Lilly's Zepbound (tirzepatide 10 mg and 15 mg) was associated with more weight loss than Wegovy HD (semaglutide injection 7.2 mg) in a new indirect treatment comparison

September 29, 2026

In this new analysis, Zepbound 15 mg showed 4.5% greater weight loss than Wegovy HD in adults with obesity

Participants receiving Zepbound 15 mg had more than three times the odds of achieving at least 20% body-weight reduction compared with Wegovy HD

INDIANAPOLIS, Sept. 29, 2026 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY), the maker of Foundayo (orforglipron), today announced results from a new analysis showing that Zepbound (tirzepatide) 10 mg and 15 mg, a dual GIP and GLP-1 receptor agonist, delivered greater weight loss than Wegovy HD (semaglutide injection 7.2 mg) in adults with obesity. The findings come from an indirect treatment comparison of Zepbound and Wegovy HD, drawing on data from the SURMOUNT-1 and STEP UP trials.[1,2,3] These results, presented at the 62nd Annual Meeting of the European Association for the Study of Diabetes (EASD) in Milan, Italy, add to the growing body of evidence comparing Zepbound and Wegovy, including SURMOUNT-5, a randomized controlled Phase 3b trial in which Zepbound 10 mg and 15 mg demonstrated superior weight loss compared with Wegovy 1.7 mg and 2.4 mg.

"For people living with obesity, the choice of treatment matters, and clinicians increasingly want evidence on how the available options compare," said John Wilding, DM, professor of medicine at the University of Liverpool. "Tirzepatide 10 mg and 15 mg and semaglutide 1.7 mg and 2.4 mg were compared directly in SURMOUNT-5, where tirzepatide helped people with obesity lose more weight. In the absence of a head-to-head trial comparing tirzepatide 15 mg against semaglutide 7.2 mg, this indirect comparison offers useful evidence for physicians as they make treatment decisions."

In the indirect treatment comparison, which was covariate-adjusted for gender, age, baseline weight and baseline A1C, Zepbound 10 mg and 15 mg were associated with greater reductions in body weight than Wegovy HD at 72 weeks using the treatment-regimen estimand.[4,5] Participants taking Zepbound 15 mg lost 4.5% more of their body weight (95.0% CrI: -6.3, -2.8) on average, and those taking 10 mg lost 3.2% more of their body weight (95.0% CrI: -5.0, -1.4). Using the efficacy estimand, Zepbound 15 mg and 10 mg were associated with 1.8% (95.0% CrI: -3.8, 0.1) and 0.7% (95.0% CrI: -2.6, 1.3) greater mean weight reduction than Wegovy HD, respectively, though these differences did not reach statistical significance.[6]

"People with obesity have more treatment options than ever before, and their healthcare providers deserve as much information as possible to help guide their decisions," said Thomas Seck, M.D., senior vice president of product development, Lilly Cardiometabolic Health. "In a head-to-head Phase 3 clinical trial, Zepbound 10 mg and 15 mg delivered greater weight loss than Wegovy 1.7 mg and 2.4 mg, and a new indirect treatment comparison suggests the same doses of Zepbound may outperform Wegovy HD, as well. Together, these results offer physicians more information as they choose a treatment path."

In addition to achieving greater weight loss, participants taking Zepbound 15 mg were four times more likely to achieve 20% or greater body weight reduction compared with Wegovy HD using the efficacy estimand (odds ratio 4.15; 95.0% CrI: 1.02, 15.64), and more than three times more likely using the treatment-regimen estimand (odds ratio 3.54; 95.0% CrI: 1.05, 11.05). While not statistically significant, participants taking Zepbound 10 mg had more than two times the odds of achieving at least 20% body-weight reduction compared with Wegovy HD using the efficacy (odds ratio 2.8; 95.0% CrI: 0.7, 10.8) and treatment-regimen estimands (odds ratio 2.46; 95.0% CrI: 0.7, 7.8).

Zepbound 10 mg and 15 mg showed comparable rates of treatment discontinuation due to adverse events versus Wegovy HD across both estimands.

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.

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.

About SURMOUNT-5
SURMOUNT-5 (NCT05822830) was a 72-week, multi-center, randomized, open-label, Phase 3b trial evaluating the efficacy and safety of Zepbound (tirzepatide) compared with Wegovy (semaglutide) in adults with obesity, or overweight with at least one of the following comorbidities: hypertension, dyslipidemia, obstructive sleep apnea (OSA) or cardiovascular disease, who did not have diabetes. Participants in both treatment groups received counseling on a reduced-calorie diet and increased physical activity. The trial randomized 751 participants across the U.S. and Puerto Rico in a 1:1 ratio to receive maximum tolerated dose of Zepbound (10 mg or 15 mg) or Wegovy (1.7 mg or 2.4 mg). With tirzepatide, 89.3% received at least one dose of the 15 mg dose and with semaglutide 92.8% received at least one dose of the 2.4 mg dose. The primary objective of the study was to demonstrate Zepbound's superiority in percent change from baseline in body weight at 72 weeks compared to Wegovy.

For the primary endpoint, participants treated with Zepbound achieved an average weight reduction of 20.2% compared to 13.7% with Wegovy at 72 weeks using the treatment-regimen estimand, a 47% greater relative weight loss. Participants using Zepbound lost an average of 50.3 lbs (22.8 kg)

and participants on Wegovy lost an average of 33.1 lbs (15.0 kg).

About Zepbound (tirzepatide) injection
Zepbound (tirzepatide) is the first and only dual GIP (glucose-dependent insulinotropic polypeptide) and GLP-1 (glucagon-like peptide-1) receptor agonist obesity medication. Zepbound tackles an underlying cause of excess weight. It reduces appetite and how much you eat. Zepbound is indicated for adults with obesity, or some adults who are overweight and also have at least one weight-related medical problem, to lose weight and keep it off. Additionally, Zepbound is FDA-approved to treat adults with moderate-to-severe obstructive sleep apnea and obesity. Zepbound should be used with a reduced calorie diet and increased physical activity.

Endnotes and References

1. Jastreboff AM, Aronne LJ, Ahmad NN, et al. Tirzepatide once weekly for the treatment of obesity. New England Journal of Medicine. 2022;387(3):205-216. doi:10.1056/NEJMoa2206038.
2. Wharton S, Freitas P, Hjelmesæth J, et al. Once-weekly semaglutide 7.2 mg in adults with obesity (STEP UP): a randomised, controlled, phase 3b trial. The Lancet Diabetes & Endocrinology, 2025; 13, 949-963. https://doi.org/10.1016/S2213-8587(25)00226-8
3. Wilding J, Postma MJ, Jacobi D, et al. Tirzepatide 10 and 15 mg (SURMOUNT-1) vs semaglutide 7.2 mg (STEP UP) in adults with obesity without type 2 diabetes: an indirect treatment comparison. Presented at the 62nd Annual Meeting of the European Association for the Study of Diabetes (EASD).
4. Weight loss data represent an ML-NMR analysis.
5. Treatment-regimen estimand represents the estimated average treatment effect regardless of treatment discontinuation.
6. Efficacy estimand represents efficacy prior to discontinuation of study drug.

U.S. ZEPBOUND INDICATIONS AND SAFETY SUMMARY WITH WARNINGS
Zepbound® (ZEHP-bownd) is an injectable prescription medicine used with a reduced-calorie diet and increased physical activity to 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.
- moderate-to-severe obstructive sleep apnea (OSA) and obesity to improve their OSA.
- 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.

KwikPen®: Do not share your KwikPen with other people, even if the pen needle has been changed. You may give other people a serious infection or get a serious infection from them.

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.

Dehydration leading to kidney problems. 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. Tell your healthcare provider right away if you have nausea, vomiting, or diarrhea that does not go away.

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 nausea or 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.

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.**
- **Talk to your healthcare provider about low blood sugar and how to manage it. Tell your healthcare provider if you are taking medicines to treat diabetes including an insulin or sulfonylurea.**
- **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 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. Zepbound may pass 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 is 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 call 1-844-524-0039 or email at MILEregistry@thermofisher.com or visit https://pregnancyregistry.lilly.com/zepbound.

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.
- Inject Zepbound under the skin (subcutaneously) of your stomach (abdomen), thigh, or have another person inject in the back of the upper arm. **Do not** inject ZEPBOUND into a muscle (intramuscularly) or vein (intravenously).
- **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, call the Poison Help line at 1-800-222-1222 or go to the nearest hospital emergency room right away.

Zepbound is approved as a 2.5 mg, 5 mg, 7.5 mg, 10 mg, 12.5 mg, and 15 mg injection.

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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U.S. FOUNDAYO INDICATION AND SAFETY SUMMARY WITH WARNINGS
Foundayo™ (fown-DAY-oh) is a prescription medicine used with a reduced-calorie diet and increased physical activity to 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.

- Foundayo should not be used with other GLP-1 receptor agonist medicines.
- It is not known if Foundayo is safe and effective for use in children.

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

Foundayo may cause serious side effects, including:

Inflammation of the pancreas (pancreatitis). Stop taking Foundayo 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 nausea or vomiting. Sometimes you may feel the pain from your abdomen to your back.

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

Dehydration leading to kidney problems. 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. Tell your healthcare provider right away if you have nausea, vomiting, or diarrhea that does not go away.

Low blood sugar (hypoglycemia). Your risk for getting low blood sugar may be higher if you use Foundayo with medicines that can cause low blood sugar, such as an insulin or sulfonylurea. **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.

Serious allergic reactions. Stop using Foundayo 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.

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

Gallbladder problems. Gallbladder problems have happened in some people who use Foundayo. 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.

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

Common side effects
The most common side effects of Foundayo include nausea, constipation, diarrhea, vomiting, indigestion, stomach (abdominal) pain, headache, swollen belly, feeling tired, belching, heartburn, gas, and hair loss. These are not all the possible side effects of Foundayo. 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 taking Foundayo

- **Tell your healthcare provider about all the medicines you take.** Foundayo may affect the way some medicines work, and some medicines may affect the way Foundayo works.
- **Pregnancy Exposure Registry**: There will be a pregnancy exposure registry for women who have taken Foundayo 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 Eli Lilly and Company at 1-800-LillyRx (1-800-545-5979).
- **If you take birth control pills by mouth, talk to your healthcare provider before you take Foundayo. Birth control pills may not work as well while taking Foundayo.** Your healthcare provider may recommend another type of birth control for 30 days after starting Foundayo and for 30 days after each dose increase of Foundayo.
- **Talk to your healthcare provider about low blood sugar and how to manage it.** Tell your healthcare provider if you are taking medicines to treat diabetes including an insulin or sulfonylurea.

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 liver, severe problems with your stomach, such as slowed emptying of your stomach (gastroparesis) or problems digesting food?
❑ 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 or plan to become pregnant? Foundayo may harm your unborn baby.
❑ Are you breastfeeding or plan to breastfeed? Breastfeeding is not recommended during treatment with Foundayo.
❑ Do you take any other prescriptions or over-the-counter medicines, vitamins, or herbal supplements?

How to take

- Take Foundayo exactly as your healthcare provider tells you to.

- Use Foundayo with a reduced-calorie diet and increased physical activity.
- Take Foundayo by mouth 1 time each day, with or without food.
- Swallow tablets whole. Do not break, crush, or chew the tablet.
- If you miss a dose, take it as soon as possible. **Do not** take **2** doses of Foundayo in the same day.
- **Do not take more than 1 tablet per day.**
- If you miss taking Foundayo for 7 or more days in a row, call your healthcare provider to talk about how to restart your treatment.
- If you take too much Foundayo, call your healthcare provider or Poison Help line at 1-800-222-1222 or go to the nearest hospital emergency room right away.

Learn more
Foundayo is a prescription medicine available in 0.8 mg, 2.5 mg, 5.5 mg, 9 mg, 14.5 mg, or 17.2 mg oral tablets. For more information, call 1-800-545-5979 or go to **foundayo.lilly.com**.

This summary provides basic information about Foundayo 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 doctor. Be sure to talk to your doctor or other healthcare provider about Foundayo and how to take it. Your doctor is the best person to help you decide if Foundayo is right for you.

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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 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

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 Zepbound (tirzepatide) as a treatment for 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 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, or that Zepbound will receive additional regulatory approvals. 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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