Lilly's oral GLP-1, orforglipron, demonstrated meaningful weight loss and cardiometabolic improvements in complete ATTAIN-1 results published in The New England Journal of Medicine

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The investigational once-daily oral pill led to an average weight loss of 27.3 lbs (12.4%) at the highest dose at week 72 in the Phase 3 study

Orforglipron demonstrated significant improvements across key cardiometabolic risk factors, supporting its potential as a treatment option for millions living with obesity

INDIANAPOLIS, Sept. 16, 2025 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) today announced detailed results from the Phase 3 ATTAIN-1 trial, evaluating the safety and efficacy of orforglipron, an investigational oral glucagon-like peptide-1 (GLP-1) receptor agonist, in adults with obesity, or overweight with a weight-related medical problem and without diabetes. At 72 weeks, all three doses (6 mg, 12 mg and 36 mg) of orforglipron met the primary endpoint of superior body weight reduction compared to placebo. In addition, all three doses delivered clinically meaningful results compared to placebo across the key secondary endpoints of body weight reduction (≥10%, ≥15% and ≥20%), and waist circumference reduction.[1] Results from the trial were presented at the European Association for the Study of Diabetes (EASD) Annual Meeting 2025 and simultaneously published in *The New England Journal of Medicine*.

"Obesity is a complex, global health challenge — and patients need treatment options that are both effective and easy to integrate into everyday life," said Sean Wharton, M.D., director at Wharton Medical Clinic and lead investigator. "In this Phase 3 study, orforglipron demonstrated strong efficacy results and safety consistent with the GLP-1 class, reinforcing its potential as a first-line treatment in primary care. Additionally, orforglipron could help reduce known markers of cardiovascular risk associated with obesity and support meaningful improvements in public health."

In the ATTAIN-1 trial, orforglipron met the primary endpoint of superior body weight reduction compared to placebo, with participants taking the highest dose losing an average of 27.3 lbs (12.4%) at 72 weeks using the efficacy estimand.[2] In key secondary endpoints, 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. Among the 1,127 participants who had prediabetes at the start of the study, up to 91% of those taking orforglipron achieved near-normal blood sugar levels compared to 42% of those taking placebo at 72 weeks.[3,4] Additionally, orforglipron showed clinically meaningful improvements across key cardiovascular risk factors often associated with obesity, including non-HDL cholesterol, systolic blood pressure and triglycerides. In a pre-specified exploratory analysis, the highest dose of orforglipron reduced high-sensitivity C-reactive protein (hsCRP) levels, a marker of inflammation, by 47.7%.

Full 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]	Efficacy estimand	-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)
	Treatment-regimen estimand[5]	-7.5% (-7.8 kg; -17.2 lbs)	-8.4% (-8.6 kg; -19.0 lbs)	-11.2% (-11.3 kg; -25.0 lbs)	-2.1% (-2.4 kg; -5.3 lbs)
Key Secondary Endpoints					
Percentage of participants achieving body weight reductions of ≥5%[i]	Efficacy estimand	63.8 %	69.3 %	77.1 %	22.1 %
	Treatment-regimen estimand	60.6 %	63.5 %	71.8 %	26.8 %
Percentage of participants achieving body weight reductions of ≥10%[i]	Efficacy estimand	35.9 %	45.1 %	59.6 %	8.6 %
	Treatment-regimen estimand	33.3 %	40.0 %	54.6 %	12.9 %
Percentage of participants achieving body weight reductions of ≥15%[i]	Efficacy estimand	16.5 %	24.0 %	39.6 %	3.6 %
	Treatment-regimen estimand	15.1 %	20.3 %	36.0 %	5.9 %
Percentage of participants achieving body weight reductions of ≥20%[i,ii]	Efficacy estimand	7.2 %	11.4 %	20.1 %	1.6 %
	Treatment-regimen estimand	6.4 %	9.0 %	18.4 %	2.8 %

Change in waist circumference from average baseline of 112.4 cm (44.25 in)[i]	Efficacy estimand	-7.5 cm (-3.0 in)	-9.0 cm (-3.5 in)	-11.1 cm (-4.4 in)	-2.1 cm (-0.8 in)
	Treatment-regimen estimand	-7.1 cm (-2.8 in)	-8.2 cm (-3.2 in)	-10.1 cm (-4.0 in)	-3.1 cm (-1.2 in)
Mean percent change in non-HDL cholesterol from baseline of 146.4 mg/dL[iii]	Efficacy estimand	-5.9 %	-8.3 %	-8.5 %	-1.4 %
	Treatment-regimen estimand	-5.4 %	-7.0 %	-7.7 %	-1.9 %
Mean percent change in triglycerides from baseline of 138.8 mg/dL[iii]	Efficacy estimand	-12.1 %	-15.2 %	-21.6 %	-4.8 %
	Treatment-regimen estimand	-10.4 %	-13.5 %	-20.2 %	-3.8 %
Mean change in systolic blood pressure from baseline of 125.5 mm Hg[iii]	Efficacy estimand	-5.8 mm Hg	-5.9 mm Hg	-6.7 mm Hg	-0.8 mm Hg
	Treatment-regimen estimand	-5.7 mm Hg	-5.1 mm Hg	-6.3 mm Hg	-1.4 mm Hg

[i]Controlled for family-wise type 1 error rate.

[ii]Percentage of participants achieving body weight reductions of ≥20% with orforglipron 6 mg was not controlled for family-wise type 1 error rate.

[iii]Family-wise type 1 error rate was controlled for the pooled orforglipron doses compared to the placebo.

"People living with obesity have broad and varied needs — whether it's improving weight, A1C, lipids, blood pressure, or other health markers that primary care physicians routinely address with their patients," said Kenneth Custer, Ph.D., executive vice president and president of Lilly Cardiometabolic Health. "We're encouraged to see orforglipron improve many of these areas in ATTAIN-1. As a convenient, once-daily pill that can be scaled globally, orforglipron could be ideally suited for early adoption in primary care — where proactive intervention has the potential to lead to meaningful, long-term health improvements."

The 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, and vomiting (13.0%, 21.4% and 24.0%) vs. 3.5% with placebo. Treatment discontinuation rates due to adverse events were 5.3% (6 mg), 7.9% (12 mg) and 10.3% (36 mg) for orforglipron vs. 2.7% with placebo. No hepatic safety signal was observed.

Lilly is advancing orforglipron toward global regulatory submissions for the treatment of obesity, with regulatory action expected to occur as early as next year. Submission for the treatment of type 2 diabetes is anticipated in 2026.

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.[6] 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.[7] 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 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 a monotherapy to placebo in adults with obesity, or overweight with at least one of the following comorbidities: hypertension, dyslipidemia, obstructive sleep apnea or cardiovascular disease, who did not have diabetes. The trial is the first Phase 3 study of this patient population in which treatment was evaluated as an adjunct to exercise and a balanced, healthy diet rather than a reduced-calorie diet. 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.

Endnotes and References

1. Percentage of participants achieving body weight reductions of ≥20% with orforglipron 6 mg was not controlled for family-wise type 1 error rate.
2. 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.
3. American Diabetes Association. Standards of Care in Diabetes—2020 Abridged for Primary Care Providers. Clinical Diabetes 2020; 38(1):10–38. https://doi.org/10.2337/cd20-as01
4. Not controlled for family-wise type 1 error rate.
5. The treatment-regimen estimand represents the estimated average treatment effect regardless of adherence to study intervention or initiation of prohibited weight management treatments.
6. 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

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7. Kawai T, Sun B, Yoshino H, Feng D, Suzuki Y, Fukazawa M, Nagao S, Wainscott DB, Showalter AD, Droz BA, Kobilka TS, Coghlan MP, Willard FS, Kawabe Y, Kobilka BK, Sloop KW. 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).

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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 regulatory submissions, 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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