Lilly's tirzepatide delivered up to 22.5% weight loss in adults with obesity or overweight in SURMOUNT-1

April 28, 2022

Participants taking tirzepatide lost up to 52 lb. (24 kg) in this 72-week phase 3 study

63% of participants taking tirzepatide 15 mg achieved at least 20% body weight reductions as a key secondary endpoint

INDIANAPOLIS, April 28, 2022 /PRNewswire/ -- Tirzepatide (5 mg, 10 mg, 15 mg) achieved superior weight loss compared to placebo at 72 weeks of treatment in topline results from Eli Lilly and Company's (NYSE: LLY) SURMOUNT-1 clinical trial, with participants losing up to 22.5% (52 lb. or 24 kg) of their body weight for the efficacy estimand[i]. This study enrolled 2,539 participants and was the first phase 3 global registration trial evaluating the efficacy and safety of tirzepatide in adults with obesity, or overweight with at least one comorbidity, who do not have diabetes. Tirzepatide met both co-primary endpoints of superior mean percent change in body weight from baseline and greater percentage of participants achieving body weight reductions of at least 5% compared to placebo for both estimands[ii]. The study also achieved all key secondary endpoints at 72 weeks.

For the efficacy estimand, participants taking tirzepatide achieved average weight reductions of 16.0% (35 lb. or 16 kg on 5 mg), 21.4% (49 lb. or 22 kg on 10 mg) and 22.5% (52 lb. or 24 kg on 15 mg), compared to placebo (2.4%, 5 lb. or 2 kg). Additionally, 89% (5 mg) and 96% (10 mg and 15 mg) of people taking tirzepatide achieved at least 5% body weight reductions compared to 28% of those taking placebo.

In a key secondary endpoint, 55% (10 mg) and 63% (15 mg) of people taking tirzepatide achieved at least 20% body weight reductions compared to 1.3% of those taking placebo. In an additional secondary endpoint not controlled for type 1 error, 32% of participants taking tirzepatide 5 mg achieved at least 20% body weight reductions. The mean baseline body weight of participants was 231 lb. (105 kg).

"Obesity is a chronic disease that often does not receive the same standard of care as other conditions, despite its impact on physical, psychological and metabolic health, which can include increased risk of hypertension, heart disease, cancer and decreased survival," said Louis J. Aronne, MD, FACP, DABOM, director of the Comprehensive Weight Control Center and the Sanford I. Weill Professor of Metabolic Research at Weill Cornell Medicine, obesity expert at NewYork-Presbyterian/Weill Cornell Medical Center and Investigator of SURMOUNT-1. "Tirzepatide delivered impressive body weight reductions in SURMOUNT-1, which could represent an important step forward for helping the patient and physician partnership treat this complex disease."

For the treatment-regimen estimand[iii], results showed:

- Average body weight reductions: 15.0% (5 mg), 19.5% (10 mg), 20.9% (15 mg), 3.1% (placebo)
- Percentage of participants achieving body weight reductions of ≥5%: 85% (5 mg), 89% (10 mg), 91% (15 mg), 35% (placebo)
- Percentage of participants achieving body weight reductions of ≥20%: 30% (5 mg, not controlled for type 1 error), 50% (10 mg), 57% (15 mg), 3.1% (placebo)

The overall safety and tolerability profile of tirzepatide was similar to other incretin-based therapies approved for the treatment of obesity. The most commonly reported adverse events were gastrointestinal-related and generally mild to moderate in severity, usually occurring during the dose escalation period. For those treated with tirzepatide (5 mg, 10 mg and 15 mg, respectively), nausea (24.6%, 33.3%, 31.0%), diarrhea (18.7%, 21.2%, 23.0%), vomiting (8.3%, 10.7%, 12.2%) and constipation (16.8%, 17.1%, 11.7%) were more frequently experienced compared to placebo (9.5% [nausea], 7.3% [diarrhea], 1.7% [vomiting], 5.8% [constipation]).

Treatment discontinuation rates due to adverse events were 4.3% (5 mg), 7.1% (10 mg), 6.2% (15 mg) and 2.6% (placebo). The overall treatment discontinuation rates were 14.3% (5 mg), 16.4% (10 mg), 15.1% (15 mg) and 26.4% (placebo).

Participants who had pre-diabetes at study commencement will remain 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 the potential differences in progression to type 2 diabetes at three years of treatment with tirzepatide compared to placebo.

"Tirzepatide is the first investigational medicine to deliver more than 20 percent weight loss on average in a phase 3 study, reinforcing our confidence in its potential to help people living with obesity," said Jeff Emmick, MD, Ph.D., vice president, product development, Lilly. "Obesity is a chronic disease that requires effective treatment options, and Lilly is working relentlessly to support people with obesity and modernize how this disease is approached. We're proud to research and develop potentially innovative treatments like tirzepatide, which helped nearly two thirds of participants on the highest dose reduce their body weight by at least 20 percent in SURMOUNT-1."

Tirzepatide is a novel investigational once-weekly GIP (glucose-dependent insulinotropic polypeptide) receptor and GLP-1 (glucagon-like peptide-1) receptor agonist, representing a new class of medicines being studied for the treatment of obesity. Tirzepatide is a single peptide that activates the body's receptors for GIP and GLP-1, two natural incretin hormones. Obesity is a chronic, progressive disease caused by disruptions in the mechanisms that control body weight, often leading to an increase in food intake and/or a decrease in energy expenditure. These disruptions are multifactorial and can be related to genetic, developmental, behavioral, environmental and social factors. To learn more, visit Lilly.com/obesity.

Lilly will continue to evaluate the SURMOUNT-1 results, which will be presented at an upcoming medical meeting and submitted to a peer-reviewed

journal. Additional studies are ongoing for tirzepatide as a potential treatment for obesity or overweight.

About tirzepatide

Tirzepatide is a once-weekly GIP (glucose-dependent insulinotropic polypeptide) receptor and GLP-1 (glucagon-like peptide-1) receptor agonist that integrates the actions of both incretins into a single novel molecule. GIP is a hormone that may complement the effects of GLP-1 receptor agonists. In preclinical models, GIP has been shown to decrease food intake and increase energy expenditure therefore resulting in weight reductions, and when combined with GLP-1 receptor agonism, may result in greater effects on markers of metabolic dysregulation such as body weight, glucose and lipids. Tirzepatide is in phase 3 development for adults with obesity or overweight with weight-related comorbidity and is currently under regulatory review as a treatment for adults with type 2 diabetes. It is also being studied as a potential treatment for non-alcoholic steatohepatitis (NASH) and heart failure with preserved ejection fraction (HFpEF). Studies of tirzepatide in obstructive sleep apnea (OSA) and in morbidity/mortality in obesity are planned as well.

About SURMOUNT-1 and the SURMOUNT clinical trial program

SURMOUNT-1 (NCT04184622) is 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 have obesity, or overweight with at least one of the following comorbidities: hypertension, dyslipidemia, obstructive sleep apnea or cardiovascular disease. The trial randomized 2,539 participants across the U.S., Argentina, Brazil, China, India, Japan, Mexico, Russia and Taiwan in a 1:1:1:1 ratio to receive either tirzepatide 5 mg, 10 mg or 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 percentage of body weight reductions from baseline and percentage of participants achieving ≥5% body weight reduction at 72 weeks compared to placebo. Participants who had pre-diabetes at study commencement will remain 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.

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 step-wise approach at four-week intervals to their final randomized maintenance dose of 5 mg (via a 2.5 mg step), 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 SURMOUNT phase 3 global clinical development program for tirzepatide began in late 2019 and has enrolled more than 5,000 people with obesity or overweight across six clinical trials, four of which are global studies. Results from SURMOUNT-2, -3, and -4 are anticipated in 2023.

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 47 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**

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 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 research development and commercialization. Among other things, there can be no guarantee that the studies will be completed as planned, that future study results will be consistent with the results to date or that tirzepatide will receive regulatory approvals. 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.

Dr. Aronne is co-founder, chief scientific advisor and member of the board of directors for Intellihealth. Dr. Aronne is also a paid scientific advisory board member for Eli Lilly and Company.

[i] Efficacy estimand represents efficacy prior to discontinuation of study drug.

[ii] Treatment differences for two estimands – efficacy and treatment-regimen – were evaluated for three tirzepatide doses (5 mg, 10 mg and 15 mg) compared to placebo.

[iii] Treatment-regimen estimand represents the estimated average treatment effect regardless of treatment discontinuation.

Refer to: Maggie Pfeiffer; monson_maggie@lilly.com; 317-650-5939 (Media)
Kevin Hern; hern_kevin_r@lilly.com; 317-277-1838 (Investors)



View original content to download multimedia:https://www.prnewswire.com/news-releases/lillys-tirzepatide-delivered-up-to-22-5-weight-loss-in-adults-with-obesity-or-overweight-in-surmount-1--301534871.html

SOURCE Eli Lilly and Company