



Lilly's triple agonist, retatrutide, delivered weight loss of up to an average of 71.2 lbs along with substantial relief from osteoarthritis pain in first successful Phase 3 trial

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In TRIUMPH-4, participants with obesity and knee osteoarthritis taking retatrutide 12 mg lost an average of 28.7% of their body weight at 68 weeks

Retatrutide reduced WOMAC pain scores by up to an average of 4.5 points (75.8%) and significantly improved measures of physical function, with more than 1 out of 8 retatrutide-treated patients completely free from knee pain at the end of the trial

Seven additional Phase 3 trials evaluating the investigational once-weekly treatment in obesity and type 2 diabetes are expected to complete in 2026

INDIANAPOLIS, Dec. 11, 2025 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) today announced positive topline results from the Phase 3 TRIUMPH-4 clinical trial evaluating the safety and efficacy of the two highest investigational doses of retatrutide, a first-in-class GIP, GLP-1 and glucagon triple hormone receptor agonist, in adults with obesity or overweight and knee osteoarthritis, and without diabetes, as an adjunct to healthy diet and physical activity. In this global registration trial, where 84.0% of participants had a baseline BMI of ≥ 35 kg/m², each dose of retatrutide (9 mg and 12 mg) met all primary and key secondary endpoints, delivering significant weight loss and improvements in pain and physical function at 68 weeks using both the efficacy and treatment-regimen estimands.^{1,2} For the co-primary endpoints, retatrutide lowered weight by up to an average of 28.7% (71.2 lbs) and reduced pain by up to an average of 4.5 points (75.8%) using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain score.³

"People with obesity and knee osteoarthritis often live with pain and restricted mobility, and may eventually require total joint replacement," said Kenneth Custer, Ph.D., executive vice president and president, Lilly Cardiometabolic Health. "We are encouraged by the results of TRIUMPH-4, which highlight the powerful effect of retatrutide, a first-in-class triple agonist, on body weight, pain and physical function. With seven additional Phase 3 readouts expected in 2026, we believe retatrutide could become an important option for patients with significant weight loss needs and certain complications, including knee osteoarthritis."

TRIUMPH-4 Efficacy Estimand Results

	Retatrutide 9 mg	Retatrutide 12 mg	Placebo
Co-Primary Endpoints			
Percent change in body weight from avg. baseline of 112.7 kg (248.5 lbs; 40.4 kg/m ² BMI)	-26.4% (-29.1 kg; -64.2 lbs)	-28.7% (-32.3 kg; -71.2 lbs)	-2.1% (-2.1 kg; -4.6 lbs)
Change in WOMAC pain subscale score from avg. baseline of 6.0 points	-4.5 points (-75.8%) ⁱ	-4.4 points (-74.3%) ⁱ	-2.4 points (-40.3%) ⁱ
Secondary Endpoints			
Achieved $\geq 25\%$ weight loss	47.7 %	58.6 %	1.3 %
Achieved $\geq 30\%$ weight loss ⁱⁱ	30.5 %	39.4 %	0.8 %
Achieved $\geq 35\%$ weight loss ⁱⁱ	18.2 %	23.7 %	0.0 %
Change in WOMAC physical function subscale score from avg. baseline of 5.8 points	-4.1 points (-71.8%) ⁱ	-4.2 points (-73.7%) ⁱ	-2.1 points (-35.6%) ⁱ
Achieved $\geq 70\%$ reduction in WOMAC pain subscale ⁱⁱ	73.0 %	67.7 %	26.2 %

ⁱPercent change in the WOMAC pain subscale score and percent change in the WOMAC physical function subscale score were not pre-specified and were estimated from a post-hoc analysis.

ⁱⁱNot controlled for multiplicity.

In additional secondary endpoints, retatrutide reduced known markers of cardiovascular risk, including non-HDL cholesterol, triglycerides, and high-sensitivity C-reactive protein (hsCRP), and at the highest dose lowered systolic blood pressure by 14.0 mmHg, using the efficacy estimand.⁴ In an additional post-hoc analysis, 14.1% of patients on retatrutide 9 mg and 12.0% patients on retatrutide 12 mg were completely free of knee pain at 68 weeks compared to 4.2% on placebo, based on the observed efficacy estimand data.

For the treatment-regimen estimand, each dose level of retatrutide led to statistically significant improvements in both co-primary and all secondary endpoints. The treatment-regimen estimand results for the co-primary endpoints were:

- Percent change in body weight: -20.0% (-22.9 kg; -50.5 lbs; 9 mg); -23.7% (-27.2 kg; -60.0 lbs; 12 mg) and -4.6% (-5.3 kg; -11.7 lbs; placebo)
- Change in WOMAC pain subscale score: -4.0 points (-67.2%; 9 mg), -3.7 points (-62.6%; 12 mg) and -2.1 points (-35.1%; placebo)⁵

Consistent with the types of adverse events seen in clinical trials for other incretins, the most common adverse events among participants treated with retatrutide (9 mg and 12 mg, respectively) were nausea (38.1% and 43.2%) vs. 10.7% with placebo, diarrhea (34.7% and 33.1%) vs. 13.4% with placebo, constipation (21.8% and 25.0%) vs. 8.7% with placebo, vomiting (20.4% and 20.9%) vs. 0.0% with placebo, and decreased appetite (19.0% and 18.2%) vs. 9.4% with placebo. Dysesthesia occurred in 8.8% and 20.9% (9 mg and 12 mg, respectively) of patients treated with retatrutide, compared to 0.7% with placebo. These dysesthesia events were generally mild and rarely led to treatment discontinuation. Overall treatment discontinuation rates were similar across the retatrutide and placebo treatment arms. Discontinuation rates due to adverse events were 12.2% and 18.2% with retatrutide 9 mg and 12 mg, respectively, compared to 4.0% with placebo. These rates were highly correlated with baseline BMI and included discontinuations for perceived excessive weight loss. For patients with a baseline BMI ≥ 35 , discontinuation rates due to adverse events were 8.8% and 12.1% for the 9 mg and 12 mg doses, respectively, compared to 4.8% with placebo.

Detailed TRIUMPH-4 results will be presented at a future medical meeting and published in a peer-reviewed journal. Additional results from the TRIUMPH program, which include a maintenance dose of 4 mg in addition to the 9 mg and 12 mg doses tested in this trial, are expected in 2026.

About retatrutide

Retatrutide is an investigational once-weekly triple hormone receptor agonist. Retatrutide is a single molecule that activates the body's receptors for glucose-dependent insulinotropic polypeptide (GIP), glucagon-like peptide-1 (GLP-1), and glucagon. Lilly is studying retatrutide in several Phase 3 clinical trials to evaluate its potential efficacy and safety in obesity and overweight with at least one weight-related medical problem, type 2 diabetes, knee osteoarthritis, moderate-to-severe obstructive sleep apnea, chronic low back pain, cardiovascular and renal outcomes, and metabolic dysfunction-associated steatotic liver disease.

About TRIUMPH-4 and the TRIUMPH clinical trial program

TRIUMPH-4 (NCT05931367) is a Phase 3, 68-week, randomized, double-blind, placebo-controlled study comparing the efficacy and safety of retatrutide with placebo in adults with obesity or overweight and knee osteoarthritis. The study randomized 445 participants in a 1:1:1 ratio to receive either retatrutide 9 mg or 12 mg, or placebo. The objective of the study was to demonstrate that retatrutide is superior to placebo in WOMAC pain subscale score reduction and in body weight reduction from baseline to week 68 in people with a BMI ≥ 27.0 kg/m² and who met American College of Rheumatology Criteria (clinical and radiological) for knee osteoarthritis. Participants randomized to retatrutide initiated treatment with 2 mg once weekly and increased the dose in a step-wise approach every four weeks until reaching the target dose of 9 mg (via steps at 2 mg, 4 mg and 6 mg) or 12 mg (via steps at 2 mg, 4 mg, 6 mg and 9 mg).

The initial TRIUMPH Phase 3 global registrational clinical development program is evaluating the safety and efficacy of retatrutide for the treatment of obesity and overweight, obstructive sleep apnea and knee osteoarthritis in people with obesity and overweight across four global registrational trials. The program, which began in 2023, has enrolled more than 5,800 participants and additional results are anticipated next year. The TRIUMPH clinical trial program includes five doses of retatrutide: 2 mg, 4 mg, 6 mg, 9 mg and 12 mg. Across all studies, participants randomized to retatrutide initiated treatment with 2 mg once weekly and increased the dose every four weeks until reaching their target dose. The target doses in TRIUMPH-1 and TRIUMPH-2 are 4 mg, 9 mg and 12 mg, while target doses in TRIUMPH-3 and TRIUMPH-4 are 9 mg and 12 mg.

Endnotes and References

1. The efficacy estimand with weight management represents efficacy in all randomized participants who remained on the study intervention (with possible dose modifications) without initiating prohibited weight management treatments. The efficacy estimand with knee osteoarthritis pain represents efficacy in all randomized participants who remained on the study intervention (with possible dose modifications) without initiating prohibited weight management and/or pain treatments.
2. The treatment-regimen estimand with weight management represents the estimated average treatment effect regardless of adherence to study intervention or initiation of prohibited weight management treatments. The treatment-regimen estimand with knee osteoarthritis pain represents the estimated average treatment effect regardless of adherence to study intervention assuming no treatment benefit should participants need significant actions associated with lack of efficacy.
3. WOMAC is a patient-reported questionnaire validated in osteoarthritis for assessing pain, stiffness and physical function, with scores normalized to a 0–10 scale where higher values indicate worse symptoms.
4. Not controlled for multiplicity.
5. Percent change in the WOMAC pain and physical function subscale scores were not pre-specified and were estimated from a post-hoc analysis.

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 curbing 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](https://www.lilly.com) and [Lilly.com/news](https://www.lilly.com/news), or follow us on [Facebook](https://www.facebook.com/lilly), [Instagram](https://www.instagram.com/lilly) and [LinkedIn](https://www.linkedin.com/company/lilly). 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 retatrutide as a potential treatment for adults with obesity or overweight and knee osteoarthritis, potential efficacy and tolerability of retatrutide, and the timeline for future readouts, presentations, and other milestones relating to retatrutide 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 retatrutide will prove to be a safe and effective treatment for

obesity or overweight and knee osteoarthritis or other potential indications, that retatrutide 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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The Lilly logo is rendered in a vibrant red, cursive script. The letters are fluid and interconnected, with a classic, elegant feel. The 'L' is particularly large and prominent, leading into the 'i', 'l', 'l', 'e', and 'y' which follow in a similar flowing style. The overall appearance is that of a handwritten signature or a stylized brand mark.

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