*in*Thought takes #1

Wegovy leadership in obesity remains strong as Lilly doubles down on emerging entry with tirzepatide

A BATTLE OF THE HEAVYWEIGHTS

While Novo Nordisk continues to have a virtual monopoly on the GLP space for obesity, posting huge growth in uptake and sales of Wegovy, Lilly is close on their heels, releasing impressive topline results from the SURMOUNT-2 trial of tirzepatide in obese patients with type 2 diabetes (T2D). Tirzepatide is expected to reach approval in obesity by the end of 2023. Many expect that some Wegovy patients will switch to tirzepatide, and new patients will begin to preferentially start on tirzepatide over Wegovy. Lilly is doubling down on their potential best-in-class status by initiating a head-to-head trial which will compare weight loss on tirzepatide directly to Wegovy. They are also advancing their oral GLP-1 orforglipron to Phase 3 trials, which could match Novo Nordisk's oral formulation of semaglutide.

However, Novo Nordisk is likely to maintain their leadership in the obesity space for quite a while longer. The demand for Wegovy continues to outstrip supply even as Novo Nordisk brings more manufacturers online. They recently announced that they would be limiting the supply of lower doses in the US to curb new patient starts, and the rollout in the EU remains slow and uneven. The obesity market is currently underexploited, so demand for Wegovy is expected to remain high even when new competitors enter the market. Additionally, Novo Nordisk is close to bringing an oral formulation of Wegovy to the market, which would be the first oral GLP therapeutic to gain approval. The oral formulation will be more convenient for many patients and can likely be prescribed in the primary care setting, which will drive up demand even more.

Lilly

1. Lilly releases positive topline data for Phase SURMOUNT-2 trial of tirzepatide in patients with obesity and Type 2 diabetes (T2D). Patients lost an average of 15.7% of their bodyweight at the highest dose, and >80% of patients on tirzepatide lost 5% or more of their bodyweight. Lilly plans to present full results at the American Diabetes Association 83rd Scientific Sessions. Lilly aims to complete the rolling submission of tirzepatide for the treatment of obesity shortly, which will put them on track for an approval decision by the end of 2023.

Although the weight loss results are not as high as in the SURMOUNT 1 trial of patients with obesity without T2D, these results are still an improvement over clinical data for Wegovy, showing its best-in-class potential.

With its dual-action mechanism and superior clinical data, KOLs are expected to begin switching some patients and starting new patients on tirzepatide over Wegovy, cutting into Wegovy's sales growth somewhat. However, the obesity market remains largely underexploited in the US, and it is likely that sales will continue to boom for Wegovy even as tirzepatide enters the market.

2. Lilly registers the SURMOUNT-5 head-to-head trial comparing tirzepatide with semaglutide in obesity (N=700). The primary endpoint is percent body weight reduction at 72 weeks. Results are expected in Q2 2025

To date, clinical data has favored tirzepatide over semaglutide, the active ingredient of Wegovy, so it is very likely that the results of SURMOUNT-5 will confirm tirzepatide's superiority in efficacy. While we already predict KOL's to prefer tirzepatide over Wegovy once approved for the obesity indication, the results of this trial will likely accelerate this trend.

3. Lilly initiates the ACHIEVE-4 study of orforglipron, a Phase 3 trial in patients with obesity and heart failure. This is the first Phase 3 trial registered for orforglipron. Lilly has commented that they initiated this trial first because it will be the longest trial in the Phase 3 program, but they anticipate initiating the rest of the Phase 3 program soon

Orforglipron is an oral GLP-1 medicine. Oral formulations of these therapeutics are expected to become very important for a few reasons. First, oral therapeutics are more convenient for many patients over a once weekly injection. They can also be cheaper to manufacture with less material, which is crucial for easing supply issues. They also have the potential to be prescribed through the primary care setting, whereas current offerings are typically supposed to be prescribed through a specialty weight management clinic.

Novo Nordisk is currently ahead in the development of an oral GLP-1 therapeutic, with approval of an oral semaglutide expected in 2024. Novo Nordisk and Lilly are trailed by Pfizer, who have two oral GLP-1 therapeutics in Phase 2 trials. Pfizer expects to advance one of these assets to Phase 3, though there has not been guidance on that timing yet.

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1. Novo Nordisk showed continued dominance and massive growth for Wegovy. Their obesity franchise claims a 54% market share of the anti-obesity market, and sales have grown 124% YoY

Novo Nordisk is currently seeing exponential growth with Wegovy sales and is currently limited by the supply they can produce. This underscores the huge potential of the obesity market

2. Novo Nordisk officially relaunched Wegovy in the US in January 2023, and they have brought a second contract manufacturer online. However, to maintain continuity of care, the company announced that they are temporarily limiting the supply of lower Wegovy dose strengths.

Restricting lower dose strengths of Wegovy will curb new patients from starting on the drug, since patients typically titrate up from low dose strengths to higher ones. Novo Nordisk is taking this move to ensure that patients already on the drug do not have their supply disrupted.

This shows that Novo Nordisk still is not able to meet demand for Wegovy even as they temporarily halted and then launched Wegovy in the US. As other products enter the market, we will begin to see whether the supply issues are due to lack of investment from Novo Nordisk or a general lack of capacity in the global supply chain and what steps can be made to stably increase supply

3. Wegovy has launched in Denmark and Norway with further plans to gradually roll out internationally

It is interesting to note that the UK is not on the list of countries where Wegovy has launched. The UK has been bracing for its launch, which was expected to happen imminently. However, the company has decided to delay the launch there to build enough supply, frustrating many UK patients.

We can expect further roll out internationally to happen slowly until the supply can be stabilized in the US, which will likely be the biggest market for the drug.

4. Topline results from the PIONEER PLUS study of oral semaglutide in T2D patients showed 4.5%, 7%, and 9.2% weight reduction at the 14 mg, 25 mg, and 50 mg doses, respectively

Although not an obesity trial, these results may foreshadow the upcoming readout for OASIS 1, the trial of oral semaglutide in obese patients.

With a readout of the OASIS 1 trial expected in late Q2 2023 and assuming a standard review timeline, we can expect that oral semaglutide will be approved for obesity in 2024. This will be key for Novo Nordisk to continue their dominance of the market as new injectables from Eli Lilly enter the competition