ACHIEVE-4, the longest Phase 3 study of Lilly's Foundayo (orforglipron) to date, reaffirmed its cardiovascular and overall safety profile as well as consistent improvements across key measures of cardiometabolic health

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In ACHIEVE-4, Foundayo met the primary objective of non-inferiority vs. insulin glargine with a 16% lower risk of MACE-4 events and a 23% lower risk of MACE-3 events

In a pre-planned analysis, the risk of all-cause death was 57% lower for Foundayo vs. insulin glargine, showing the potential for more comprehensive health benefits

With these data, Lilly plans to submit Foundayo for the treatment of type 2 diabetes to the U.S. Food and Drug Administration by the end of Q2

INDIANAPOLIS, April 16, 2026 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) today announced positive topline results from the Phase 3 ACHIEVE-4 trial evaluating the efficacy and safety of Foundayo (orforglipron), compared to insulin glargine in adults with type 2 diabetes and obesity or overweight at increased cardiovascular risk. ACHIEVE-4, the largest and longest study of Foundayo in type 2 diabetes to date, enrolled more than 2,700 participants across 15 countries. In the trial, Foundayo met the primary endpoint by demonstrating a non-inferior risk of major adverse cardiovascular events (MACE-4), including cardiovascular death, heart attack, stroke or hospitalization for unstable and sudden chest pain, compared to insulin glargine. In addition, Foundayo showed superior improvements in A1C and body weight at 52 weeks vs. insulin glargine, which persisted through 104 weeks of therapy. While not controlled for multiplicity, the risk of all-cause death was significantly lower for Foundayo vs. insulin glargine.

"Across seven Phase 3 studies enrolling more than 11,000 patients, Foundayo has demonstrated a consistent safety and efficacy profile," said Thomas Seck, M.D., senior vice president of product development, Lilly Cardiometabolic Health. "ACHIEVE-4 adds a new dimension to that evidence — cardiovascular safety and a lower observed risk of all-cause death in patients who carry elevated cardiovascular risk. Together with the simplicity of a once-daily pill that requires no food or water restrictions, we believe Foundayo could be an important new treatment option for people with type 2 diabetes."

In the trial, the risk of cardiovascular death, heart attack, stroke, or hospitalization for unstable sudden chest pain was 16% lower for Foundayo vs. insulin glargine (hazard ratio: 0.84; 95.0% CI: 0.59 to 1.20), meeting the prespecified criteria for demonstrating non-inferiority (upper limit of 95.0% CI of the hazard ratio < 1.8).[1] The risk of all-cause death was 57% lower with Foundayo vs. insulin glargine (hazard ratio: 0.43; 95.0% CI: 0.25 to 0.75; nominal p = 0.002).[2] Foundayo also showed clinically meaningful improvements from baseline across several cardiovascular risk factors, including non-HDL cholesterol, systolic blood pressure, triglycerides, and hsCRP.[2]

ACHIEVE-4 Topline Results:

<table>
<tr><th></th><th>Foundayo</th><th>Insulin Glargine</th></tr>
<tr><td colspan="3">Primary Endpoint</td></tr>
<tr><td>Time to first occurrence of MACE-4[i]</td><td colspan="2">Hazard ratio = 0.84
95.0% CI: 0.59 to 1.20[ii]
p = 0.336</td></tr>
<tr><td colspan="3">Key Secondary Endpoints</td></tr>
<tr><td>Time to first occurrence of MACE-3[i]</td><td colspan="2">Hazard ratio = 0.77
95.0% CI: 0.52 to 1.13
p = 0.181</td></tr>
<tr><td rowspan="2">Change in A1C from mean baseline of 8.22% at 52 weeks[iii]</td><td>-1.6 %</td><td>-1.0 %</td></tr>
<tr><td colspan="2">Estimated treatment difference:
-0.66 (95.0% CI: -0.74 to -0.58)
p < 0.001</td></tr>
<tr><td rowspan="2">Change in body weight from mean baseline of 90.9 kg (200.4 lbs) at 52 weeks[iii]</td><td>-8.8%
(-8.1 kg / -17.9 lbs)</td><td>+1.7%
(+1.4 kg / +3.1 lbs)</td></tr>
<tr><td colspan="2">Estimated treatment difference:
-10.42% (95.0% CI: -10.92 to -9.93)
p < 0.001</td></tr>
<tr><td colspan="3">Additional Pre-Planned Analysis</td></tr>
<tr><td>All-cause death[i,iv]</td><td colspan="2">Hazard ratio = 0.43
95.0% CI: 0.25 to 0.75
p = 0.002</td></tr>
</table>

[i]Time to first event analysis using Cox proportional hazard model for CI and log-rank for p-value. All data from randomization to end of the study were included in the analysis.

[ii]Non-inferiority (upper limit of 95% CI of the hazard ratio < 1.8).

[iii] *Results of A1C and body weight were based on efficacy estimand.*[3]

[iv] *Not controlled for family-wise type 1 error.*

The overall safety and tolerability profile of Foundayo in ACHIEVE-4 was generally consistent with previous trials and with the GLP-1 class. The most common adverse events for patients taking Foundayo were nausea, vomiting, diarrhea, decreased appetite, and constipation. During the 52-week minimum treatment period, 10.6% of patients taking Foundayo discontinued treatment due to adverse events. ACHIEVE-4 included a thorough analysis of potential drug-induced liver injury (DILI), and these analyses confirmed there was no hepatic safety signal, consistent with all prior studies in the ACHIEVE and ATTAIN programs.

Lilly will submit Foundayo for the treatment of type 2 diabetes to the U.S. FDA by the end of the second quarter under the Commissioner's National Priority Review Voucher.

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.[4] Orforglipron was discovered by Chugai Pharmaceutical Co., Ltd. and licensed by Lilly in 2018. In addition to chronic weight management, Foundayo 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-4 and ACHIEVE clinical trial program
ACHIEVE-4 (NCT05803421) is a Phase 3, event-driven, randomized, open-label trial evaluating the efficacy and safety of Foundayo compared with insulin glargine in adults with type 2 diabetes and obesity or overweight (BMI ≥25 kg/m^2) with increased risk of cardiovascular events. The trial randomized 2,749 participants across the U.S., Argentina, Austria, Brazil, Czechia, Germany, Greece, India, Italy, Mexico, Puerto Rico, Romania, Slovakia, South Korea, Spain and Turkey to receive either escalating doses of Foundayo or insulin glargine. The primary objective of the study was to demonstrate that Foundayo was non-inferior in the risk of major adverse cardiovascular events (MACE-4) compared to insulin glargine in adults with type 2 diabetes and obesity or overweight with increased risk for cardiovascular events who have taken at least one and no more than three oral anti-diabetic medications for at least 90 days prior to study start. Study participants had an A1C between ≥7.0% and ≤10.5% (≥7.5% and ≤10.5% if background diabetes medication includes a sulfonylurea) and a BMI of ≥25 kg/m^2 with stable weight (±5%) for at least 90 days prior to study start. Participants randomized to Foundayo initiated treatment with 1 mg capsule (corresponds to 0.8 mg tablets) once daily and increased the dose every four weeks until reaching a maximum tolerated dose (up to 36 mg capsule/17.2 mg tablet).

The ACHIEVE Phase 3 global clinical development program for Foundayo began in 2023 and enrolled more than 6,000 people with type 2 diabetes across five global registrational trials.

Endnotes and References

1. Time to first event analysis using Cox proportional hazard model using all randomized participants exposed to ≥1 dose of study intervention.
2. All-cause death, serum lipids, blood pressure, and hsCRP were not controlled for family-wise type 1 error.
3. The efficacy estimand represents efficacy had all randomized participants remained on study intervention (with possible dose interruptions) without initiating additional antihyperglycemic medications (>14 days of use).
4. Ma X, Liu R, Pratt EJ, Benson CT, Bhattachar SN, Sloop KW. Effect of Food Consumption on the Pharmacokinetics, Safety, and Tolerability of Once-Daily Orally Administered Orforglipron (LY3502970), a Non-peptide GLP-1 Receptor Agonist. Diabetes Ther. 2024 Apr;15(4):819-832. https://doi.org/10.1007/s13300-024-01554-1. Epub 2024 Feb 24. PMID: 38402332; PMCID: PMC10951152. https://doi.org/10.1073/pnas.2014879117(2020)

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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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, potential efficacy and tolerability of Foundayo, and the timeline for future readouts, presentations, and other milestones relating to Foundayo 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 expectations or study results to date, that Foundayo will prove to be a safe and effective treatment for 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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