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CITELINE COMMERCIAL

08 Aug 2023 | **Analysis**

Lilly Expects Mounjaro To Benefit From Novo Nordisk Cardiovascular Trial

by Alaric DeArment

An exec said results from the SELECT trial of Wegovy could benefit the GLP-1 agonist class, given that employers tend to opt into drug classes when covering obesity treatments.

Eli Lilly and Company had a lot to discuss in its second quarter 2023 earnings, but most of the excitement was about a competitor's announcement of positive results from a cardiovascular outcomes trial (CVOT) of a GLP-1 agonist for obesity, because of the potential those results have to drive payer coverage for Lilly's own GLP-1/GIP agonist, Mounjaro (tirzepatide), approved for type 2 diabetes and pending approval for obesity.

The Indianapolis-based drug maker announced its second quarter results on 8 August, with Mounjaro's rapid increase in sales to blockbuster levels since the comparable period last year playing a key role. In the second quarter, Mounjaro's sales were $979.7m, compared with $16m in the second quarter of 2022. Year to date, the drug's sales were $1.5bn, compared with $16m in the first half of 2022.

However, after *Novo Nordisk A/S*'s revealed that the Phase III SELECT trial of Wegovy (semaglutide) showed a statistically significant reduction in major adverse cardiovascular events (MACE) of 20%, the same-day announcement generated even greater excitement than Lilly's Q2 Mounjaro sales. That is because the results for Novo's obesity drug have the potential to read-through to Lilly's product, which is undergoing its own CVOT in obese patients, SURMOUNT-MMO, which is expected to yield data in 2027. (Also see "*SELECT: Novo Nordisk Comes Roaring Back*" - Scrip, 8 Aug, 2023.)

During Lilly's 8 August earnings call, chief scientific and medical officer Daniel Skovronsky noted that the firm applied for US Food and Drug Administration approval of Mounjaro for chronic weight management in the second quarter and anticipates an FDA decision by the end of the year.

In June, the company presented data from the Phase III SURMOUNT-2 study at the American Diabetes Association meeting, which showed a mean weight loss of 13.4% among patients receiving the 10mg dose and 15.7% for the 15mg dose after 72 weeks in overweight and obese patients with type 2 diabetes. (Also see "*Lilly Wows ADA Crowd With Obesity Data Across Three-Drug Incretin Portfolio*" - Scrip, 26 Jun, 2023.) Lilly Diabetes president Michael Mason told Lilly's 8 August earnings call that the company would decide at the time of approval whether to market the drug for obesity under the Mounjaro brand or split the brand.

Potential Read-Through From SELECT

To be sure, there are some important differences between Mounjaro and Wegovy as well as between SURMOUNT-MMO and SELECT. Mounjaro is a GLP-1/GIP agonist, while Wegovy is a GLP-1 agonist. SURMOUNT-MMO includes patients with type 2 diabetes, while SELECT excludes them. Moreover, SURMOUNT has a different primary endpoint – time to first occurrence of any component event of the composite endpoint – while using the three-point MACE as a secondary endpoint.

But while he highlighted some of the differences on Lilly's earnings call, Skovronsky remained confident in SURMOUNT-MMO's potential for success. "Of course, we expect tirzepatide to show a very important benefit," he said.

In an 8 August note ahead of Lilly's call, Truist Securities analyst Robyn Karnauskas said that given the data for Mounjaro so far, she believes it could show a better benefit. However, a key question would be how insurance companies will view reimbursement of the class for weight loss in light of the data and if pricing would play a role in formulary access.

Many of the questions on the earnings call dealt with Mounjaro or the SELECT results' implications for it. Despite Wegovy being at the moment the only drug in the GLP-1 class to have a proven cardiovascular benefit in obesity, Mason said he expects the SELECT results to ultimately benefit the entire class in terms of things like payer coverage rather than benefiting Wegovy to the detriment of its competitors.

"What we've seen is payers opt into the class, not a particular drug, so I don't think that'll give [Novo Nordisk] differential impact within payer access,"

Obesity Market Potential Is Huge, But Access To Drugs An Increasing Challenge

By Mandy Jackson

14 Jul 2023

Despite double-digit weight loss across several drugs presented at ADA, experts note access to obesity therapies will be constrained without outcomes data to justify their widespread use and cost.

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he told the call. “I think commercially, typically, health care professionals, when they see results like this, it really helps the class more than any one individual product.”

Wolfe Research analyst Tim Anderson said in an 8 August note that the SELECT results have “broad ramifications” for obesity drugs in general, especially from a payer perspective. He noted that Mounjaro’s revenue beat his prediction of $743m. “Another important prediction by management,” Anderson added, “it believes Mounjaro should be able to deliver an even bigger benefit vs SELECT (but note: results may not be out until 2027 from [Lilly’s] similar trial).”

If Lilly’s prediction proves correct, Wegovy’s gain stands to be Mounjaro’s as well. In March, Novo Nordisk CEO Lars Jørgensen told the CNBC Health Returns conference that positive results could better position Wegovy for broader reimbursement in the US and Europe alike. (Also see "*Wegovy CVOT Data Could Pave The Way For Broad Reimbursement, CEO Says*" - Scrip, 29 Mar, 2023.)

More Obesity Treatments On The Way

One area Lilly is stressing differences between obesity therapeutics is safety, in particular liver toxicity. *Pfizer Inc.* announced in June that it would terminate development of its GLP-1 agonist lotiglipron after elevated liver transaminases were observed in Phase I and Phase II development. (Also see "*Pfizer Sees Once Daily Danuglipron In The “Reasonable Future”*" - Scrip, 2 Aug, 2023.) Skovronsky told the earnings call that Lilly did not see any read-through from that for one of its other GLP-1 agonists under development for obesity, the orally available Phase III orforglipron, pointing to published data indicating an improvement in liver enzymes for patients on that drug. Lilly additionally is developing a third candidate for obesity, the Phase III GLP-1/GIP/glucagon receptor drug retatrutide.

“I think I’ve frequently cautioned on all of our molecules that Phase III is really the place where you can get surprised by any new safety findings,” he said. “So we’ll be watching liver safety closely, but not with any particularly heightened concern versus other adverse events that we’ll also be watching carefully.”

Lilly presented Phase II data for orforglipron and retatrutide at the ADA meeting in June and also initiated Phase III trials for orforglipron – in obesity and type 2 diabetes – in the second quarter, with the expectation of having results in 2025. (Also see "*Lilly Wows ADA Crowd With Obesity Data Across Three-Drug Incretin Portfolio*" - Scrip, 26 Jun, 2023.) Meanwhile, four Phase III trials under the TRIUMPH program are evaluating retatrutide for chronic weight management, obstructive sleep apnea and knee osteoarthritis in overweight and obese patients, which will run for between 68 and 80 weeks.

CEO David Ricks told the call that the news about the Wegovy results will “only expand the opportunity” in obesity, but it was unclear if Mounjaro would be able to meet demand.

“[Other] molecules, and orforglipron in particular, could play a big role in meeting global demand for obesity treatment and all the related complications because it’s a completely different technology in that it’s using [an] oral solid, and there’s quite a bit of capacity around the globe for that,” he said.

But Novo Nordisk has also faced issues with supply for Wegovy as well as for Ozempic, its version of semaglutide for diabetes. Despite ramping up manufacturing, the Danish company said in its fourth quarter earnings in February that it was still unable to produce enough Wegovy to meet demand, meaning that the potential revenue benefit from SELECT might take some time to materialize. (Also see "*Novo’s Wegovy Back On Track In Q4 But Broader Supply Issues Remain*" - Scrip, 1 Feb, 2023.)

Mason said there had been tight supply for Mounjaro, which Lilly expects to see continue in the short term. Consequently, he said, it is working on bringing on new manufacturing capacity for Mounjaro in North Carolina and other areas and the company expects to see some benefit from that supply as production ramps up, as it would help build up inventories and eliminate “any spot outage that we see.”

“In the short term, because we’re seeing really unprecedented demand, we do still expect to see tight supply and some spot outages on Mounjaro through the end of the year, but I think ultimately as that manufacturing capacity ramps up, we will be out of the spot outage that we see,” he said. “But in the next couple of months and quarters, I think we’ll see tight inventory.”