



Tirzepatide demonstrated significant and superior weight loss compared to placebo in two pivotal studies

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Participants in SURMOUNT-3, after 12 weeks of intensive lifestyle intervention, achieved an additional 21.1% mean weight loss with tirzepatide for a total mean weight loss of 26.6% from study entry over 84 weeks

Participants in SURMOUNT-4 achieved 21.1% weight loss during a 36-week tirzepatide lead-in period and an additional 6.7% weight loss during a 52-week continued treatment period, for a total mean weight loss of 26.0% over 88 weeks

INDIANAPOLIS, July 27, 2023 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) announced results of two phase 3 tirzepatide studies in adults with obesity or overweight with weight-related comorbidities, excluding type 2 diabetes. SURMOUNT-3 and SURMOUNT-4 met all primary and key secondary objectives for tirzepatide compared to placebo. Across SURMOUNT-3 and SURMOUNT-4, participants on tirzepatide following intensive lifestyle intervention or with continued tirzepatide treatment, achieved up to 26.6% mean weight loss, for the efficacy estimandⁱ.

The overall safety profile of tirzepatide in both studies was similar to previously reported SURMOUNT and SURPASS trials and to that of incretin-based therapies approved for the treatment of obesity and overweight. The most commonly reported adverse events in both trials were gastrointestinal-related and generally mild to moderate in severity.

"The results of SURMOUNT-3 and -4 showed the highest level of weight loss observed in the SURMOUNT program to date," said Jeff Emmick, MD, Ph.D., senior vice president, product development, Lilly. "Whether taking tirzepatide for 88 weeks in SURMOUNT-4 or taking tirzepatide for 72 weeks following intensive caloric restriction in SURMOUNT-3, participants achieved similar mean weight reduction — about 26%. The findings from SURMOUNT-3 challenge the notion that patients living with obesity or overweight can achieve their weight loss goals with diet and exercise alone. Additionally, the findings from SURMOUNT-4 reinforce that obesity should be regarded like other chronic diseases where chronic therapy may be needed to maintain treatment benefits."

Results from SURMOUNT-3

SURMOUNT-3 evaluated the efficacy and safety of tirzepatide compared to placebo for 72 weeks after a 12-week intensive lifestyle intervention lead-in period that included a low-calorie diet, exercise and weekly counseling sessions. The trial randomized adults with obesity or overweight who had at least 5% body weight reduction by the end of the 12-week lead-in period to placebo or tirzepatide. At study entry, the mean body weight was 241.4 lb. (109.5 kg). At the end of the 12-week lead-in period, participants achieved 6.9% mean weight loss.

Tirzepatide met both co-primary endpoints demonstrating superiority to placebo during the 72-week double-blind treatment period. For the efficacy estimand, those taking tirzepatide, on average, lost an additional 21.1% of their body weight from randomization, a co-primary endpoint, compared to those taking placebo who experienced mean weight regain of 3.3% over 72 weeks, for a placebo-adjusted net weight change of -24.5%. In addition, 94.4% of those taking tirzepatide achieved an additional $\geq 5\%$ body weight reduction from randomization, the other co-primary endpoint, compared to 10.7% in the placebo group over 72 weeks. In a secondary endpoint, participants receiving tirzepatide had a total mean weight reduction of 26.6% from study entry after 12 weeks of intensive lifestyle intervention followed by 72 weeks of tirzepatide treatment.

For the treatment-regimen estimandⁱⁱ, those taking tirzepatide, on average, lost an additional 18.4% of their body weight from randomization compared to those taking placebo who experienced mean weight regain of 2.5% over 72 weeks. In addition, 87.5% of those taking tirzepatide achieved an additional $\geq 5\%$ body weight reduction from randomization compared with 16.5% in the placebo group over 72 weeks. Participants receiving tirzepatide had a total mean weight reduction of 24.3% from study entry after 12 weeks of intensive lifestyle intervention followed by 72 weeks of tirzepatide treatment.

The full results of the SURMOUNT-3 study will be presented at the ObesityWeek conference in October and submitted for publication in a peer-reviewed journal.

Results from SURMOUNT-4

SURMOUNT-4 evaluated the efficacy and safety of tirzepatide compared to placebo for 52 weeks after a 36-week open-label tirzepatide lead-in period. The trial had two periods: a 36-week open-label lead-in period during which all participants took tirzepatide, followed by a 52-week double-blind treatment period during which participants were randomized to either continue on tirzepatide or switch to placebo. For randomized participants, the mean body weight was 236.6 lb. (107.3 kg) at study entry. At the end of the 36-week tirzepatide lead-in period, they achieved 21.1% mean weight loss.

Tirzepatide met the primary endpoint of superior mean percent change in body weight compared to placebo from 36 weeks to 88 weeks, indicating sustained weight loss. For the efficacy estimand, those taking tirzepatide, on average, lost an additional 6.7% of their body weight from randomization, compared to those taking placebo who experienced mean weight regain of 14.8% from randomization at 88 weeks, for a placebo-adjusted net weight change of -21.4%. In a secondary endpoint, participants who remained on tirzepatide after randomization achieved a total of 26.0% mean body weight loss from study entry over the entire 88-week period.

For the treatment-regimen estimand, those taking tirzepatide, on average, lost an additional 5.5% of their body weight from randomization, compared to those taking placebo who experienced mean weight regain of 14.0% from randomization at 88 weeks. Participants who remained on tirzepatide after randomization achieved a total of 25.3% mean body weight loss from study entry over the entire 88-week period.

The full results of the SURMOUNT-4 study will be presented at the European Association for the Study of Diabetes Annual Meeting in October and submitted for publication in a peer-reviewed journal.

About SURMOUNT-3, SURMOUNT-4 and the SURMOUNT clinical trial program¹

SURMOUNT-3 (NCT04657016) was a multi-center, randomized, double-blind, parallel, placebo-controlled trial comparing the efficacy and safety of tirzepatide to placebo for 72 weeks after a 12-week intensive lifestyle intervention lead-in period in adults with obesity or overweight with weight-related comorbidities, excluding type 2 diabetes. The trial enrolled 806 participants across the U.S., Argentina, Brazil and Puerto Rico to a lead-in period with intensive lifestyle intervention. After 12 weeks, 579 participants achieved at least 5% body weight reduction and were randomized in a 1:1 ratio to receive tirzepatide or placebo. The co-primary objectives of the study were to demonstrate that tirzepatide is superior in percentage change in body weight from randomization and percentage of participants achieving $\geq 5\%$ body weight reduction from randomization at 72 weeks compared to placebo.

SURMOUNT-4 (NCT04660643) was a multi-center, randomized, double-blind, parallel, placebo-controlled trial comparing the efficacy and safety of tirzepatide to placebo in adults with obesity or overweight with weight-related comorbidities, excluding type 2 diabetes. The trial had two periods: a 36-week open-label lead-in period in which all participants took tirzepatide, and a subsequent 52-week double-blind treatment period in which participants were randomized to either continue on tirzepatide or switch to placebo. The trial enrolled 783 participants across the U.S., Argentina, Brazil, Puerto Rico and Taiwan into the open-label lead-in period and 670 participants were randomized in a 1:1 ratio in the 52-week double-blind treatment period to receive tirzepatide or placebo. The primary objective of the study was to demonstrate that tirzepatide is superior in percentage change in body weight from randomization at 88 weeks compared to placebo.

While SURMOUNT-1 and SURMOUNT-2 had fixed weekly tirzepatide doses, participants in SURMOUNT-3 and SURMOUNT-4 utilized a maximum tolerated dose of 10 mg or 15 mg once-weekly. The starting dose of 2.5 mg tirzepatide was increased by 2.5 mg every four weeks until maximum tolerated dose was achieved. Participants who tolerated 15 mg continued on 15 mg as their maximum tolerated dose. Participants who tolerated 10 mg but did not tolerate 15 mg continued on 10 mg as their maximum tolerated dose.

The SURMOUNT phase 3 global clinical development program for tirzepatide in chronic weight management began in late 2019 and has enrolled more than 5,000 people with obesity or overweight across six registration studies, four of which are global studies. The primary period of SURMOUNT-1 was completed in 2022 and SURMOUNT-2 was completed in the first half of 2023.

About tirzepatide

Tirzepatide is a once-weekly GIP (glucose-dependent insulinotropic polypeptide) receptor and GLP-1 (glucagon-like peptide-1) receptor agonist. Tirzepatide is a single molecule that activates the body's receptors for GIP and GLP-1, which are natural incretin hormones. Both GIP and GLP-1 receptors are found in areas of the human brain important for appetite regulation. Tirzepatide has been shown to decrease food intake and modulate fat utilization. Tirzepatide is in phase 3 development for adults with obesity or overweight with weight-related comorbidities. It is also being studied as a potential treatment for people with obesity and/or overweight with heart failure with preserved ejection fraction (HFpEF), obstructive sleep apnea (OSA) and non-alcoholic steatohepatitis (NASH). Studies of tirzepatide in chronic kidney disease (CKD) and in morbidity/mortality in obesity (MMO) are also ongoing.

Tirzepatide was approved as Mounjaro[®] (tirzepatide) by the FDA on May 13, 2022. Mounjaro is a glucose-dependent insulinotropic polypeptide (GIP) receptor and glucagon-like peptide-1 (GLP-1) receptor agonist indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes.

About Lilly

Lilly unites caring with discovery to create medicines that make life better for people around the world. We've been pioneering life-changing discoveries for nearly 150 years, and today our medicines help more than 51 million people across the globe. Harnessing the power of biotechnology, chemistry and genetic medicine, our scientists are urgently advancing new discoveries to solve some of the world's most significant health challenges, redefining diabetes care, treating obesity and curtailing its most devastating long-term effects, advancing the fight against Alzheimer's disease, providing solutions to some of the most debilitating immune system disorders, and transforming the most difficult-to-treat cancers into manageable diseases. With each step toward a healthier world, we're motivated by one thing: making life better for millions more people. That includes delivering innovative clinical trials that reflect the diversity of our world and working to ensure our medicines are accessible and affordable. To learn more, visit [Lilly.com](https://www.lilly.com) and [Lilly.com/newsroom](https://www.lilly.com/newsroom) or follow us on [Facebook](https://www.facebook.com/lilly), [Instagram](https://www.instagram.com/lilly), [Twitter](https://twitter.com/lilly) and [LinkedIn](https://www.linkedin.com/company/lilly). P-LLY.

INDICATION AND SAFETY SUMMARY WITH WARNINGS

Mounjaro[®] (moun-JAHR-OH) is an injectable medicine for adults with type 2 diabetes used along with diet and exercise to improve blood sugar (glucose).

- It is not known if Mounjaro can be used in people who have had inflammation of the pancreas (pancreatitis). Mounjaro is not for use in people with type 1 diabetes. It is not known if Mounjaro is safe and effective for use in children under 18 years of age.

Warnings - Mounjaro may cause tumors in the thyroid, including thyroid cancer. Watch for possible symptoms, such as a lump or swelling in the neck, hoarseness, trouble swallowing, or shortness of breath. If you have any of these symptoms, tell your healthcare provider.

- Do not use Mounjaro if you or any of your family have ever had a type of thyroid cancer called medullary thyroid carcinoma (MTC).
- Do not use Mounjaro if you have Multiple Endocrine Neoplasia syndrome type 2 (MEN 2).
- Do not use Mounjaro if you are allergic to it or any of the ingredients in Mounjaro.

Mounjaro may cause serious side effects, including:

Inflammation of the pancreas (pancreatitis). Stop using Mounjaro and call your healthcare provider right away if you have severe pain in your

stomach area (abdomen) that will not go away, with or without vomiting. You may feel the pain from your abdomen to your back.

Low blood sugar (hypoglycemia). Your risk for getting low blood sugar may be higher if you use Mounjaro with another medicine that can cause low blood sugar, such as a sulfonylurea or insulin. **Signs and symptoms of low blood sugar may include** dizziness or light-headedness, sweating, confusion or drowsiness, headache, blurred vision, slurred speech, shakiness, fast heartbeat, anxiety, irritability, or mood changes, hunger, weakness and feeling jittery.

Serious allergic reactions. Stop using Mounjaro and get medical help right away if you have any symptoms of a serious allergic reaction, including swelling of your face, lips, tongue or throat, problems breathing or swallowing, severe rash or itching, fainting or feeling dizzy, and very rapid heartbeat.

Kidney problems (kidney failure). In people who have kidney problems, diarrhea, nausea, and vomiting may cause a loss of fluids (dehydration), which may cause kidney problems to get worse. It is important for you to drink fluids to help reduce your chance of dehydration.

Severe stomach problems. Stomach problems, sometimes severe, have been reported in people who use Mounjaro. Tell your healthcare provider if you have stomach problems that are severe or will not go away.

Changes in vision. Tell your healthcare provider if you have changes in vision during treatment with Mounjaro.

Gallbladder problems. Gallbladder problems have happened in some people who use Mounjaro. Tell your healthcare provider right away if you get symptoms of gallbladder problems, which may include pain in your upper stomach (abdomen), fever, yellowing of skin or eyes (jaundice), and clay-colored stools.

Common side effects

The most common side effects of Mounjaro include nausea, diarrhea, decreased appetite, vomiting, constipation, indigestion, and stomach (abdominal) pain. These are not all the possible side effects of Mounjaro. Talk to your healthcare provider about any side effect that bothers you or doesn't go away.

Tell your healthcare provider if you have any side effects. **You can report side effects at 1-800-FDA-1088 or www.fda.gov/medwatch.**

Before using Mounjaro

- **Your healthcare provider should show you how to use Mounjaro before you use it for the first time.**
- **Talk to your healthcare provider about low blood sugar and how to manage it.**
- **If you take birth control pills by mouth, talk to your healthcare provider before you use Mounjaro. Birth control pills may not work as well while using Mounjaro.** Your healthcare provider may recommend another type of birth control for 4 weeks after you start Mounjaro and for 4 weeks after each increase in your dose of Mounjaro.

Review these questions with your healthcare provider:

- ☐ Do you have other medical conditions, including problems with your pancreas or kidneys, or severe problems with your stomach, such as slowed emptying of your stomach (gastroparesis) or problems digesting food?
- ☐ Do you take other diabetes medicines, such as insulin or sulfonylureas?
- ☐ Do you have a history of diabetic retinopathy?
- ☐ Are you pregnant, plan to become pregnant, breastfeeding, or plan to breastfeed? It is not known if Mounjaro will harm your unborn baby or pass into your breast milk.
- ☐ Do you take any other prescription medicines or over-the-counter drugs, vitamins, or herbal supplements?

How to take

- Read the **Instructions for Use** that come with Mounjaro.
- Use Mounjaro exactly as your healthcare provider says.
- Mounjaro is injected under the skin (subcutaneously) of your stomach (abdomen), thigh, or upper arm.
- **Use Mounjaro 1 time each week, at any time of the day.**
- **Do not** mix insulin and Mounjaro together in the same injection.
- You may give an injection of Mounjaro and insulin in the same body area (such as your stomach area), but not right next to each other.
- Change (rotate) your injection site with each weekly injection. **Do not** use the same site for each injection.
- If you take too much Mounjaro, call your healthcare provider or seek medical advice promptly.

Learn more

Mounjaro is a prescription medicine. For more information, call 1-833-807-MJRO (833-807-6576) or go to www.mounjaro.com.

This summary provides basic information about Mounjaro but does not include all information known about this medicine. Read the information that comes with your prescription each time your prescription is filled. This information does not take the place of talking with your healthcare provider. Be sure to talk to your healthcare provider about Mounjaro and how to take it. Your healthcare provider is the best person to help you decide if Mounjaro is right for you.

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ⁱ The efficacy estimand represents efficacy prior to discontinuation of study drug.

ⁱⁱ The treatment-regimen estimand represents the estimated average treatment effect regardless of treatment discontinuation.

Lilly Cautionary Statement Regarding Forward-Looking Statements

This press release contains forward-looking statements (as that term is defined in the Private Securities Litigation Reform Act of 1995) about tirzepatide as a potential treatment for adults with obesity or overweight and the timeline for regulatory submissions, future readouts, presentations and other milestones relating to tirzepatide and its clinical trials, and reflects Lilly's current belief and expectations. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of drug research, development, and commercialization. Among other things, there can be no guarantee that planned or ongoing studies will be completed as planned, that future study results will be consistent with the results to date, that tirzepatide will receive additional regulatory approvals, or that tirzepatide will be commercially successful. For further discussion of these and other risks and uncertainties, see Lilly's most recent Form 10-K and Form 10-Q filings with the United States Securities and Exchange Commission. Except as required by law, Lilly undertakes no duty to update forward-looking statements to reflect events after the date of this release.

References

1. le Roux, C., Zhang, S., Aronne, L. et. al. Tirzepatide for the Treatment of Obesity: Rationale and Design of the SURMOUNT Clinical Development Program 2022 Obesity doi: 10.1002/oby.23612

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