Article Title: Lilly's obesity portfolio in 'all-of-the-above mode'

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Eli Lilly is in "all-of-the-above mode" in obesity, with the research teams moving as fast as possible to advance an oral candidate and build a portfolio of complementary treatments.

The company is advancing the oral therapy orforglipron, testing new doses for tirzepatide—known as Mounjaro as approved for diabetes—as well as preparing a slate of earlier stage candidates to further deepen the possible weight loss seen with the GLP-1 class. The sprawling obesity research program was the headline from Lilly's third-quarter earnings call held Thursday.

Analysts tried to tease out any concerns Lilly may have on safety issues for orforglipron, the Indianapolis pharma's next-gen oral GLP-1 agonist, and other late-stage obesity trials underway. While the company brushed off concerns of liver toxicity last quarter in light of Pfizer's decision to drop an oral obesity candidate for that reason, the questions still came fast and furious.

"We've invested quite a lot in those phase 3 programs. They're robust, cover multiple indications, so there's no hesitation or trepidation there at all," said Dan Skovronsky, M.D., Ph.D., Lilly's chief scientific and medical officer, as well as president of Lilly Research Laboratories.

Asked why Lilly is testing higher doses of tirzepatide, a combo GLP-1 and GIP agonist, which is already approved for diabetes but is also awaiting an FDA decision in obesity, Skovronsky said the company believes they haven't truly maximized dose response yet. Higher doses are therefore being tested in phase 2.

"We've had enough patients on this drug for long enough that I expect the risk of uncovering a new safety signal with sort of marginally higher doses is extremely low, so not worried about that at all," he said.

Skovronsky also urged investors not to pit one obesity program against the other in Lilly's pipeline: "That's not really the mindset in which we're pursuing this.

"We see ourselves as a leader in the space and have a unique opportunity. And our goal is to exploit every single idea until we get data that says we shouldn't," Skovronsky said. "So high dose tirzepatide is just another version of that. But it doesn't have read-through to other things. We're just in all-the-above mode in obesity."

One massive hurdle Lilly—and other key players in the space like Novo Nordisk—is going to have to overcome is treatment adherence. Data shows that patients must stay on GLP-1s to maintain weight loss. Once they stop taking the injectable treatments, appetite comes back and weight returns.

An analyst pointed out that long-term adherence is always an issue for chronic conditions. But even without oral candidates ready, Lilly believes that patients will keep taking tirzepatide to maintain their weight loss. That's been the case with patients who have started on Mounjaro for diabetes, especially as compared to those who kept taking Lilly's other diabetes med Trulicity.

Lilly does not yet have data to show the long-term adherence in obesity care, and president of Lilly's diabetes and obesity division Mike Mason noted that Novo's Wegovy isn't a great model either due to supply constraints that have restricted availability of the product for patients.

"Time is going to tell," said Mason on the call.

With many chronic conditions, patients can stop taking a drug without seeing acute issues or immediate return of symptoms. Mason doesn't think that's the case with tirzepatide judging by data seen in the phase 3 SURROUND trials.

"Consumers will feel their appetite increase and experience weight regain when they stop tirzepatide, so this should help reinforce treatment adherence," Mason said. Lilly's market research has shown that people who lose weight want to maintain it, he added.

What could help is an oral candidate like orforglipron. Skovronsky said the team is moving as fast as possible to advance the candidate, which is already in phase 3 testing. But Lilly isn't looking to have the oral option be just one thing. Orforglipron could be used alone as an initial treatment, for maintenance of weight loss or in combination.

The therapy spurred 14.7% weight loss at 36 weeks in a phase 2 study published in the New England Journal of Medicine in June.

Lilly has another oral med called retatrutide, which was just shown in a phase 2 study to reduce weight by an average of 58 pounds at the end of 48 weeks, prompting the start of an expansive phase 3 program.