Lilly's Foundayo (orforglipron) 17.2 mg showed greater weight loss and A1C reduction than oral semaglutide 25 mg among adults with type 2 diabetes in a new indirect treatment comparison

September 29, 2026

Foundayo 17.2 mg was associated with 1.5% greater weight loss and 0.3% greater A1C reduction than oral semaglutide 25 mg at 52 weeks

These additional analyses build on findings of the ACHIEVE-3 head-to-head study, where Foundayo 9 mg and 17.2 mg delivered greater A1C and weight reductions than oral semaglutide 14 mg

INDIANAPOLIS, Sept. 29, 2026 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY), the maker of Zepbound (tirzepatide), today announced results from a new analysis showing that Foundayo (orforglipron) 17.2 mg was associated with significantly greater weight loss and better blood sugar control than oral semaglutide 25 mg in adults with type 2 diabetes. The findings are based on an indirect treatment comparison of Foundayo 17.2 mg against oral semaglutide 25 mg, drawing on data from ACHIEVE-3 and PIONEER PLUS.[1,2,3,4] Presented at the 62nd Annual Meeting of the European Association for the Study of Diabetes (EASD) in Milan, Italy, these results add to a growing body of evidence supporting Foundayo's efficacy.

"For someone managing type 2 diabetes, the choice between treatments is a decision that impacts their life every day," said Deborah Horn, D.O., director of the Center for Obesity Medicine at McGovern Medical School at UTHealth Houston. "Having data to help us compare available medications provides clinicians the opportunity to make informed treatment choices that fit each patient's needs."

In an indirect treatment comparison using data from ACHIEVE-3 and PIONEER PLUS, Foundayo 17.2 mg showed significantly greater weight loss and A1C reduction compared to oral semaglutide 25 mg at 52 weeks.[5] On average, participants taking Foundayo 17.2 mg lost 1.5% more of their body weight compared to oral semaglutide 25 mg (95% CI -2.7%, -0.2%). Additionally, Foundayo lowered A1C by 0.3% more than oral semaglutide 25 mg (95% CI -0.6%, -0.1%). This analysis was covariate-adjusted for gender, age, baseline A1C and baseline weight. Analyses using different statistical methods produced consistent results, with Foundayo 17.2 mg showing 1.5% to 2.4% greater weight loss and 0.3% to 0.6% greater A1C reduction compared to oral semaglutide 25 mg.

"Head-to-head trials ultimately provide the best comparison of two medicines, but when we don't yet have those data, then other approaches can provide informative data points," said Rachel Batterham, OBE, MBBS, Ph.D., FRCP, senior vice president of medical innovation and external engagement, Lilly Cardiometabolic Health. "Results from this indirect treatment comparison suggest that Foundayo may deliver A1C and weight lowering that is similar to the 25 mg dose of oral semaglutide. These results, paired with simple administration free of fasting or water restrictions, are what make Foundayo a potentially foundational therapy for adults managing type 2 diabetes around the world."

About Foundayo (orforglipron)
Foundayo (orforglipron) is FDA-approved for adults with obesity, or some adults with overweight who also have weight-related medical problems, to reduce excess body weight and maintain weight reduction long term, alongside a reduced-calorie diet and increased physical activity. Foundayo is a once-daily small molecule (non-peptide) oral glucagon-like peptide-1 receptor agonist that can be taken any time of the day without restrictions on food and water intake. Orforglipron was discovered by Chugai Pharmaceutical Co., Ltd. and licensed by Lilly in 2018. Orforglipron is being studied as a potential treatment for type 2 diabetes, obstructive sleep apnea, osteoarthritis knee pain, hypertension, peripheral artery disease and stress urinary incontinence.

About ACHIEVE-3 and ACHIEVE clinical trial program
ACHIEVE-3 (NCT06045221) is a Phase 3, 52-week, randomized, open-label trial evaluating the efficacy and safety of orforglipron compared with oral semaglutide (Rybelsus) in adults with type 2 diabetes inadequately controlled with metformin. The trial randomized 1,698 participants across the U.S., Argentina, China, Japan, Mexico and Puerto Rico to receive either 9 mg or 17.2 mg orforglipron or 7 mg or 14 mg oral semaglutide in a 1:1:1:1 ratio. The primary objective of the study was to demonstrate that orforglipron is non-inferior in A1C reduction from baseline after 52 weeks compared with oral semaglutide when comparing the lower and higher doses.

In ACHIEVE-3, Foundayo lowered A1C by an average of 1.9% (9 mg) and 2.2% (17.2 mg) compared to 1.1% (7 mg) and 1.4% (14 mg) with oral semaglutide at 52 weeks. Foundayo also delivered greater weight loss, with participants losing an average of 14.6 lbs (6.7%; 9 mg) and 19.7 lbs (9.2%; 17.2 mg) compared to 7.9 lbs (3.7%; 7 mg) and 11.0 lbs (5.3%; 14 mg) with oral semaglutide.

The ACHIEVE Phase 3 global clinical development program for orforglipron enrolled more than 6,000 people with type 2 diabetes across five global registration trials.

Endnotes and References

1. Rosenstock J, Yabe D, Cox D, et al. Efficacy and safety of once-daily oral orforglipron compared with oral semaglutide in adults with type 2 diabetes (ACHIEVE-3): a multinational, multicentre, non-inferiority, open-label, randomised, phase 3 trial. Lancet. 2026 Mar 21;407(10534):1147-1160. https://doi.org/10.1016/S0140-6736(26)00202-3. Epub 2026 Feb 26. PMID: 41765029.
2. Aroda V, Aberle J, Bardtrum L, et al. Efficacy and safety of once-daily oral semaglutide 25 mg and 50 mg compared with 14 mg in adults with type 2 diabetes (PIONEER PLUS): a multicentre, randomised, phase 3b trial. The Lancet, 2023; 402, 693-704. https://doi.org/10.1016/s0140-6736(23)01127-3
3. Cheng A, Jacobi D, Mojdami D, Li J, Li J, Zhao Y, Terrell K, Liu-Seifert H. Oral orforglipron 17.2 mg versus oral

semaglutide 25 mg in adults with type 2 diabetes and BMI ≥25kg/m^2: an indirect treatment comparison.

4. A 25 mg once-daily dose of oral semaglutide is not approved in the United States for the treatment of type 2 diabetes. Novo Nordisk has submitted an application to the FDA seeking approval of that dose.
5. All data referenced in this press release are based on the efficacy estimand. In ACHIEVE-3, the efficacy estimand represents treatment efficacy had all randomized participants remained on study intervention (with possible dose interruptions and/or dose modifications) for 52 weeks without initiating additional antihyperglycemic medications (>14 days of use). In PIONEER PLUS, the corresponding estimand is termed as the trial product estimand in the manuscript.

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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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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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 Foundayo (orforglipron) as a potential treatment for adults with type 2 diabetes 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 or that future study results will be consistent with study results to date, that Foundayo will prove to be a safe and effective treatment for adults with type 2 diabetes or other potential indications, that Foundayo 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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