Treatment with tirzepatide in adults with pre-diabetes and obesity or overweight resulted in sustained weight loss and nearly 99% remained diabetes-free at 176 weeks

November 13, 2024

SURMOUNT-1 results show a 94% reduction in risk of progression to type 2 diabetes across all pooled doses of tirzepatide compared to placebo over three years

Results suggest one new case of diabetes could be prevented for every nine patients treated with tirzepatide

Participants treated with tirzepatide had an average weight reduction of 22.9% (15 mg dose)

INDIANAPOLIS, Nov. 13, 2024 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) announced today detailed results from the Phase 3 SURMOUNT-1 three-year study (176-week treatment period), the longest completed study to date of tirzepatide. Weekly tirzepatide (Zepbound® and Mounjaro®) injections (pooled 5 mg, 10 mg, 15 mg doses) significantly reduced the risk of progression to type 2 diabetes in adults with pre-diabetes and obesity or overweight, compared with placebo, over 176 weeks. Tirzepatide demonstrated sustained average weight loss of 22.9% (15 mg dose) through the three-year treatment period for the efficacy estimand[i]. These findings were published in *The New England Journal of Medicine (NEJM)* and recently presented at ObesityWeek 2024.

"Individuals treated with tirzepatide lost on average up to 23% of their body weight and maintained this for over three years, while benefitting from a substantial decrease in risk of developing type 2 diabetes. In absolute terms, nearly 99% of individuals treated with tirzepatide remained diabetes-free at 176 weeks," said Ania Jastreboff, M.D., Ph.D., director of the Yale Obesity Research Center. "These results are impressive given the degree of sustained weight reduction and decrease in risk of diabetes."

Tirzepatide is the first and only approved dual GIP (glucose-dependent insulinotropic polypeptide) and GLP-1 (glucagon-like peptide-1) receptor agonist medicine. Both GIP and GLP-1 are gut hormones secreted in response to nutrient load and are responsible for the incretin effect.

"In the SURMOUNT-1 three-year study of tirzepatide, an average weight reduction of up to 22.9% was accompanied by a hazard ratio of 0.06 for progression to type 2 diabetes. This translates to a risk reduction of 94% and a number needed to treat of nine to prevent one case of diabetes," said Jeff Emmick, M.D., Ph.D., senior vice president, product development, Lilly. "These results underscore the critical role of long-term therapy with effective treatments like tirzepatide to achieve and maintain weight reduction."

In additional endpoints, the study showed an association of tirzepatide treatment with improvements in glycemic control, cardiometabolic risk factors (including fasting insulin, blood pressure and lipids) and health-related quality of life, which were sustained through 176 weeks[ii]. A post hoc mediation analysis suggested that approximately half of the observed effect in delay to onset of type 2 diabetes with tirzepatide was associated with medication-induced weight reduction, with the remaining benefit potentially attributed to other effects of tirzepatide.

The overall safety and tolerability profile of tirzepatide at 193 weeks (176 weeks followed by 17 weeks off-treatment) was consistent with the previously published results at 72 weeks for SURMOUNT-1 and other tirzepatide clinical studies conducted for weight reduction and long-term maintenance. Other than COVID-19, the most frequently reported adverse events were gastrointestinal-related and generally mild to moderate in severity. The most common gastrointestinal-related adverse events in patients treated with tirzepatide were nausea, diarrhea and constipation.

Full Results

SURMOUNT-1 Three-Year Study: Key Secondary Endpoints (p<0.0001, controlled for type 1 error)						
Key Secondary Endpoints at Week 176 (end of treatment period)						
	Efficacy Estimand[i]			**Treatment-Regimen Estimand[iii]**		
Percentage of Participants Diagnosed with Type 2 Diabetes						
Tirzepatide (5 mg, 10 mg and 15 mg pooled doses) (n=762)	1.2 %			1.3 %		
Placebo (n=270)	12.6 %			13.3 %		
Reduction in Risk of Progression to Type 2 Diabetes						
Tirzepatide (5 mg, 10 mg and 15 mg pooled doses)	Hazard Ratio=0.06			Hazard Ratio=0.07		
Tirzepatide (5 mg, 10 mg and 15 mg pooled doses)	Number Needed to Treat to Prevent One Case of Diabetes=9[ii]			Number Needed to Treat to Prevent One Case of Diabetes=9[ii]		
Average Percent Body Weight Reduction from Baseline						
Tirzepatide	5 mg[iv] (n=245)	10 mg (n=260)	15 mg (n=249)	5 mg[iv] (n=247)	10 mg (n=262)	15 mg (n=253)

	15.4 %	19.9 %	22.9 %	12.3 %	18.7 %	19.7 %
Placebo	2.1 % (n=264)			1.3 % (n=270)		
Key Secondary Endpoint[v] at Week 193 (end of 17-week off-treatment follow-up period)						
Percentage of Participants Diagnosed with Type 2 Diabetes						
Tirzepatide (5 mg, 10 mg and 15 mg pooled doses) (n=762)	2.4 %					
Placebo (n=270)	13.7 %					
Reduction in Risk of Progression to Type 2 Diabetes						
Tirzepatide (5 mg, 10 mg and 15 mg pooled doses)	Hazard Ratio=0.12					

About SURMOUNT-1
SURMOUNT-1 (NCT04184622) was a multi-center, randomized, double-blind, parallel, placebo-controlled trial comparing the efficacy and safety of tirzepatide 5 mg, 10 mg and 15 mg to placebo as an adjunct to a reduced-calorie diet and increased physical activity in adults without type 2 diabetes who had obesity, or overweight with at least one of the following comorbidities: hypertension, dyslipidemia, obstructive sleep apnea (OSA) or cardiovascular disease. The 1,032 participants who had pre-diabetes at study commencement remained enrolled in SURMOUNT-1 for an additional 104 weeks of treatment following the initial 72-week completion date to evaluate the impact on body weight and potential differences in progression to type 2 diabetes at three years of treatment with tirzepatide compared to placebo.

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 decreases calorie intake, and the effects are likely mediated by affecting appetite. Studies of tirzepatide in chronic kidney disease (CKD) and in morbidity/mortality in obesity (MMO) are ongoing. Lilly submitted data for tirzepatide in moderate-to-severe obstructive sleep apnea (OSA) and obesity to the U.S. Food and Drug Administration (FDA) and other global regulatory agencies earlier this year. Lilly plans to submit data for tirzepatide in heart failure with preserved ejection fraction (HFpEF) and obesity to the U.S. FDA and other global regulatory agencies later this year.

Tirzepatide was approved by the U.S. FDA as Mounjaro® for adults with type 2 diabetes to improve glycemic control on May 13, 2022, and as Zepbound® for adults with obesity or those who are overweight who also have at least one weight-related medical problem on November 8, 2023. Tirzepatide is also commercialized as Mounjaro® in some global markets outside the U.S. for adults with obesity or those who are overweight who also have a weight-related comorbid condition.

Tirzepatide is the only approved dual GIP and GLP-1 receptor agonist treatment to reduce excess body weight and maintain weight reduction long term. Both Mounjaro® and Zepbound® should be used in combination with diet and exercise.

INDICATION AND SAFETY SUMMARY WITH WARNINGS

Zepbound® (ZEHP-bownd) is an injectable prescription medicine that may help adults with obesity, or some adults with overweight who also have weight-related medical problems to lose excess body weight and keep the weight off. It should be used with a reduced-calorie diet and increased physical activity.

- Zepbound contains tirzepatide and should not be used with other tirzepatide-containing products or any GLP-1 receptor agonist medicines. It is not known if Zepbound is safe and effective for use in children.

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

Zepbound may cause serious side effects, including:

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

Kidney problems (kidney failure). Diarrhea, nausea, and vomiting may cause a loss of fluids (dehydration), which may cause kidney problems. It is important for you to drink fluids to help reduce your chance of dehydration.

Gallbladder problems. Gallbladder problems have happened in some people who use Zepbound. 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), or clay-colored stools.

Inflammation of the pancreas (pancreatitis). Stop using Zepbound 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.

Serious allergic reactions. Stop using Zepbound 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, or very rapid heartbeat.

Low blood sugar (hypoglycemia). Your risk for getting low blood sugar may be higher if you use Zepbound with medicines 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, mood changes, hunger, weakness or feeling jittery.

Changes in vision in patients with type 2 diabetes. Tell your healthcare provider if you have changes in vision during treatment with Zepbound.

Depression or thoughts of suicide. You should pay attention to changes in your mood, behaviors, feelings or thoughts. Call your healthcare provider right away if you have any mental changes that are new, worse, or worry you.

Food or liquid getting into the lungs during surgery or other procedures that use anesthesia or deep sleepiness (deep sedation). Zepbound may increase the chance of food getting into your lungs during surgery or other procedures. Tell all your healthcare providers that you are taking Zepbound before you are scheduled to have surgery or other procedures.

Common side effects

The most common side effects of Zepbound include nausea, diarrhea, vomiting, constipation, stomach (abdominal) pain, indigestion, injection site reactions, feeling tired, allergic reactions, belching, hair loss, and heartburn. These are not all the possible side effects of Zepbound. Talk to your healthcare provider about any side effect that bothers you or doesn't go away.

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

Before using Zepbound

- **Your healthcare provider should show you how to use Zepbound before you use it for the first time.**
- **Tell your healthcare provider if you are taking medicines to treat diabetes including an insulin or sulfonylurea which could increase your risk of low blood sugar. Talk to your healthcare provider about low blood sugar levels and how to manage them.**
- **If you take birth control pills by mouth, talk to your healthcare provider before you use Zepbound. Birth control pills may not work as well while using Zepbound.** Your healthcare provider may recommend another type of birth control for 4 weeks after you start Zepbound and for 4 weeks after each increase in your dose of Zepbound.

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 diabetes medicines, such as insulin or sulfonylureas?

❑ Do you have a history of diabetic retinopathy?

❑ Are you scheduled to have surgery or other procedures that use anesthesia or deep sleepiness (deep sedation)?

❑ Do you take any other prescription medicines or over-the-counter drugs, vitamins, or herbal supplements?

❑ Are you pregnant, plan to become pregnant, breastfeeding, or plan to breastfeed? Zepbound may harm your unborn baby. Tell your healthcare provider if you become pregnant while using Zepbound. It is not known if Zepbound passes into your breast milk. You should talk with your healthcare provider about the best way to feed your baby while using Zepbound.

- **Pregnancy Exposure Registry:** There will be a pregnancy exposure registry for women who have taken Zepbound during pregnancy. The purpose of this registry is to collect information about the health of you and your baby. Talk to your healthcare provider about how you can take part in this registry, or you may contact Lilly at 1-800-LillyRx (1-800-545-5979).

How to take

- Read the Instructions for Use that come with Zepbound.
- Use Zepbound exactly as your healthcare provider says.
- Use Zepbound with a reduced-calorie diet and increased physical activity.
- Zepbound is injected under the skin (subcutaneously) of your stomach (abdomen), thigh, or upper arm.
- **Use Zepbound 1 time each week, at any time of the day.**
- Change (rotate) your injection site with each weekly injection. **Do not** use the same site for each injection.
- If you take too much Zepbound, call your healthcare provider, seek medical advice promptly, or contact a Poison Center expert right away at 1-800-222-1222.

Learn more

Zepbound is a prescription medicine. For more information, call 1-800-LillyRx (1-800-545-5979) or go to **www.zepbound.lilly.com**.

This summary provides basic information about Zepbound 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 Zepbound and how to take it. Your healthcare provider is the best person to help you decide if Zepbound is right for you.

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INDICATION AND SAFETY SUMMARY WITH WARNINGS

Mounjaro® (mown-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.

Food or liquid getting into the lungs during surgery or other procedures that use anesthesia or deep sleepiness (deep sedation). Mounjaro may increase the chance of food getting into your lungs during surgery or other procedures. Tell all your healthcare providers that you are taking Mounjaro before you are scheduled to have surgery or other procedures.

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 scheduled to have surgery or other procedures that use anesthesia or deep sleepiness (deep sedation)?
❑ 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 available as a pre-filled single-dose pen in 2.5 mg, 5 mg, 7.5 mg, 10 mg, 12.5 mg, or 15 mg per 0.5 mL injection. For more information, call 1-833-807-MJRO (833-807-6576) [or go to **www.mounjaro.lilly.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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 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.If you take too much Mounjaro, call your healthcare provider or seek medical advice promptly.

About Lilly
Lilly is a medicine company turning science into healing to make life better for people around the world. We've been pioneering life-changing discoveries for nearly 150 years, and today our medicines help tens of millions of 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 and Lilly.com/news, or follow us on Facebook, Instagram, and LinkedIn. P-LLY

References
[i] The efficacy estimand represents efficacy had all patients remained on randomized treatment for the entire planned treatment duration (up to 176 weeks).
[ii] Not controlled for type 1 error.
[iii] The treatment-regimen estimand represents efficacy regardless of adherence to randomized treatment.
[iv] 5 mg weekly tirzepatide injections evaluating change in body weight not controlled for type 1 error.
[v] The analysis was conducted regardless of adherence to randomized treatment from randomization to the end of safety follow-up at 193 weeks.

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) including about tirzepatide injection for the treatment of adults with type 2 diabetes, tirzepatide as a potential long-term therapy for adults with pre-diabetes and obesity or overweight and the timeline for future readouts, presentations, and other milestones relating to tirzepatide and its clinical trials, and reflects Lilly's current beliefs 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 is no guarantee that planned or ongoing studies will be completed as planned, that future study results will be consistent with study results to date, that tirzepatide will receive additional regulatory approvals, or that Lilly will execute its strategy as expected. For further discussion of these and other risks and uncertainties that could cause actual results to differ from Lilly's expectations, see Lilly's 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.

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SOURCE Eli Lilly and Company