Lilly's triple agonist, retatrutide, demonstrated significant reductions in A1C and weight in first Phase 3 trial for treatment of type 2 diabetes

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For the primary endpoint, retatrutide lowered A1C by an average of 1.7% to 2.0% across doses at 40 weeks in TRANSCEND-T2D-1

Participants taking retatrutide 12 mg lost an average of 36.6 lbs (16.8%)

No weight loss plateau was observed with retatrutide, with participants continuing their weight loss trajectory through 40 weeks

INDIANAPOLIS, March 19, 2026 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) today announced positive topline results from TRANSCEND-T2D-1, a Phase 3 clinical trial evaluating the efficacy and safety of retatrutide, an investigational first-in-class GIP, GLP-1 and glucagon triple hormone receptor agonist, as an adjunct to diet and exercise. The trial enrolled adults diagnosed with type 2 diabetes with inadequate glycemic control with diet and exercise alone, and a mean duration of diabetes of 2.5 years. In the study, retatrutide met the primary and all key secondary endpoints, delivering superior A1C reduction and weight loss at 40 weeks compared to placebo, using both the efficacy and treatment-regimen estimands.[1,2] For the primary endpoint, participants taking retatrutide achieved average A1C reductions of up to 2.0%, using the efficacy estimand. For a key secondary endpoint, participants taking retatrutide lost up to an average of 36.6 lbs (16.8%), using the efficacy estimand. Weight loss continued through the end of the treatment period.

"For many people with type 2 diabetes, it is a struggle to achieve both A1C control and weight loss, since obesity has historically been harder to treat for those with type 2 diabetes," said Kenneth Custer, Ph.D., executive vice president and president, Lilly Cardiometabolic Health. "With triple agonist retatrutide, we set out to make a molecule that could help patients achieve substantial A1C reduction and weight loss. These results support the remarkable potential of this novel molecule for people living with type 2 diabetes, with up to 2% A1C improvement and nearly 17% weight loss in 40 weeks of treatment."

TRANSCEND-T2D-1 Efficacy Results

Primary Endpoint					
		Retatrutide 4 mg	**Retatrutide 9 mg**	**Retatrutide 12 mg**	**Placebo**
Change in A1C from a baseline of 7.9% at 40 weeks	Efficacy estimand	-1.7 %	-2.0 %	-1.9 %	-0.8 %
	Treatment-regimen estimand	-1.7 %	-1.9 %	-1.9 %	-0.8 %
Key Secondary Endpoint					
Percentage change in body weight at 40 weeks from a baseline of 96.9 kg (213.6 lbs; BMI of 35.8 kg/m^2)	Efficacy estimand	-11.5% (-11.1 kg; -24.5 lbs)	-15.5% (-15.1 kg; -33.3 lbs)	-16.8% (-16.6 kg; -36.6 lbs)	-2.5% (-2.8 kg; -6.2 lbs)
	Treatment-regimen estimand	-11.5% (-11.1 kg; -24.5 lbs)	-13.9% (-13.5 kg; -29.8 lbs)	-15.3% (-15.1 kg; -33.3 lbs)	-2.6% (-2.7 kg; -6.0 lbs)

Retatrutide also showed clinically meaningful improvements from baseline across key cardiovascular risk factors, including non-HDL cholesterol, triglycerides and systolic blood pressure.[3]

Consistent with the types of adverse events seen in clinical trials for other incretin-based therapies, the most common adverse events among participants treated with retatrutide (4 mg, 9 mg, 12 mg) were nausea (16.4%, 19.5%, 26.5%, respectively vs. 3.7% with placebo), diarrhea (18.7%, 26.3%, 22.8%, respectively vs. 4.5% with placebo) and vomiting (15.7%, 15.0%, 17.6%, respectively vs. 2.2% with placebo), and occurred primarily during dose escalation. Incidence of dysesthesia occurred in 4.5%, 2.3% and 4.4% (4 mg, 9 mg and 12 mg, respectively) of patients treated with retatrutide, compared to 0.0% with placebo. These dysesthesia events were generally mild, with a majority resolving during treatment. Discontinuation rates due to adverse events were 2.2%, 4.5% and 5.1% with retatrutide 4 mg, 9 mg and 12 mg, respectively, compared to 0.0% with placebo.

Detailed TRANSCEND-T2D-1 results will be presented at the American Diabetes Association Scientific Sessions in June and published in a peer-reviewed journal. Additional results from the retatrutide clinical trial program are expected over the next year.

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. Retatrutide is an investigational molecule that is legally available only to participants in Lilly's clinical trials.

About TRANSCEND-T2D-1 and the TRANSCEND-T2D clinical trial program
TRANSCEND-T2D-1 (NCT06354660) is a Phase 3, 40-week, randomized, double-blind, placebo-controlled study comparing the efficacy and safety of retatrutide with placebo in adults with type 2 diabetes and inadequate glycemic control with diet and exercise alone. The study randomized 537 participants in a 1:1:1:1 ratio to receive either retatrutide 4 mg, 9 mg or 12 mg, or placebo. The objective of the study was to demonstrate that retatrutide (4 mg, 9 mg or 12 mg) is superior to placebo in A1C reduction from baseline after 40 weeks, in adults with type 2 diabetes who have not taken any anti-diabetes medications for at least 90 days prior to visit one, and are naïve to insulin therapy except for gestational diabetes. Study participants had A1C between ≥7.0% and ≤9.5% and a BMI of ≥23 kg/m^2 at visit one. 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 4 mg (via one step at 2 mg), 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 TRANSCEND-T2D Phase 3 clinical trial program is evaluating the safety and efficacy of retatrutide for the treatment of adults with type 2 diabetes across three global registrational trials. The program, which began in 2024, has enrolled more than 2,050 participants and additional results are anticipated over the next year.

Endnotes and References

1. The efficacy estimand represents efficacy had all randomized participants remained on study intervention (with possible dose interruptions and/or dose modifications) for 40 weeks without initiating additional antihyperglycemic medications (>14 days of use).
2. The treatment-regimen estimand represents the estimated average treatment effect regardless of adherence to study intervention or initiation of additional antihyperglycemic medications.
3. Reduction in non-HDL cholesterol, triglycerides and systolic blood pressure with retatrutide was controlled for family-wise type 1 error in all dose groups except for 4 mg.

About Lilly
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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 retatrutide as a potential treatment for adults with type 2 diabetes, 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 type 2 diabetes 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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