With Once-a-Week Dosing, Insulin Efsitora Alfa Delivers A1C Reduction and Safety Profile Consistent with Daily Insulin

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Efsitora met the primary endpoint in both QWINT-2 and QWINT-4 with once-a-week dosing regimen for people living with type 2 diabetes

Efsitora was equally safe and effective among adults naïve to insulin therapy currently using and not using GLP-1 receptor agonists

INDIANAPOLIS, May 16, 2024 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) today announced positive topline results from the QWINT-2 and QWINT-4 phase 3 clinical trials evaluating once-weekly insulin efsitora alfa (efsitora) in adults with type 2 diabetes using insulin for the first time (insulin naïve) and those who require multiple daily insulin injections. In the treat-to-target clinical trials, efsitora showed non-inferior A1C reduction compared to the most commonly used daily basal insulins globally.

"The results of QWINT-2 and QWINT-4 are a significant milestone for the diabetes community and demonstrate that efsitora as a weekly insulin provides blood sugar control equivalent to daily basal insulins," said Jeff Emmick, MD, Ph.D., senior vice president, product development, Lilly. "With efsitora, we have an opportunity to provide an innovative once-weekly solution that safely achieves and maintains A1C control, reduces treatment burden of traditional daily injections and potentially improves adherence for people with diabetes."

QWINT-2 evaluated the efficacy and safety of once-weekly efsitora compared to once-daily insulin degludec for 52 weeks. The trial randomized insulin-naïve adults with type 2 diabetes to receive efsitora once weekly or insulin degludec once daily and was also designed to assess efficacy in patients using and not using GLP-1 receptor agonists.

The trial met its primary endpoint of non-inferior A1C reduction with efsitora compared to insulin degludec at week 52. For the efficacy estimand[1,2], efsitora reduced A1C by 1.34% compared to 1.26% for insulin degludec resulting in an A1C of 6.87% and 6.95% respectively[3]. In a key secondary endpoint, efsitora was non-inferior to insulin degludec in A1C change among participants using and not using GLP-1 receptor agonists. Further, participants taking efsitora spent 45 minutes more time in range[4] and 37 minutes more in tight range[5] without additional time in hypoglycemia (blood glucose <54 mg/dL) in comparison to insulin degludec.

QWINT-4 evaluated the efficacy and safety of efsitora compared 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 participants to receive efsitora once weekly or insulin glargine once daily, both of which were administered with insulin lispro.

The trial met its primary endpoint of non-inferior A1C reduction with efsitora compared to insulin glargine at week 26. For the efficacy estimand, both efsitora and insulin glargine reduced A1C by 1.07% resulting in an A1C of 7.12% and 7.11%, respectively[6,7].

In both QWINT-2 and QWINT-4, efsitora was safe and well-tolerated with estimated combined rates of severe or clinically significant (blood glucose <54 mg/dL) hypoglycemic events per patient-year of exposure of 0.58 with efsitora vs. 0.45 with insulin degludec (QWINT-2) and 6.6 with efsitora vs. 5.9 with insulin glargine (QWINT-4).

Detailed results from QWINT-2 will be presented at the European Association for the Study of Diabetes (EASD) Annual Meeting 2024. Topline readouts from QWINT-1, QWINT-3 and QWINT-5 are anticipated later 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 4,000 people living with type 1 or type 2 diabetes across five global registration studies.

QWINT-2 (NCT05362058) 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 to insulin degludec for 52 weeks in insulin-naïve adults with type 2 diabetes. The trial randomized 928 participants across the U.S., Brazil, Canada, China, Czechia (Czech Republic), Germany, Greece, Japan, Korea, Mexico and Puerto Rico to receive efsitora once weekly or insulin degludec once daily administered subcutaneously. The primary objective of the trial was to demonstrate non-inferiority in reducing A1C at week 52 with efsitora compared to insulin degludec. The trial was also designed to assess efficacy and safety for patients using and not using GLP-1 receptor agonists.

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. 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) 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 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 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.

[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 (-0.22% to 0.061%).
[3] From a baseline A1C of 8.21% for efsitora and 8.23% for insulin degludec.
[4] Blood glucose 70-180 mg/dL.
[5] Blood glucose 70-140 mg/dL.
[6] From a baseline A1C of 8.18% for efsitora and insulin glargine.
[7] 95% CI for treatment difference (-0.13% to 0.14%).

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