as non-alcoholic steatohepatitis (NASH) and sleep apnea, among many others. The potential of GLP-1s to help with a wide variety of medical conditions is causing adverse stock reactions for companies that offer more traditional treatments.

Eli Lilly's ongoing SURMOUNT-OSA clinical trial, for example, is evaluating the impact of GLP-1 on patients with sleep apnea. Given that apnea is present in approximately 40% of obese individuals, it's widely expected that this trial will demonstrate a clinical benefit. Over time, this could reduce the number of patients who need CPAP machines or other alternative treatments. Extrapolate this risk to the many other GLP-1 studies being conducted, and it's easy to see why investors are paying attention.

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Will GLP-1s lead to the downfall of all other therapeutic areas? This sounds concerning for health care investors.

We hardly think GLP-1s will render other treatments obsolete. While these drugs will be disruptive, we believe that misperceptions abound—and as doctors, patients, and investors learn more, the market will adjust. Factors that may dampen the enthusiasm around GLP-1s include:

Weight gain after stopping the drug. When a patient stops taking GLP-1s, they often regain a significant portion of the lost weight.

Side effects. The side effects seen with the first GLP-1 drug in 2005 still exist for current versions, making even short-term use potentially unsustainable—not to mention lifetime use.

Additional risk factors. Not all patients can take GLP-1s due to the increased risk of pancreatitis, and there could be additional risk factors we don't yet understand.

Cost. GLP-1s may be cost prohibitive for patients. For example, the monthly list price for Zepbound is currently over $1,000.

GLP-1s are also expanding the treatment funnel for certain procedures and spawning new scientific efforts in adjacent fields. Some treatments (including many orthopedic procedures) require patients to have a BMI below a certain threshold. GLP-1s will make it easier for these patients to lose sufficient weight, increasing the number of patients qualified for these procedures. The side effects of GLP-1s may also promote investment in adjacent fields, like muscle growth (to combat lean muscle wasting), health food suppliers (to provide low-volume, protein-dense meals), and anti-emetics manufacturers (to combat nausea and vomiting).

Are GLP-1s covered by insurance? (Asking for a friend!)

Most commercial insurers now cover GLP-1s for type 2 diabetes. As additional clinical data is presented over the coming years, it's likely GLP-1 coverage will continue to expand. However, given the cost of the drugs and quantity of patients, these drugs can be hard to access even if covered. Patients may have to try generic or lower-cost drugs first.

Medicare is an easier explanation: GLP-1s are not covered for weight loss. Years ago, laws were passed excluding medications used for weight loss from Medicare Part D coverage. However, as society's perceptions of obesity change and with clinical data proving the benefits of GLP-1s, there's new momentum in Washington, D.C., to change these laws.

Our approach to GLP-1 investment

We believe GLP-1s will negatively impact specific companies but will also create numerous investment opportunities. Already, GLP-1s have shown significant potential for long-term benefits in patients with obesity, type 2 diabetes, and cardiovascular risk. And current and future studies may show the effectiveness of GLP-1s in treating many other conditions that are exacerbated by obesity.

If these studies are successful, the addressable market for GLP-1s will expand and pressure insurers (both commercial and government) to provide greater access. In fact, it's not an exaggeration to say GLP-1s could quickly become the largest drug class we've ever seen. However, the nausea, vomiting, muscle loss, and prohibitive cost of these drugs may be an impediment to uptake and adherence.

At Kennedy Capital, we're taking a threefold approach to GLP-1 investment by identifying and investing in:

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1

Potential acquisition targets. Through our small-cap focus, we can evaluate and invest in the next-generation of GLP-1 assets that are potential acquisition targets for large pharmaceutical companies.

2

Value buys. Our sector-specific analyst team helps us quickly identify equities that are mispriced as GLP-1 fears cause stocks to overcorrect.

3

Adjacent treatments. We also look to invest in new adjacencies, such as muscle-wasting treatments, that present opportunities because of GLP-1 side effects.

In conclusion, as we all slowly digest the GLP-1 impact on the equity markets, let's remember that great innovation in health care is not the end of the road. Each great advancement simply leads to new challenges—and new opportunities—to continue to advance care for patients.

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