With once-a-week dosing, insulin efsitora alfa delivers similar A1C reduction compared to daily insulin in adults with type 1 diabetes

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Detailed results were published in The Lancet and simultaneously presented at the European Association for the Study of Diabetes (EASD) Annual Meeting 2024

INDIANAPOLIS, Sept. 10, 2024 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) today announced detailed results from the QWINT-5 phase 3 trial evaluating once-weekly insulin efsitora alfa (efsitora) compared to once-daily insulin degludec in adults with type 1 diabetes who require daily basal and multiple daily mealtime insulin injections. The data were published in *The Lancet* and simultaneously presented today at the European Association for the Study of Diabetes (EASD) Annual Meeting 2024.

In the trial, efsitora met the primary endpoint of non-inferior A1C reduction at week 26. For the efficacy estimand[1,2], efsitora reduced A1C by 0.53% compared to 0.59% for insulin degludec resulting in an A1C of 7.37% and 7.32% respectively[3].

In a key secondary endpoint, time in range[4] as measured by continuous glucose monitoring (CGM) was similar between efsitora and insulin degludec during the four weeks prior to week 26. In an additional key secondary endpoint, the estimated combined rates of patient-reported clinically significant (blood glucose <54 mg/dL) or severe nocturnal[5] hypoglycemic events per patient-year of exposure were similar between efsitora and insulin degludec over the 52-week study period.

"People with type 1 diabetes need insulin every day. Currently, they can deliver the insulin using an automated insulin delivery system or by taking a daily basal insulin injection and multiple mealtime insulin injections each day," said Richard Bergenstal, M.D., executive director of the International Diabetes Center, HealthPartners Institute. "This new data shows that with one dose a week of basal insulin, efsitora was able to achieve a similar A1C reduction as taking an injection of one of the most used background insulins every day. I look forward to further evaluation of these data, including ways to minimize hypoglycemia, so once-weekly insulin can be one option for personalizing the management of type 1 diabetes."

Full Results

QWINT-5 Study: Primary and Secondary Endpoints		
	Efficacy Estimand	**Treatment-Regimen Estimand[6]**
Primary Endpoint – A1C Reduction (Resulting A1C) at 26 Weeks		
Efsitora	-0.53% (7.37%)	-0.51% (7.41%)[7]
Insulin degludec	-0.59% (7.32%)	-0.56% (7.36%)[8]
Secondary Endpoint – Percent Time in Range During the 4 Weeks Prior to Week 26		
Efsitora	52.8 %	52.5 %
Insulin degludec	53.1 %	52.9 %
Secondary Endpoint – Estimated Rate of Clinically Significant[9] or Severe Nocturnal Hypoglycemic Events Per Patient-Year of Exposure through 52 Weeks		
Efsitora	1.99	
Insulin degludec	1.96	

In the trial, estimated combined rates of patient-reported clinically significant (blood glucose <54 mg/dL) or severe hypoglycemic events per patient-year of exposure through week 52 were 14.03 with efsitora vs. 11.59 with insulin degludec. There was no evidence of increased duration of hypoglycemia with efsitora compared to insulin degludec based on CGM data.

Estimated rates of severe hypoglycemic events per patient-year of exposure through week 52 were 0.14 with efsitora vs. 0.04 with insulin degludec. More than half (64%) of the reported severe hypoglycemic events with efsitora took place during the initial 12 weeks of the trial's treatment period and incidence of severe hypoglycemia in both treatment groups declined after week 12.

Overall incidence of treatment-emergent adverse events were comparable across treatment groups. Serious adverse events were higher in efsitora compared to insulin degludec, driven by severe hypoglycemic events.

"When we commercialized insulin more than 100 years ago, it marked the beginning of our commitment to people living with type 1 diabetes – today's announcement continues that legacy," said Jeff Emmick, M.D., Ph.D., senior vice president, product development, Lilly. "These results underscore the potential of efsitora to help some people living with type 1 diabetes lower their A1C with only one basal insulin injection per week, while also highlighting the complexity of treating this chronic disease. With the data we have seen from our phase 3 program so far, we are confident in efsitora's potential to transform diabetes care and will continue to pursue new treatment options until we can eliminate the disease entirely."

Detailed results for QWINT-2 are also being presented at EASD and simultaneously published in *The New England Journal of Medicine*.

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 4,000 people living with type 1 or type 2 diabetes across five global registration studies.

QWINT-5 (NCT05463744) is a multicenter, treat-to-target, randomized, parallel-design, open-label study comparing the efficacy and safety of efsitora as a once-weekly basal insulin to insulin degludec in participants with type 1 diabetes treated with daily basal and multiple daily mealtime insulin injections. The trial consisted of a 52-week treatment period with the primary endpoint measured at 26 weeks. 692 participants across the U.S., Argentina, Japan, Poland, Puerto Rico, Slovakia and Taiwan were randomized to receive efsitora once weekly or insulin degludec once daily administered subcutaneously. The primary objective of the study is to demonstrate non-inferiority in reducing A1C at week 26 with efsitora compared to insulin degludec. Throughout the study, participants used unblinded CGM.

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, has the potential to provide more stable glucose levels (less glucose variability) throughout the week. Efsitora is in phase 3 development for adults with type 1 and 2 diabetes.

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 more than 51 million 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

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), including statements about insulin efsitora alfa as a potential treatment for people with type 1 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 planned or ongoing studies will be completed as planned, 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 1 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.

[1] The efficacy estimand represents the treatment effect had all participants adhered to the study drug without initiating rescue therapy for persistent severe hyperglycemia.

[2] 95% CI for treatment difference (-0.075% to 0.19%).

[3] From a baseline A1C of 7.89% for efsitora and 7.93% for insulin degludec.

[4] Glucose 70-180 mg/dL.

[5] Any event that occurred between midnight and 6 a.m.

[6] Treatment-regimen estimand represents the efficacy irrespective of adherence to the investigational medicine or introduction of rescue therapy for persistent severe hyperglycemia.

[7] From a baseline A1C of 7.88% for efsitora and 7.94% for insulin degludec.

[8] 95% CI for treatment difference (-0.077% to 0.181%).

[9] Blood glucose <54 mg/dL.

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