Lilly's oral GLP-1, orforglipron, delivers weight loss of up to an average of 27.3 lbs in first of two pivotal Phase 3 trials in adults with obesity

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In ATTAIN-1, the investigational once-daily oral pill showed significant efficacy, and a safety and tolerability profile consistent with injectable GLP-1 therapies at 72 weeks

Orforglipron achieved the primary and all key secondary endpoints, including demonstrating improvements in a number of cardiovascular risk factors

With these results, Lilly is on track to submit orforglipron to global regulatory agencies by year-end and is making substantial investments to meet anticipated demand at launch

INDIANAPOLIS, Aug. 7, 2025 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) today announced positive topline results from the Phase 3 ATTAIN-1 trial, evaluating orforglipron, an investigational oral glucagon-like peptide-1 (GLP-1) receptor agonist, in 3,127 adults with obesity, or overweight with a weight-related medical problem and without diabetes. At 72 weeks, all three doses of orforglipron, met the primary endpoint and all key secondary endpoints compared to placebo, delivering clinically meaningful weight loss as an adjunct to a healthy diet and physical activity. For the primary endpoint, orforglipron 36 mg, taken once per day without food and water restrictions, lowered weight by an average of 12.4% (27.3 lbs) compared to 0.9% (2.2 lbs) with placebo using the efficacy estimand.[1]

"Obesity is one of the most pressing global health challenges of our time, driving global chronic disease burden and impacting more than one billion people worldwide," said Kenneth Custer, Ph.D., executive vice president and president of Lilly Cardiometabolic Health. "With orforglipron, we're working to transform obesity care by introducing a potential once-daily oral therapy that could support early intervention and long-term disease management, while offering a convenient alternative to injectable treatments. With these positive data in hand, we are now planning to submit orforglipron for regulatory review by year-end and are prepared for a global launch to address this urgent public health need."

In the ATTAIN-1 trial, orforglipron met the primary endpoint of superior body weight reduction compared to placebo. Participants taking the highest dose of orforglipron lost an average of 27.3 lbs (12.4%) at 72 weeks using the efficacy estimand. In a key secondary endpoint, 59.6% of participants taking the highest dose of orforglipron lost at least 10% of their body weight, while 39.6% lost at least 15% of their body weight. In addition to achieving significant weight loss, orforglipron was also associated with reductions in known markers of cardiovascular risk, including non-HDL cholesterol, triglycerides and systolic blood pressure in pooled analyses across all doses. In a pre-specified exploratory analysis, the highest dose of orforglipron reduced high-sensitivity C-reactive protein (hsCRP) levels by 47.7%.

Efficacy Estimand Results				
	Orforglipron 6 mg	**Orforglipron 12 mg**	**Orforglipron 36 mg**	**Placebo**
Primary Endpoint				
Mean percent change in body weight from avg. baseline of 103.2 kg (227.5 lbs) and 37.0 BMI[i]	-7.8% (-8.0 kg; -17.6 lbs)	-9.3% (-9.4 kg; -20.7 lbs)	-12.4% (-12.4 kg; -27.3 lbs)	-0.9% (-1.0 kg; -2.2 lbs)
Key Secondary Endpoints				
Percentage of participants achieving body weight reductions of ≥10%[i]	35.9 %	45.1 %	59.6 %	8.6 %
Percentage of participants achieving body weight reductions of ≥15%[i]	16.5 %	24.0 %	39.6 %	3.6 %

[i] *Superiority test was adjusted for multiplicity.*

For the treatment-regimen estimand,[2] each dose of orforglipron led to statistically significant improvements across the primary and all key secondary endpoints.

- Percent weight reduction: -7.5% (-7.8 kg; 17.2 lbs; 6 mg), -8.4% (-8.6 kg; 19.0 lbs; 12 mg), -11.2% (-11.3 kg; 25.0 lbs; 36 mg), -2.1% (-2.4 kg; 5.3 lbs; placebo)
- Percentage of participants achieving body weight reductions of ≥10%: 33.3% (6 mg), 40.0% (12 mg), 54.6% (36 mg), 12.9% (placebo)
- Percentage of participants achieving body weight reductions of ≥15%: 15.1% (6 mg), 20.3% (12 mg), 36.0% (36 mg), 5.9% (placebo)

The overall safety profile of orforglipron in ATTAIN-1 was consistent with the established GLP-1 receptor agonist class. The most commonly reported adverse events were gastrointestinal-related and generally mild-to-moderate in severity. The most common adverse events for participants treated with orforglipron (6 mg, 12 mg and 36 mg, respectively) were nausea (28.9%, 35.9% and 33.7%) vs. 10.4% with placebo, constipation (21.7%, 29.8% and 25.4%) vs. 9.3% with placebo, diarrhea (21.0%, 22.8% and 23.1%) vs. 9.6% with placebo, vomiting (13.0%, 21.4% and 24.0%) vs. 3.5% with placebo, and dyspepsia (13.0%, 16.2% and 14.1%) vs. 5.0% with placebo. Treatment discontinuation rates due to adverse events were 5.1% (6 mg), 7.7% (12 mg) and 10.3% (36 mg) for orforglipron vs. 2.6% with placebo. The overall treatment discontinuation rates were 21.9% (6 mg), 22.5% (12 mg) and 24.4% (36 mg) for orforglipron vs. 29.9% with placebo. No hepatic safety signal was observed.

The detailed ATTAIN-1 results will be presented next month at the European Association for the Study of Diabetes (EASD) Annual Meeting 2025 and published in a peer-reviewed journal. More results from the ATTAIN Phase 3 clinical trial program will be shared later this year, along with findings from the ACHIEVE Phase 3 clinical trial program evaluating orforglipron for adults with type 2 diabetes.

About orforglipron
Orforglipron (or-for-GLIP-ron) is an investigational, 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.[3] Orforglipron was discovered by Chugai Pharmaceutical Co., Ltd. and licensed by Lilly in 2018. Chugai and Lilly published the preclinical pharmacology data of this molecule together.[4] Lilly is running Phase 3 studies on orforglipron for the treatment of type 2 diabetes and for weight management in adults with obesity or overweight with at least one weight-related medical problem. It is also being studied as a potential treatment for obstructive sleep apnea (OSA) and hypertension in adults with obesity.

About ATTAIN-1 and ATTAIN clinical trial program
ATTAIN-1 (NCT05869903) is a Phase 3, 72-week, randomized, double-blind, placebo-controlled trial comparing the efficacy and safety of orforglipron 6 mg, 12 mg and 36 mg as monotherapy to placebo in adults with obesity, or overweight with at least one of the following comorbidities: hypertension, dyslipidemia, OSA or cardiovascular disease, who did not have diabetes. The trial randomized 3,127 participants across the U.S., Brazil, China, India, Japan, South Korea, Puerto Rico, Slovakia, Spain and Taiwan in 3:3:3:4 ratio to receive either 6 mg, 12 mg or 36 mg orforglipron or placebo. The primary objective of the study was to demonstrate that orforglipron (6 mg, 12 mg, 36 mg) is superior to placebo in body weight reduction from baseline after 72 weeks in people with a BMI ≥30.0 kg/m² or a BMI ≥27.0 kg/m² with at least one weight-related comorbidity and a history of at least one self-reported unsuccessful dietary effort to lose body weight. All participants in the orforglipron treatment arms started the study at a dose of orforglipron 1 mg once-daily and then increased the dose in a step-wise approach at four-week intervals to their final randomized maintenance dose of 6 mg (via steps at 1 mg and 3 mg), 12 mg (via steps at 1 mg, 3 mg and 6 mg) or 36 mg (via steps at 1 mg, 3 mg, 6 mg, 12 mg and 24 mg). Dose reduction was only allowed for GI tolerability if other mitigations failed.

The ATTAIN Phase 3 global clinical development program for orforglipron has enrolled more than 4,500 people with obesity or overweight across two global registration trials. The program began in 2023 with additional results anticipated this year.

About Lilly
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 nearly 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

Endnotes and References:

1. The efficacy estimand represents efficacy had all randomized participants remained on study intervention (with possible dose interruptions and modifications) for 72 weeks without initiating prohibited weight management treatments.
2. The treatment-regimen estimand represents the estimated average treatment effect regardless of adherence to study intervention or initiation of prohibited weight management treatments.
3. 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. doi: 10.1007/s13300-024-01554-1. Epub 2024 Feb 24. PMID: 38402332; PMCID: PMC10951152.
4. T. Kawai, B. Sun, H. Yoshino, D. Feng, Y. Suzuki, M. Fukazawa, S. Nagao, D.B. Wainscott, A.D. Showalter, B.A. Droz, T.S. Kobilka, M.P. Coghlan, F.S. Willard, Y. Kawabe, B.K. Kobilka, & K.W. Sloop, Structural basis for GLP-1 receptor activation by LY3502970, an orally active nonpeptide agonist, Proc. Natl. Acad. Sci. U.S.A. 117 (47) 29959-29967, https://doi.org/10.1073/pnas.2014879117 (2020).

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 orforglipron as a potential treatment for adults with obesity or overweight, Lilly's ability to supply orforglipron, if approved, and the timeline for future readouts, presentations, and other milestones relating to orforglipron 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 study results to date, that orforglipron will prove to be a safe and effective treatment for obesity or overweight, that orforglipron will receive regulatory approval, 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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