Lilly's once-weekly insulin efsitora alfa demonstrated A1C reduction and a safety profile consistent with daily insulin in multiple Phase 3 trials

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Results from the fixed-dose QWINT-1 study, along with the QWINT-3 and QWINT-4 studies, reinforce efsitora's potential to simplify insulin management with weekly dosing

Lilly plans to submit efsitora for the treatment of adults with type 2 diabetes to global regulatory agencies by the end of this year

INDIANAPOLIS, June 22, 2025 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) today announced detailed results from QWINT-1, QWINT-3, and QWINT-4 Phase 3 clinical trials evaluating the safety and efficacy of investigational once-weekly insulin efsitora alfa (efsitora) in adults with type 2 diabetes who used insulin for the first time, previously used daily basal insulin, and previously used daily basal insulin and mealtime insulin, respectively. In each trial, once-weekly efsitora met the primary endpoint of non-inferior A1C reduction compared to daily basal insulin. The complete results from these studies were presented at the American Diabetes Association (ADA) 85th Scientific Sessions 2025. Simultaneously, results from QWINT-1, a first-of-its-kind fixed-dose study, were published in *The New England Journal of Medicine*, while results from QWINT-3 and QWINT-4 were published in *The Lancet*.

In QWINT-1, efsitora reduced A1C by 1.31% compared to 1.27% for insulin glargine at week 52 for the efficacy estimand.[1,2] In the trial, efsitora was titrated to four fixed doses at four-week intervals, as needed for blood glucose control.[3] In QWINT-3, efsitora reduced A1C by 0.86% compared to 0.75% for insulin degludec at week 26 for the efficacy estimand.[4] In QWINT-4, efsitora reduced A1C by 1.07% compared to 1.07% for insulin glargine at week 26 for the efficacy estimand.[5] In these two trials, efsitora was administered using traditional insulin dosing with adjustments based on each patient's glucose level.

"The novel fixed-dose regimen used in QWINT-1 for once-weekly efsitora, which consisted of only four single-dose titration options, has the potential to facilitate and simplify insulin therapy, reducing the hesitation often associated with starting insulin to treat type 2 diabetes," said Dr. Julio Rosenstock, senior scientific advisor for Velocity Clinical Research at Medical City Dallas, clinical professor of medicine, University of Texas Southwestern Medical Center, and lead trial investigator for QWINT-1. "A simpler, once-weekly regimen with efsitora may help people with type 2 diabetes initiate and manage insulin therapy with the goal of improving blood sugar levels. Across all QWINT trials, the results showed that once-weekly efsitora controlled glucose as effectively as the most popular once-daily basal insulins."

QWINT-1 Primary Endpoint

	Efficacy Estimand	**Treatment-Regimen Estimand**[6]
Primary Endpoint – A1C Reduction (Resulting A1C) at Week 52		
Efsitora	-1.31 % (6.92 %)	-1.19 % (7.05 %)
Glargine	-1.27 % (6.96 %)	-1.16 % (7.08 %)

QWINT-3 Primary and Key Secondary Endpoints

	Efficacy Estimand	**Treatment-Regimen Estimand**
Primary Endpoint – A1C Reduction (Resulting A1C) at Week 26		
Efsitora	-0.86 % (6.93 %)	-0.81 % (6.99 %)
Degludec	-0.75 % (7.03 %)	-0.72 % (7.08 %)
Key Secondary Endpoint – Rates of Clinically Significant or Severe Nocturnal Hypoglycemic Events Per Patient-Year of Exposure up to Week 78[7,8]		
Efsitora	0.11	
Degludec	0.10	
Key Secondary Endpoint – Percent Time in Range (70-180 mg/dL) During the Four Weeks Prior to Week 26		
Efsitora	62.8 %	61.4 %
Degludec	61.3 %	61.0 %

QWINT-4 Primary and Key Secondary Endpoints

	Efficacy Estimand	**Treatment-Regimen Estimand**
Primary Endpoint – A1C Reduction (Resulting A1C) at Week 26		
Efsitora	-1.07 % (7.12 %)	-1.01 % (7.17 %)
Glargine	-1.07 % (7.11 %)	-1.00 % (7.18 %)

Key Secondary Endpoint – Participants Achieving A1C <7% at Week 26 Without Nocturnal Hypoglycemia		
Efsitora	39.5 %	38.6 %
Glargine	36.6 %	35.9 %
Key Secondary Endpoint – Rates of Clinically Significant or Severe Nocturnal Hypoglycemic Events Per Patient-Year of Exposure up to Week 26		
Efsitora	0.67	
Glargine	1.00	

"Building on Lilly's legacy of innovation in insulin therapy, once-weekly efsitora may offer a significant advancement for people with type 2 diabetes who need insulin by eliminating over 300 injections per year," said Jeff Emmick, M.D., Ph.D., senior vice president of product development at Lilly. "These results reinforce the potential for once-weekly efsitora to help reduce the overall burden of insulin therapy through a simplified treatment approach. We look forward to working with regulatory agencies to bring this innovation to patients around the world."

Across the three trials, efsitora demonstrated an overall safety profile similar to two of the most commonly used daily basal insulin therapies for the treatment of type 2 diabetes. In QWINT-1, efsitora resulted in approximately 40% fewer hypoglycemic events compared to insulin glargine, with estimated combined rates of severe or clinically significant hypoglycemic events per patient-year of exposure of 0.50 with efsitora vs. 0.88 with insulin glargine at 52 weeks. In QWINT-3, these rates were 0.84 with efsitora vs. 0.74 with insulin degludec at 78 weeks. In QWINT-4, estimated combined rates of severe or clinically significant hypoglycemic events per patient-year of exposure were 6.6 with efsitora vs. 5.9 with insulin glargine at 26 weeks.

Lilly plans to submit efsitora for the treatment of adults with type 2 diabetes to global regulatory agencies by the end of this year.

About the QWINT clinical trial program
The QWINT Phase 3 global clinical development program for insulin efsitora alfa (efsitora) in diabetes began in 2022 and has enrolled more than 3,000 people living with type 2 diabetes across four global registration studies.

QWINT-1 (NCT05662332) was a parallel-design, open-label, treat-to-target, randomized controlled clinical trial comparing the efficacy and safety of efsitora as a once-weekly basal insulin using a fixed dose escalation to daily insulin glargine for 52 weeks in insulin-naïve adults with type 2 diabetes. The trial randomized 795 participants across the U.S., Argentina and Mexico to receive efsitora once weekly or insulin glargine once daily, administered subcutaneously. Participants treated with efsitora received a starting dose of 100 units of insulin, followed by escalation to fixed dosages of 150 units, 250 units and 400 units every four weeks, as needed, until achieving a target fasting blood glucose of 80-130 mg/dL. Participants with fasting blood glucose greater than 130 mg/dL on or after 16 weeks were transferred to flexible dosing. The primary objective of the trial was to demonstrate non-inferiority in reducing A1C at week 52 with efsitora compared to daily use of insulin glargine.

QWINT-3 (NCT05275400) was a multicenter, randomized, parallel-design, open-label trial comparing the efficacy and safety of efsitora as a once-weekly basal insulin to insulin degludec for 78 weeks after a three-week lead-in followed by a five-week safety follow up period, in adults with type 2 diabetes who are currently treated with basal insulin. The trial randomized 986 participants across the U.S., Argentina, Hungary, Japan, Korea, Poland, Puerto Rico, Slovakia, Spain and Taiwan to receive efsitora once weekly or insulin degludec once daily, administered subcutaneously. The primary objective of the study was to demonstrate non-inferiority in reducing A1C at week 26 with efsitora compared to insulin degludec.

QWINT-4 (NCT05462756) was a parallel-design, open-label, treat-to-target, randomized controlled clinical trial comparing the efficacy and safety of efsitora as a weekly basal insulin to insulin glargine for 26 weeks in adults with type 2 diabetes who have previously been treated with basal insulin and at least two injections per day of mealtime insulin. The trial randomized 730 participants across the U.S., Argentina, Germany, India, Italy, Mexico, Puerto Rico and Spain to receive efsitora once weekly or insulin glargine once daily, both of which were administered subcutaneously along with insulin lispro. The primary objective of the trial was to demonstrate non-inferiority in reducing A1C at week 26 with efsitora compared to insulin glargine.

About insulin efsitora alfa
Insulin efsitora alfa (efsitora) is a once-weekly basal insulin, a fusion protein that combines a novel single-chain variant of insulin with a human IgG2 Fc domain. It is specifically designed for once-weekly subcutaneous administration, and with its low peak-to-trough ratio, it has the potential to provide more stable glucose levels (less glucose variability) throughout the week.

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

1. The efficacy estimand represents the treatment effect on all participants who adhered to the study drug without initiating rescue therapy for persistent severe hyperglycemia.
2. From a baseline of 8.20% for efsitora and 8.28% for insulin glargine.
3. Participants treated with efsitora received a starting dose of 100 units of insulin, followed by escalation to fixed dosages of 150 units, 250 units and 400 units every four weeks, as needed, until achieving a target fasting blood glucose of 80-130 mg/dL. Participants with fasting blood glucose greater than 130 mg/dL on or after 16 weeks were transferred to flexible dosing.

4. From a baseline of 7.80% for both efsitora and insulin degludec.
5. From a baseline of 8.18% for both efsitora and insulin glargine.
6. The treatment-regimen estimand represents the estimated average treatment effect regardless of treatment discontinuation or introduction of rescue therapy for persistent severe hyperglycemia.
7. Blood glucose <54 mg/dL.
8. Nocturnal hypoglycemia was defined as any event that occurred at night between midnight and 6 a.m.

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 insulin efsitora alfa as a potential treatment for people with type 2 diabetes and the timeline for future readouts, presentations, and other milestones relating to insulin efsitora alfa 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 future study results will be consistent with study results to date, that insulin efsitora alfa will prove to be a safe and effective treatment for type 2 diabetes, that insulin efsitora alfa 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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Refer to: Niki Biro; niki_biro@lilly.com; 317-358-9074 (Media)
Michael Czapar; czapar_michael_c@lilly.com; 317-617-0983 (Investors)

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