Lilly's phase 2 results published in the New England Journal of Medicine show orforglipron, a once-daily oral nonpeptide GLP-1 receptor agonist, achieved up to 14.7% mean weight reduction at 36 weeks in adults with obesity or overweight

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In additional phase 2 data, published in The Lancet, orforglipron achieved mean reduction in A1C up to 2.1% at 26 weeks in adults with type 2 diabetes

Lilly is investigating orforglipron, its first nonpeptide oral GLP-1 receptor agonist, for chronic weight management in the ATTAIN phase 3 clinical program and for type 2 diabetes in the ACHIEVE phase 3 clinical program

INDIANAPOLIS, June 23, 2023 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) announced today new phase 2 data for orforglipron, its first nonpeptide oral glucagon-like peptide-1 (GLP-1) receptor agonist being studied for chronic weight management in participants with obesity or overweight[i]. The results were shared during an oral presentation at the American Diabetes Association's® 83rd Scientific Sessions and were simultaneously published in the *New England Journal of Medicine*. Orforglipron met both primary and secondary endpoints for the efficacy estimand[ii] and demonstrated clinically significant weight reductions in adults with obesity or overweight, with at least one weight-related comorbidity (not including type 2 diabetes).

At the 26-week primary endpoint, orforglipron (12 mg, 24 mg, 36 mg or 45 mg) showed statistically significant dose-dependent body weight reductions for all doses ranging from 8.6% (19.8 lb. or 9.0 kg) to 12.6% (29.3 lb. or 13.3 kg) compared to 2.0% (4.6 lb. or 2.1 kg) for placebo. For those taking orforglipron, body weight continued to decrease at 36 weeks where all doses achieved body weight reductions ranging from 9.4% (21.6 lb. or 9.8 kg) to 14.7% (34.0 lb. or 15.4 kg) compared to 2.3% (5.3 lb. or 2.4 kg) for placebo. The mean baseline body weight of participants was 240 lb. (109 kg).

The safety profile of orforglipron was similar to other incretin-based therapies. Gastrointestinal side effects were the most commonly reported adverse events, were generally mild-to-moderate in severity, and usually occurred during the dose escalation period.

"We recognize that obesity is a global epidemic and there is a need for a variety of effective medications and administration routes," said Dr. Sean Wharton, Director at Wharton Medical Clinic. "We are working to address these needs by researching different options, including a daily oral pill called orforglipron. In a phase 2 study, orforglipron demonstrated an average of up to 14.7% weight reduction. These exciting results indicate that orforglipron may be an effective, once-daily oral that can be taken without food or water restrictions."

All four tested doses of orforglipron achieved all key secondary endpoints at 36 weeks of treatment for the efficacy estimand, including participants achieving:

- Body weight reductions of ≥5%: 72% (12 mg), 90% (24 mg), 92% (36 mg) and 90% (45 mg) compared to 24% with placebo
- Body weight reductions of ≥10%: 47% (12 mg), 62% (24 mg), 75% (36 mg) and 69% (45 mg) compared to 9% with placebo
- BMI reduction from baseline: 3.4 kg/m2 (12 mg), 4.7 kg/m2 (24 mg), 5.0 kg/m2 (36 mg) and 5.5 kg/m2 (45 mg) compared to 0.9 kg/m2 with placebo
- Waist circumference reduction from baseline: 9.6 cm (12 mg), 11.2 cm (24 mg), 10.6 cm (36 mg) and 13.6 cm (45 mg) compared to 4 cm with placebo

An additional phase 2 study evaluated orforglipron for the treatment of type 2 diabetes compared to placebo and dulaglutide. Data were presented at the American Diabetes Association's 83rd Scientific Sessions and simultaneously published in *The Lancet*. The study met its primary and secondary endpoints, demonstrating orforglipron achieved meaningful reductions in A1C and body weight at 26 weeks with an adverse events profile consistent with other GLP-1 receptor agonists. In that study, for the efficacy estimand, mean reduction in A1C (from a mean baseline of 8.1%) with orforglipron at 26 weeks was up to 2.1% compared to 0.4% with placebo and 1.1% with dulaglutide. Orforglipron (3 mg, 12 mg, 24 mg, 36 mg or 45 mg) also demonstrated weight reductions up to 10.1 kg (or 22.3 lb.) in adults with type 2 diabetes (from a mean baseline of 100.3 kg or 221.1 lb.) compared to 2.2 kg (or 4.9 lb.) with placebo and 3.9 kg (or 8.6 lb.) for dulaglutide. With orforglipron, 65% to 96% of participants achieved an A1C of less than 7.0% at 26 weeks versus 64% in the dulaglutide group and 24% in the placebo group. An A1C of less than 5.7% was demonstrated with orforglipron doses greater than 3 mg in 18% to 34% of participants.

"People living with chronic diseases such as type 2 diabetes and obesity deserve options – including oral treatments – to meet their treatment needs. In two phase 2 studies, orforglipron demonstrated the ability to lower weight and A1C in both patient populations," said Jeff Emmick, MD, Ph.D., senior vice president, product development, Lilly. "These study results support the continued development of orforglipron in phase 3. We look forward to those results and the continued development of our pipeline assets that explore novel treatments for type 2 diabetes and obesity."

Lilly has initiated phase 3 development programs to further study the efficacy and safety of orforglipron for the treatment of obesity and overweight (ATTAIN trials) and type 2 diabetes (ACHIEVE trials).

About The Obesity Study (NCT05051579)

The phase 2 study was a 36-week, multicenter, randomized, double-blind, parallel, placebo-controlled study evaluating the efficacy and safety of orforglipron (12 mg, 24 mg, 36 mg or 45 mg) compared to placebo in people with obesity or overweight with at least one weight-related comorbidity, not including type 2 diabetes. Orforglipron or placebo was administered daily by an oral capsule in the morning without food or water restrictions. All participants were provided healthy eating and exercise education by study personnel throughout the trial.

The primary endpoint was percent change in weight from baseline at 26 weeks, and secondary endpoints included change from baseline at 36 weeks in weight, waist circumference and BMI, and participants achieving weight reductions of ≥5% and ≥10%.

About The Type 2 Diabetes Study (NCT05048719)
The phase 2 study was a 26-week, double-blind, randomised, multicenter study evaluating the efficacy and safety of orforglipron (3 mg, 12 mg, 24 mg, 36 mg or 45 mg) compared to placebo and dulaglutide in adults with type 2 diabetes.

The primary endpoint was mean change in A1C from baseline with orforglipron compared to placebo at 26 weeks.

About Lilly

Lilly unites caring with discovery to create medicines that 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/newsroom or follow us on Facebook, Instagram, Twitter and LinkedIn. P-LLY

Orforglipron was discovered by Chugai Pharmaceutical Co., Ltd. and licensed to Lilly in 2018. Chugai and Lilly published the preclinical pharmacology data of this molecule together (PNAS 2020).

Trulicity (dulaglutide) Indications

Trulicity® (Trū-li-si-tee) is for adults and children 10 years of age and older with type 2 diabetes used along with diet and exercise to improve blood sugar (glucose). Trulicity is also used in adults with type 2 diabetes to reduce the risk of major cardiovascular events (problems having to do with the heart and blood vessels) such as death, heart attack, or stroke in people who have heart disease or multiple cardiovascular risk factors.

- It is not known if TRULICITY can be used in people who have had inflammation of the pancreas (pancreatitis). TRULICITY is not for use in people with type 1 diabetes and is not recommended for use in people with severe stomach or intestinal problems. It is not known if TRULICITY is safe and effective in children under 10 years of age.
- Trulicity is given through an injection (needle). You take it once a week by injecting it under the skin of your stomach, thigh, or upper arm.

Safety Summary with Warnings

Warnings:
Trulicity may cause tumors in the thyroid, including thyroid cancer. Watch for possible symptoms, such as a lump or swelling in the neck, trouble swallowing, hoarseness, or shortness of breath. If you have any of these symptoms, tell your healthcare provider.

- Do not use Trulicity if you or any of your family have ever had a type of thyroid cancer called medullary thyroid carcinoma (MTC).
- Do not use Trulicity if you have Multiple Endocrine Neoplasia syndrome type 2 (MEN 2).
- Do not use Trulicity if you are allergic to dulaglutide or other ingredients in Trulicity.

Ask your healthcare provider how to recognize possible serious side effects and what to do:

Inflamed pancreas (pancreatitis). Stop using Trulicity and call your healthcare provider right away if you have severe pain in your stomach area (abdomen), with or without vomiting, that will not go away. You may feel the pain from your abdomen to your back.
Low blood sugar (hypoglycemia). Your risk for getting low blood sugar may be higher if you use TRULICITY with another medicine that can cause low blood sugar, such as a sulfonylurea or insulin.

Signs and symptoms of low blood sugar may include dizziness or light-headedness, confusion or drowsiness, headache, blurred vision, slurred speech, fast heartbeat, sweating, hunger, shakiness, feeling jittery, weakness, anxiety, irritability, or mood changes.

Serious allergic reactions. Stop using Trulicity and get medical help right away if you have any symptoms of a serious allergic reaction which may include swelling of your face, lips, tongue or throat, problems breathing or swallowing, severe rash or itching, fainting, or feeling dizzy, or very rapid heartbeat.

Acute kidney injury. In people who have kidney problems, diarrhea, nausea, and vomiting may cause a loss of fluids (dehydration). This may cause kidney problems to get worse.

Severe stomach problems. Trulicity may cause stomach problems, which could be severe.
Changes in vision. Tell your healthcare provider if you have changes in your eyesight (vision) during treatment with Trulicity.

Gallbladder problems. Gallbladder problems have happened in some people who take Trulicity. Tell your healthcare provider right away if you get symptoms of gallbladder problems, which may include pain in your upper stomach (abdomen), fever, yellowing of skin or eyes (jaundice), clay-colored stools.

Common side effects

The most common side effects of Trulicity include nausea, diarrhea, vomiting, abdominal pain and decreased appetite, indigestion, and fatigue.

These are not all the possible side effects of Trulicity.

Tell your healthcare provider if you have any side effects. **You can report side effects at 1-800-FDA-1088 or** www.fda.gov/medwatch.

Before using

- **Your healthcare provider should show you how to use Trulicity before you use it for the first time.**
- **Before you use Trulicity, talk to your healthcare provider about low blood sugar and how to manage it.**

Review these questions with your healthcare provider:

- Do you have other medical conditions, including problems with your pancreas, kidneys, liver, or stomach, or have a history of diabetic retinopathy (vision problems related to diabetes)?
- Do you take other diabetes medicines, such as insulin or sulfonylureas?
- Are you pregnant or plan to become pregnant or breastfeeding or plan to breastfeed?
- Do you take any other prescription medicines or over-the-counter drugs, vitamins, or herbal supplements?

How to take

- Read the Instructions for Use that come with Trulicity.
- Use Trulicity exactly as your healthcare provider says.
- Do not share your Trulicity pen, syringe, or needles with another person.
- Do not give Trulicity to other people.
- If you take too much Trulicity, call your healthcare provider or seek medical advice promptly.

Learn more

Trulicity is a prescription medicine. For more information, call 1-844-TRU-INFO (1-844-878-4636) or go to www.TRULICITY.com.

This summary provides basic information about Trulicity but does not include all information known about this medicine. Read the information that comes with your prescription each time your prescription is filled. This information does not take the place of talking with your healthcare provider. Be sure to talk to your healthcare provider about Trulicity and how to take it. Your healthcare provider is the best person to help you decide if Trulicity is right for you.

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[i] For the obesity study (NCT05051579), trial participants needed to have a Body Mass Index (BMI) of ≥27 kg/m2 to be classified as overweight.

[ii] The efficacy estimand is the primary estimand which evaluates the treatment effect of all randomized eligible participants while adhering to treatment.

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 orforglipron as a potential treatment for people with obesity or overweight and the timeline for future readouts, presentations, and other milestones relating to orforglipron 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 orforglipron will prove to be a safe and effective treatment for obesity, that orforglipron 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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