

Introduction

Obesity is a global problem with a history of troubled treatment options. The significant health risks associated with obesity make it a critical focus for the medical community, and there are some promising treatments being developed that could have not only significant health benefits, but investment implications for the companies developing them. In this piece we will take a closer look at the obesity epidemic and what is currently in the pipeline to address this global issue.

What is Obesity?

The Centers for Disease Control and Prevention (CDC) defines obesity as weight that is higher than what is considered normal for a given height. Body Mass Index (BMI) is used as a screening tool for determining obesity. BMI between 18.5 and 24.9 is considered normal, between 25 and 29.9 is considered overweight, over 30 is considered obese and over 40 is considered severely obese¹.

Obesity is a global problem. Its prevalence of about 11.4% in 2010 (511 million) is expected to increase to 16% (892 million) in 2025 and 17.5% (1 billion) by 2030 (Figure 1). In the U.S., obesity rate has increased from 30.5% in 2000 to 41.9% in 2020. The rate of severely obese has almost doubled from 4.7% to 9.2% in that period¹ (Figure 2). Obesity is a significant risk factor for many diseases such as diabetes, heart disease and cancer. The CDC estimates that the medical costs for individuals with obesity are \$1,861 per year higher than those with healthy weights and the cost of obesity to the U.S. healthcare system is approximately \$173 billion per year³.

Figure 1: Global Adult Obesity Rate ²

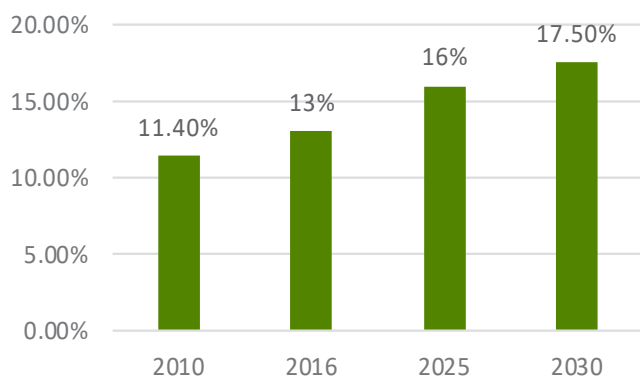
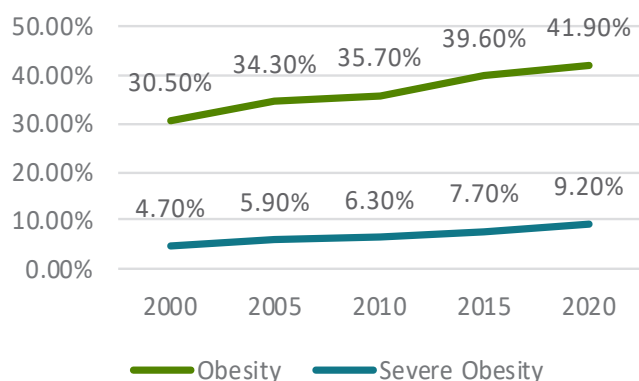


Figure 2: Obesity Rate in the U.S.⁴



Treatments of Obesity

Obesity was always considered to be the result of lifestyle and not a disease. As a result, most treatments involved lifestyle changes, which were difficult to maintain and thus not effective in the long term. So, people have always looked for a “magic pill” for weight loss. However, most weight loss drugs have had a troubled past. For example, amphetamines were popular for weight loss in the 1960s while the drug combination “fen-phen” was popular in 1990s. These drugs were taken off the market due to severe side effects like heart valve defects for “fen-phen” or were restricted by the FDA due to their addiction potential (amphetamines). Lorcaserin was the latest weight loss drug to be withdrawn from the market in 2020, due to increased cancer risk. These drugs accounted for, on average, about 5% weight loss and did not treat diabetes which can develop as a result of obesity⁵.

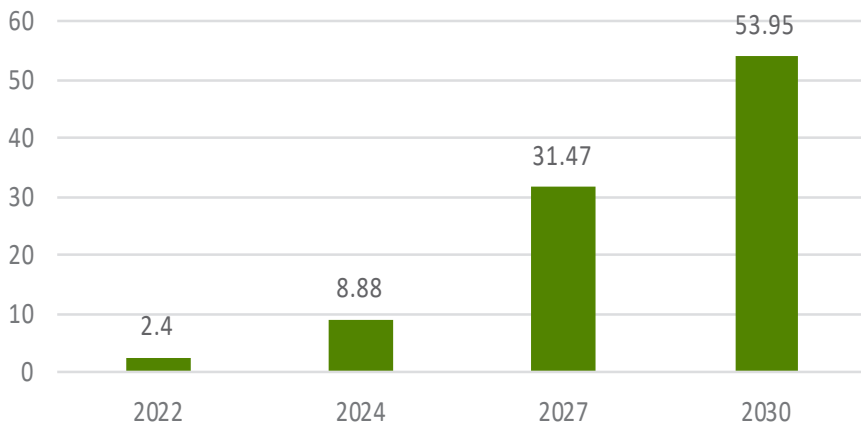
Semaglutides

There is new promise in semaglutides, which are glucagon like peptide-1 (GLP-1) agonist which mimics the effect of the hormone incretin. Incretins are hormones that are secreted by the digestive tract minutes after food consumption. Incretins stimulate insulin secretion from the pancreas and inhibit the release of glucagon which stimulates sugar production. Incretins also act on the brain to suppress appetite. Semaglutides, which were developed for Type 2 (T2D), are the first class of drugs to target both diabetes and obesity. Moreover, weight loss experienced with semaglutides is much greater than that with older drugs (15-21% vs. 5-10%) and is comparable to weight loss achieved by bariatric surgery. The most common side effects are mainly gastrointestinal symptoms like nausea and have not resulted in discontinuation of the drugs. As a result, there is a lot of excitement about this drug class. WeightWatchers recently announced (March 6, 2023) its plan to buy Sequence, a telehealth platform, in order to provide weight loss drugs, along with lifestyle changes, to its customers. T2D drugs like Ozempic, that have not been approved for weight loss, are currently in short supply due to off label use for weight loss.

Investment Case

Despite being labeled as a chronic disease in 1973 by the World Health Organization (WHO), the American Medical Association (AMA) did not classify it as a disease till 2013 and the European Commission till 2021. While Medicare covers weight loss counseling and bariatric surgery, current law prohibits Medicare from covering weight loss drugs. Since private insurance coverage typically follows Medicare, most private health plans do not cover these treatments. The average out of pocket cost for the recently approved weight loss drug Wegovy is about \$1350 per month, which limits its accessibility. To add weight loss drugs to Medicare, lawmakers, advocacy groups as well as drug companies are backing the proposed Treat and Reduce Obesity Act (TROA) which has been pending in the Congress for many years. Novo Nordisk (NVO) and Eli LLY (LLY) are conducting phase 3 trials to study the effect of semaglutides in lowering risk of cardiovascular events and data is expected in 2024. Most analysts expect price reductions along with positive data from cardiovascular risk trials will be the catalysts for the passage of TROA in 2024. By 2030, Medicare as well as private insurance coverage for semaglutides is expected to increase, over three-fold, the percent of patients seeking medical intervention from the current estimated 7% to 25% and the market for obesity drugs, over four-fold, from an estimated \$2.4B in 2022 to about \$54B (Figure 3).

Figure 3: Obesity Drugs (\$B)⁶



While many pharmaceutical companies are developing semaglutides, NVO and LLY are frontrunners and competitor semaglutides are not expected on the market till at least 2027 (Table 1). Currently, only two semaglutides, NVO’s Saxenda and Wegovy, are approved for treatment of chronic weight loss in patients with BMI greater than 30 and for patients with BMI greater than 27 who have at least one weight related ailment like diabetes, high cholesterol, or hypertension. LLY’s Mounjaro was approved in 2022 for T2 diabetes. Mounjaro is a dual incretin and acts on both GLP-1 and GIP receptors making it more effective. Average weight loss with Mounjaro was 21% compared to 15% weight loss from Wegovy (highest dose). Weight loss with Saxenda was 5%.The FDA has fast tracked Mounjaro for obesity treatment and approval is expected in 2023. Based on current data, NVO and LLY are expected to have the largest market share of the semaglutide for obesity market.

Currently, NVO’s Rybelsus is the only FDA approved oral GLP-1 for T2D. However, its weight loss profile is not as attractive as that of either Wegovy or Mounjaro. Several companies including LLY are testing next

generation oral GLP-1 for weight loss. Most of these are still in phase 2 clinical trials.

Since semaglutides target both T2D and obesity, these drugs are expected to be blockbuster drugs. Analysts expect LLY's Mounjaro to generate revenue of \$17.5B and NVO's Wegovy to generate revenue of \$11B in 2028.

Company	Molecule	Phase	Form/Dosage	Status
Novo Nordisk	Saxenda		Daily injection	Approved
	Wegovy		Weekly injection	Approved
	CagriSema	Phase 3	Weekly injection	Data 2025
Eli Lilly	Mounjaro	Phase 3	Weekly injection	FDA filing 2Q2023
	LY3437943	Phase 2	Weekly injection	Data November 2022
	Orforglipron	Phase 2	Daily oral	Trial completed Nov 2022
Pfizer	GLP-1	Phase 2	Daily oral	Data 2H2023
Amgen	Dual GLP	Phase 2	Weekly injection	Data April2023
Boehringer/Zeland Pharma	Dual GLP	Phase 2	Weekly injection	Data September 2022

Source: 7: Untapped obesity market poses an underappreciated opportunity for LLY : BofA Global Research, March 2022

Summary

Obesity is a global problem that is expected to rise significantly from 11% in 2010 to 17.5% by 2030. The U.S. obesity rate has grown from 30% in 2010 to over 40% in 2020. Obesity is a significant risk factor for many diseases such as diabetes, heart disease and cancer and the cost of obesity to the U.S. healthcare system is approximately \$173 billion per year³. Obesity, which was viewed as a lifestyle choice is now classified as a chronic disease. Semaglutides, which were developed for diabetes, are the first class of drugs to target both diabetes and obesity. Currently, Medicare as well as most private health plans do not cover weight loss drugs. However, data from clinical trials showing reduction of cardiovascular risk by semaglutides along with lower pricing is expected to enable the passage of Treat and Reduce Obesity Act (TROA) in 2024. This will then expand the market for obesity drugs from an estimated \$2.4B in 2022 to about \$54B by 2030⁵. Novo Nordisk and Eli Lilly have the most advanced products and are expected to be the market leaders.

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