



Lilly's tirzepatide shows additional 21.1% weight loss after 12 weeks of intensive lifestyle intervention, for a total mean weight loss of 26.6% from study entry over 84 weeks

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The full results of the SURMOUNT-3 trial were published in *Nature Medicine* and simultaneously presented at ObesityWeek® 2023

INDIANAPOLIS, Oct. 15, 2023 /PRNewswire/ -- Detailed results from Eli Lilly and Company's (NYSE: LLY) phase 3 SURMOUNT-3 clinical trial evaluating tirzepatide in adults with obesity or overweight with weight-related comorbidities, excluding type 2 diabetes, were published in [Nature Medicine](#) and simultaneously presented at ObesityWeek® 2023. Tirzepatide met both co-primary endpoints for the efficacy estimandⁱ and treatment-regimenⁱⁱ estimand, demonstrating superiority to placebo during the 72-week double-blind treatment period.

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 frequent 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% (7.6 kg or 16.8 lb.) mean weight loss. In a co-primary endpoint, following the lead-in period, participants taking tirzepatide achieved an additional 21.1% mean weight loss. In a secondary endpoint, participants achieved a total mean weight loss of 26.6% (29.2 kg or 64.4 lb.) from study entry over 84 weeks. Participants on placebo achieved a total mean weight loss of 3.8% (4.1 kg or 9.0 lb.) from study entry over 84 weeks.

"In this study, people who added tirzepatide to diet and exercise saw greater, longer-lasting weight reduction than those taking placebo," said Jeff Emmick, MD, Ph.D., senior vice president, product development, Lilly. "While intensive lifestyle intervention is an important part of obesity management, these results underscore the difficulty some people face maintaining weight loss with diet and exercise alone."

	Treatment-Regimen Estimand Results from Randomization (Week 0) to Week 72		Efficacy Estimand Results from Randomization (Week 0) to Week 72	
	Tirzepatide	Placebo	Tirzepatide	Placebo
Co-Primary Endpoints				
Percent change in body weight*	-18.4 %	2.5 %	-21.1 %	3.3 %
Percentage of participants achieving ≥5% weight reduction*	87.5 %	16.5 %	94.4 %	10.7 %
Key Secondary Endpoints				
Percentage of participants achieving ≥20% weight reduction*	44.7 %	2.2 %	54.9 %	1.0 %
Percentage of participants who maintained ≥80% of the body weight lost during lead-in at week 72*	94.0 %	43.8 %	98.6 %	37.8 %
Change in waist circumference*	-14.6 cm	0.2 cm	-16.8 cm	1.1 cm

*Tested for superiority, controlled for type 1 error.

The overall safety profile of tirzepatide in SURMOUNT-3 was similar to previously reported SURMOUNT and SURPASS trials. The most commonly reported adverse events in SURMOUNT-3 were gastrointestinal-related and generally mild to moderate in severity. The most frequent events reported by those on tirzepatide compared with placebo, respectively, were nausea (39.7% vs. 14.0%), diarrhea (31.0% vs. 9.2%), constipation (23.0% vs. 6.8%), COVID-19 (23.0% vs. 25.3%) and vomiting (18.1% vs. 1.4%). Adverse events led to discontinuation of study treatment in 10.5% of participants taking tirzepatide and 2.1% taking placebo.

About SURMOUNT-3 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., including Puerto Rico, Argentina and Brazil 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 percent change in body weight from randomization and percentage of participants achieving ≥5% body weight reduction from randomization at 72 weeks compared to placebo.

SURMOUNT-3 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. Topline data for SURMOUNT-3 and SURMOUNT-4 were announced on July 27, 2023; full results for SURMOUNT-4 were presented this month at the European Association for the Study of Diabetes Annual Meeting (EASD 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 under review by the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) for adults living 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/news](https://www.lilly.com/news) 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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SOURCE Eli Lilly and Company