Lilly's SURMOUNT-2 results published in The Lancet show tirzepatide achieved a mean weight reduction of 15.7% at the highest dose (15 mg) in adults with obesity or overweight and type 2 diabetes

June 24, 2023

Detailed results presented at the American Diabetes Association's® 83rd Scientific Sessions

Lilly has completed tirzepatide's submission for chronic weight management to the FDA

INDIANAPOLIS, June 24, 2023 /PRNewswire/ -- Detailed results from SURMOUNT-2, a phase 3 clinical trial evaluating the efficacy and safety of Eli Lilly and Company's (NYSE: LLY) tirzepatide (10 mg and 15 mg) for chronic weight management in participants with obesity or overweight[i] and type 2 diabetes, showed that tirzepatide led to superior weight reduction versus placebo for both doses. The data were presented during a symposium at the American Diabetes Association's® (ADA) 83rd Scientific Sessions and were simultaneously published in *The Lancet*.

Tirzepatide met both co-primary endpoints and all key secondary endpoints compared to placebo for both estimands, with those taking tirzepatide achieving a mean weight reduction of 13.4% (29.8 lb. or 13.5 kg) on 10 mg and 15.7% (34.4 lb. or 15.6 kg) on 15 mg compared to 3.3% (7.0 lb. or 3.2 kg) on placebo for the efficacy estimand, which evaluates the treatment effect if all participants adhered to treatment. For the efficacy estimand, 81.6% (10 mg) and 86.4% (15 mg) of people taking tirzepatide achieved at least 5% body weight reduction, compared to 30.5% of those taking placebo.

Both doses of tirzepatide achieved all key secondary endpoints at 72 weeks of treatment for the efficacy estimand, including:

- Percentage of participants taking the 15 mg tirzepatide dose achieving ≥15% and ≥20% body weight reductions: 51.8% (≥15% reduction) and 34.0% (≥20% reduction), compared to 2.6% and 1.0% with placebo
- Percentage of participants achieving A1C of <5.7%: 55.3% (10 mg) and 50.2% (15 mg), compared to 2.8% with placebo
- Reduction in waist circumference: 11.2 cm (10 mg) and 13.8 cm (15 mg), compared to 3.4 cm with placebo
- Reduction in fasting glucose: 49.2 mg/dL (10 mg) and 51.7 mg/dL (15 mg), compared to 2.4 mg/dL with placebo

Pooled tirzepatide doses (10 mg and 15 mg) resulted in significantly greater improvements compared to placebo in systolic blood pressure (-7.2 mmHg vs. -1.0 mmHg), fasting triglycerides (-28.6% vs. -5.8%), HDL-cholesterol (8.2% vs. 1.1%) and non-HDL-cholesterol (-6.6% vs. 2.3%).

"People living with type 2 diabetes in many cases have been exposed to excess weight for years and often face increased difficulties in achieving weight loss results, typically losing 30% less weight than those who have obesity without type 2 diabetes. They need options to help overcome those challenges and achieve meaningful weight reductions," said W. Timothy Garvey, MD, MACE, MABOM, Professor of Medicine at the University of Alabama at Birmingham (UAB), Director of the UAB Diabetes Research Center and Principal Investigator of SURMOUNT-2. "Tirzepatide not only helped people achieve body weight reductions of up to 15.7%, but also helped to significantly lower A1C without severe hypoglycemia and led to improvements in other cardiometabolic endpoints."

Additionally, tirzepatide met the co-primary and all key secondary endpoints for the treatment-regimen estimand, which represents the average results of all study participants regardless of treatment adherence, including:

- Mean body weight reductions: 12.8% (10 mg), 14.7% (15 mg), 3.2% (placebo)
- Percentage of participants achieving body weight reductions of ≥5%: 79.2% (10 mg), 82.8% (15 mg), 32.5% (placebo)
- Percentage of participants achieving at least ≥20% body weight reduction: 21.5% (10 mg) and 30.8% (15 mg), compared to 1.0% with placebo
- Percentage of participants achieving A1C of <5.7%: 46.0% (10 mg) and 48.6% (15 mg), compared to 3.9% with placebo

The overall safety profile of tirzepatide was consistent with previously reported SURMOUNT and SURPASS trials and similar to incretin-based therapies approved for the treatment of obesity and overweight. The most commonly reported adverse events were gastrointestinal-related and were generally mild to moderate in severity, and usually occurred during the dose-escalation period. For those treated with tirzepatide (10 mg and 15 mg, respectively), nausea (20.2%, 21.9%), diarrhea (19.9%, 21.5%), vomiting (10.9%, 13.2%) and constipation (8.0%, 9.0%) were more frequently reported compared to placebo (6.3% [nausea], 8.9% [diarrhea], 3.2% [vomiting], 4.1% [constipation]).

"At Lilly, bringing new treatments to people with obesity is a priority and we are proud to share more evidence that solidifies our belief in tirzepatide as a treatment that will impact the way patients manage this disease," said Mike Mason, Executive Vice President and President, Lilly Diabetes and Obesity. "With these results in hand, we have completed our submission for chronic weight management to the U.S. FDA. We look forward to the future of obesity care and the opportunity to bring potential new treatments, like tirzepatide, to people with obesity and overweight."

Regulatory action for the U.S. submission for tirzepatide in adults with obesity, or overweight with weight-related comorbidities is expected by the end of 2023.

About SURMOUNT-2 and the SURMOUNT clinical trial program[1,2]

SURMOUNT-2 (NCT04657003) was a multi-center, randomized, double-blind, parallel, placebo-controlled trial comparing the efficacy and safety of

tirzepatide 10 mg and 15 mg to placebo as an adjunct to a reduced-calorie diet and increased physical activity in adults with obesity or overweight and type 2 diabetes. The trial randomized 938 participants across the U.S., Argentina, Brazil, India, Japan, Puerto Rico, Russia and Taiwan in a 1:1:1 ratio to receive tirzepatide 10 mg, 15 mg or placebo. The co-primary objectives of the study were to demonstrate that tirzepatide 10 mg and/or 15 mg is superior in mean percentage change in body weight from baseline and percentage of participants achieving ≥5% body weight reduction at 72 weeks compared to placebo.

All participants in the tirzepatide treatment arms started the study at a dose of tirzepatide 2.5 mg once-weekly and then increased the dose in a stepwise approach at four-week intervals to their final randomized maintenance dose of 10 mg (via steps at 2.5 mg, 5 mg and 7.5 mg) or 15 mg (via steps at 2.5 mg, 5 mg, 7.5 mg, 10 mg and 12.5 mg).

The race and ethnicity of the U.S. participants in SURMOUNT-2 were mostly representative of the U.S. population. About 18% of U.S. participants were African American or Black and about 41% of U.S. participants were Hispanic. Lilly continues to prioritize efforts to increase enrollment of racially and ethnically diverse patients in our clinical trials.

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 results from SURMOUNT-3 and -4 are anticipated this year.

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 comorbidity. 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 mellitus.

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 and Lilly.com/newsroom or follow us on Facebook, Instagram, Twitter and LinkedIn. P-LLY

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.

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.

TR CON CBS 14SEP2022

Mounjaro® and its delivery device base are registered trademarks owned or licensed by Eli Lilly and Company, its subsidiaries, or affiliates.

[i] For the SURMOUNT-2 clinical trial, participants needed to have a Body Mass Index (BMI) of ≥27 kg/m2 to be classified as overweight.

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 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 prove to be a safe and effective treatment for adults with obesity or overweight, 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.

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
2. Jastreboff, A., Arrone, J., Ahmad, N. et. al. Tirzepatide Once Weekly for the Treatment of Obesity. N Engl J Med 2022; 387:205-216 DOI: 10.1056/NEJMoa2206038

©Lilly USA, LLC 2023. All rights reserved.

Refer to: Jessica Thompson; thompson_jessica@lilly.com, 317-499-2042 (Media)
Joe Fletcher; jfletcher@lilly.com, 317-296-2884 (Investors)

View original content to download multimedia:https://www.prnewswire.com/news-releases/lillys-surmount-2-results-published-in-the-lancet-show-tirzepatide-achieved-a-mean-weight-reduction-of-15-7-at-the-highest-dose-15-mg-in-adults-with-obesity-or-overweight-and-type-2-diabetes-301862487.html

SOURCE Eli Lilly and Company