Tirzepatide reduced sleep apnea severity by up to nearly two-thirds in adults with obstructive sleep apnea (OSA) and obesity

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Tirzepatide achieved a mean apnea-hypopnea index reduction of up to 63% (about 30 fewer events per hour), meeting all primary and key secondary endpoints in two phase 3 clinical trials

Tirzepatide meaningfully improved sleep apnea symptoms in those with moderate-to-severe OSA and obesity with and without PAP therapy, and based on these results Lilly plans to submit these data for global regulatory reviews

INDIANAPOLIS, April 17, 2024 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) today announced positive topline results of the SURMOUNT-OSA phase 3 clinical trials that showed tirzepatide injection (10 mg or 15 mg) significantly reduced the apnea-hypopnea index (AHI) compared to placebo, achieving the primary endpoints. Percentage change in AHI was a key secondary endpoint in both studies. AHI records the number of times a person's breathing shows a restricted or complete block of airflow per hour of sleep and is used to evaluate the severity of obstructive sleep apnea (OSA) and the effectiveness of treatment outcomes. Tirzepatide is the only approved GIP (glucose-dependent insulinotropic polypeptide) and GLP-1 (glucagon-like peptide-1) treatment for chronic weight management, commercialized as Zepbound® in the U.S. and Mounjaro® in some global markets outside the U.S.

SURMOUNT-OSA Study 1 evaluated tirzepatide in adults with moderate-to-severe OSA and obesity who were not on positive airway pressure (PAP) therapy for 52 weeks. For the efficacy estimand[i], at 52 weeks, tirzepatide led to a mean AHI reduction from baseline of 27.4 events per hour compared to a mean AHI reduction from baseline of 4.8 events per hour for placebo. In key secondary outcomes, tirzepatide led to a mean AHI reduction from baseline of 55.0% compared to 5.0% from baseline for placebo; tirzepatide also led to a mean body weight reduction of 18.1% from baseline, compared to 1.3% from baseline for placebo.

SURMOUNT-OSA Study 2 evaluated tirzepatide in adults with moderate-to-severe OSA and obesity who were on and planned to continue to use PAP therapy for 52 weeks. In this population for the efficacy estimand, at 52 weeks, tirzepatide led to a mean AHI reduction from baseline of 30.4 events per hour compared to a mean AHI reduction from baseline of 6.0 events per hour for placebo. In key secondary outcomes, tirzepatide led to a mean AHI reduction from baseline of 62.8% compared to 6.4% from baseline for placebo; tirzepatide also led to a mean body weight reduction of 20.1% from baseline, compared to 2.3% from baseline for placebo.

The weight loss observed at 52 weeks with tirzepatide (10 mg and 15 mg) across the two studies was nearly 20% in a patient population that was comprised of approximately 70% males, who are known to achieve less weight loss with incretin therapy than females.

OSA is a sleep-related breathing disorder characterized by complete or partial collapses of the upper airway during sleep, which can lead to apnea or hypopnea and a potential decrease in oxygen saturation and/or waking from sleep. OSA can have serious cardiometabolic complications, contributing to hypertension, coronary heart disease, stroke, heart failure, atrial fibrillation and type 2 diabetes.[1]

"OSA impacts 80 million adults in the U.S., with more than 20 million living with moderate-to-severe OSA. However, 85% of OSA cases go undiagnosed and therefore untreated,[2,3]" said Jeff Emmick, MD, Ph.D., senior vice president, product development, Lilly. "Addressing this unmet need head-on is critical, and while there are pharmaceutical treatments for the excessive sleepiness associated with OSA, tirzepatide has the potential to be the first pharmaceutical treatment for the underlying disease."

Topline Results

SURMOUNT-OSA Study 1 – Participants Not on PAP Therapy		
	Efficacy Estimand Results at 52 Weeks	**Treatment-Regimen Estimand[ii] Results at 52 Weeks**
Primary Endpoint – Change in AHI from Baseline		
Tirzepatide*	-27.4	-25.3
Placebo	-4.8	-5.3
Secondary Endpoint – Percent Change in AHI from Baseline		
Tirzepatide*	-55.0 %	-50.7 %
Placebo	-5.0 %	-3.0 %
Secondary Endpoint – Percent Change in Body Weight from Baseline		
Tirzepatide*	-18.1 %	-17.7 %
Placebo	-1.3 %	-1.6 %

SURMOUNT-OSA Study 2 Participants Used PAP Therapy		
	Efficacy Estimand Results at 52 Weeks	**Treatment-Regimen Estimand Results at 52 Weeks**

Primary Endpoint – Change in AHI from Baseline		
Tirzepatide*	-30.4	-29.3
Placebo	-6.0	-5.5
Secondary Endpoint – Percent Change in AHI from Baseline		
Tirzepatide*	-62.8 %	-58.7 %
Placebo	-6.4 %	-2.5 %
Secondary Endpoint – Percent Change in Body Weight from Baseline		
Tirzepatide*	-20.1 %	-19.6 %
Placebo	-2.3 %	-2.3 %

**Tirzepatide MTD is 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 overall safety profile of tirzepatide in SURMOUNT-OSA studies was similar to previously reported SURMOUNT and SURPASS trials. The most commonly reported adverse events in SURMOUNT-OSA were gastrointestinal-related and generally mild to moderate in severity. The most commonly reported adverse events for patients treated with tirzepatide were diarrhea, nausea and vomiting in SURMOUNT-OSA Study 1, and diarrhea, nausea and constipation in SURMOUNT-OSA Study 2.

SURMOUNT-OSA trials will be presented during a symposium at the American Diabetes Association's 84th Scientific Sessions on June 21 at 3:45 p.m. ET and submitted to a peer-reviewed journal. Based on these results, Lilly plans to submit to the U.S. Food and Drug Administration (FDA) and other global regulatory agencies beginning mid-year. Lilly received FDA Fast Track designation for moderate-to-severe OSA and obesity.

About SURMOUNT-OSA
SURMOUNT-OSA (NCT05412004) was a multi-center, randomized, double-blind, parallel, placebo-master protocol comparing the efficacy and safety of tirzepatide to placebo in adults living with moderate-to-severe obstructive sleep apnea and obesity who were unable or unwilling to use positive airway pressure (PAP) therapy (Study 1) and those who were and planned to stay on PAP therapy during the duration of the trial (Study 2). Under a master protocol, the trials randomized 469 participants across the U.S., Australia, Brazil, China, Czechia, Germany, Japan, Mexico and Taiwan in a 1:1 ratio to receive tirzepatide maximum tolerated dose (MTD) 10 mg or 15 mg or placebo. The primary objective of both studies was to demonstrate that tirzepatide is superior in change in apnea-hypopnea index (AHI) from baseline at 52 weeks as compared to placebo.

SURMOUNT-OSA utilized a MTD 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 MTD. Participants who tolerated 10 mg but did not tolerate 15 mg continued on 10 mg as their MTD.

INDICATION AND SAFETY SUMMARY WITH WARNINGS

Zepbound™ (ZEHP-bownd) is an injectable prescription medicine that may help adults with obesity, or with excess weight (overweight) who also have weight-related medical problems, lose weight and keep it 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 when taken with other prescription, over-the-counter, or herbal weight loss products. It is not known if Zepbound can be used in people who have had pancreatitis. It is not known if Zepbound is safe and effective for use in children under 18 years of age.

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.

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 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 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 insulin or sulfonylureas 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?
❑ 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.

How to take

- Read the **Instructions for Use** that come with Zepbound.
- Use Zepbound exactly as your healthcare provider says.
- 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, 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.

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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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/news, or follow us on Facebook, Instagram and LinkedIn. P-LLY

[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 moderate-to-severe obstructive sleep apnea and obesity 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.

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