



Results from Two Phase 3 Studies Show Lilly's Ultra Rapid Lispro (URLi) Met Primary Efficacy Endpoint in People with Type 1 and Type 2 Diabetes

October 2, 2018

Both studies also showed greater reductions in glucose excursions after mealtime

INDIANAPOLIS, Oct. 2, 2018 /PRNewswire/ -- Readouts from two phase 3 clinical trials demonstrated that Eli Lilly and Company's (NYSE: LLY) Ultra Rapid Lispro (URLi) met the primary efficacy endpoint of non-inferior A1C reduction from baseline compared to Humalog® (insulin lispro) and also demonstrated significantly improved post-meal glucose control in people with type 1 and type 2 diabetes.

URLi is Lilly's novel mealtime insulin formulation that was developed to help better control blood glucose levels after meals by more closely mirroring the way insulin works in people without diabetes.

The two phase 3 studies, PRONTO-T1D and PRONTO-T2D, evaluated the safety and efficacy of URLi compared to Humalog in people with type 1 and type 2 diabetes, respectively. The primary efficacy endpoint of non-inferiority to Humalog, as measured by A1C reduction from baseline, was met in both studies at 26 weeks. In both populations, URLi demonstrated superior reduction in glucose excursions at both one and two hours during a meal test. The studies showed no significant difference in severe, nocturnal or overall hypoglycemia rates reported by study participants.

"Despite progress in insulin and diabetes management, many people with diabetes find controlling high blood sugar levels after meals frustrating. If approved, URLi will be a new option in mealtime insulin therapy designed to help keep blood sugar in range after eating," said Thomas Hardy, Senior Medical Director, Insulins Product Development, Lilly Diabetes. "We are encouraged by these data showing that URLi was non-inferior to Humalog in controlling A1C, an overall measure of glucose control, while significantly lowering blood glucose levels during a meal test."

In both studies, URLi showed overall safety and tolerability similar to Humalog. Lilly plans to present detailed results from these studies in 2019. Based on these results, Lilly will submit URLi to regulatory authorities in 2019.

About the PRONTO Studies

PRONTO-T1D and PRONTO-T2D were randomized, double-blind, controlled, treat-to-target comparisons of ultra rapid lispro (URLi) and Humalog (insulin lispro), both in combination with either insulin glargine or insulin degludec in adults with type 1 and type 2 diabetes, respectively. The primary objective of each study, conducted in 1,222 and 673 participants, respectively, was to evaluate whether URLi is non-inferior to Humalog in reducing A1C from baseline after 26 weeks of treatment. Comparisons of one and two hour post-prandial glucose and A1C superiority were included in the statistical plan. Those comparisons were performed after the primary endpoint of non-inferiority was achieved.

Important Safety Information for Humalog

What is the most important information I should know about Humalog?

- o Do not share your Humalog KwikPen, Humalog Junior KwikPen, cartridges, reusable pen compatible with Lilly 3 mL cartridges, or syringes with other people, even if the needle has been changed. You may give other people a serious infection or get a serious infection from them.
- o Do not change the insulin you use without talking to your healthcare provider. Changes may make you more likely to experience low or high blood sugar. Changes should be made cautiously under the supervision of your healthcare provider.
- o Test your blood sugar levels as your healthcare provider instructs.
- o Your insulin dose may need to change because of illness, stress, other medicines you take, change in diet, or change in physical activity or exercise.
- o When used in a pump, do not mix or dilute Humalog with any other insulin or liquid.

Who should not take Humalog?

- o Do not take Humalog if your blood sugar is too low (hypoglycemia) or if you are allergic to insulin lispro or any of the ingredients in Humalog.

Before using Humalog, what should I tell my healthcare providers?

- o About all of your medical conditions, including liver, kidney, or heart failure or other heart problems.
- o If you are pregnant, planning to become pregnant, or are breastfeeding.
- o About all the medicines you take, including prescription (especially ones commonly called TZDs [thiazolidinediones]) and nonprescription medicines, vitamins, and herbal supplements.

How should I use Humalog?

- Humalog is a rapid-acting insulin. Take Humalog within fifteen minutes before eating or right after eating a meal.
- Always make sure you receive the correct type of Humalog from the pharmacy.
- Do not use Humalog if it is cloudy, colored, or has solid particles or clumps in it.
- Inject Humalog under your skin (subcutaneously). Never inject into a vein or muscle. Change (rotate) your injection site with each dose. Make sure you inject the correct insulin and dose.
- Do not re-use needles. Always use a new needle for each injection. Re-use of needles can cause you to receive the wrong dose of Humalog and result in infection.
- Do not drive or operate heavy machinery until you know how Humalog affects you. Do not use alcohol while using Humalog.

What are the possible side effects of Humalog?

- Severe low blood sugar can cause unconsciousness (passing out), seizures, and death. Low blood sugar is the most common side effect. There are many causes of low blood sugar, including taking too much Humalog. It is important to treat it quickly. You can treat mild to moderate low blood sugar by drinking or eating a quick source of sugar right away. Symptoms may be different for each person. Be sure to talk to your healthcare provider about low blood sugar symptoms and treatment.
- Severe life-threatening allergic reactions (whole-body reactions) can happen. Get medical help right away if you develop a rash over your whole body, have trouble breathing, have a fast heartbeat, or are sweating.
- Humalog can cause life-threatening low potassium in your blood (hypokalemia), which can cause severe breathing problems, irregular heartbeat, and death.
- Serious side effects can include swelling of your hands and feet and heart failure when taking certain pills called thiazolidinediones or "TZDs" with Humalog. This may occur in some people even if they have not had heart problems before. Tell your healthcare provider if you have shortness of breath, swelling of your ankles or feet, or sudden weight gain, which may be symptoms of heart failure. Your healthcare provider may need to adjust or stop your treatment with TZDs or Humalog.
- Failure of your insulin pump or infusion set or degradation of the insulin in the pump can cause hyperglycemia and ketoacidosis. Always carry an alternate form of insulin administration in case of pump failure.
- The most common side effects of Humalog include low blood sugar, allergic reactions, including reactions at your injection site, skin thickening or pits at the injection site (lipodystrophy), itching, and rash. These are not all of the possible side effects. Ask your healthcare provider for more information or for medical advice about side effects.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Humalog is available by prescription only.

For additional information, talk to your healthcare providers and please [click to access](#) Full Prescribing Information and Patient Prescribing Information.

Please see Instructions for Use included with the Humalog KwikPen.

HI CON ISI 06JUN2017

About Diabetes

Approximately 30 million Americans¹ and an estimated 425 million adults worldwide have diabetes.² Type 2 diabetes is the most common type internationally, accounting for an estimated 90 to 95 percent of all diabetes cases in the United States alone.¹ Diabetes is a chronic disease that occurs when the body does not properly produce or use the hormone insulin.

About Lilly Diabetes

Lilly has been a global leader in diabetes care since 1923, when we introduced the world's first commercial insulin. Today we are building upon this heritage by working to meet the diverse needs of people with diabetes and those who care for them. Through research, collaboration and quality manufacturing we strive to make life better for people affected by diabetes. We offer a wide range of therapies and a continued determination to provide real solutions—from medicines and technologies to support programs and more. For the latest updates, visit <http://www.lillydiabetes.com/> or follow us on Twitter: [@LillyDiabetes](#) and Facebook: [LillyDiabetesUS](#).

About Eli Lilly and Company

Lilly is a global healthcare leader that unites caring with discovery to make life better for people around the world. We were founded more than a century ago by a man committed to creating high-quality medicines that meet real needs, and today we remain true to that mission in all our work. Across the globe, Lilly employees work to discover and bring life-changing medicines to those who need them, improve the understanding and management of disease, and give back to communities through philanthropy and volunteerism. To learn more about Lilly, please visit us at

www.lilly.com and www.lilly.com/newsroom/social-channels. P-LLY

This press release contains forward-looking statements (as that term is defined in the Private Securities Litigation Reform Act of 1995) about Ultra Rapid Lispro as a treatment of type 1 and type 2 diabetes, and Lilly's current beliefs. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of development and commercialization. Among other things, there can be no guarantee that future study results will be consistent with study findings to date, that Ultra Rapid Lispro will receive regulatory approvals or that Ultra Rapid Lispro will prove to be commercially successful. For further discussion of these and other risks and uncertainties, see Lilly's most recent 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.

©LillyUSA, LLC 2018. All rights reserved.

Refer to: DeShong Perry-Smitherman; perry_smitherman_deshong@lilly.com; 317-719-4612 (media)
Greg Kueterman; kueterman_gregory_andrew@lilly.com; 317-432-5195 (media)
Kevin Hern; hern_kevin_r@lilly.com; 317-277-1838 (investors)

References

1. Centers for Disease Control and Prevention. National Diabetes Statistics Report, 2017. Atlanta, GA: Centers for Disease Control and Prevention, U.S. Dept of Health and Human Services; 2017.
2. International Diabetes Federation. *IDF Diabetes Atlas*, 8th edn. Brussels, Belgium: International Diabetes Federation, 2017. <http://www.diabetesatlas.org>.

The Lilly logo is rendered in a vibrant red, cursive script font. 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 traditional, handwritten-style brand mark.

 View original content to download multimedia: <http://www.prnewswire.com/news-releases/results-from-two-phase-3-studies-show-lillys-ultra-rapid-lispro-urli-met-primary-efficacy-endpoint-in-people-with-type-1-and-type-2-diabetes-300722380.html>

SOURCE Eli Lilly and Company