CHMP Issues Positive Opinion to Expand Trulicity® (dulaglutide) Label to Include Results from REWIND Cardiovascular Outcomes Trial

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INDIANAPOLIS, Sept. 20, 2019 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) announced today that the European Medicines Agency'sCommittee for Medicinal Products for Human Use (CHMP) issued a positive opinion recommending an update to the Trulicity® (dulaglutide) label and indication statement. The committee agreed the label should include results from the REWIND cardiovascular (CV) outcomes trial, which achieved a significant 12 percent risk reduction in major adverse cardiovascular events (MACE).

The CHMP has recommended updating the Trulicity® indication to reflect both glycemic control and the impact on cardiovascular events as fundamental considerations in a treatment for people with type 2 diabetes. Additionally, the updated label will reflect the consistent MACE risk reduction with Trulicity across major demographic and disease subgroups.

"Millions of people with diabetes are at a higher risk for developing cardiovascular disease. The REWIND trial found that Trulicity significantly reduced major cardiovascular events and had a consistent effect in people with and without established cardiovascular disease," said Dawn Brooks, Ph.D., global development leader, Trulicity, Lilly. "We are pleased with this opinion recognizing the importance of these data, which demonstrate the benefits of Trulicity in a broad range of people with type 2 diabetes."

REWIND is the longest CV outcomes trial in the glucagon-like peptide-1 receptor agonist (GLP-1 RA) class (median follow-up of 5.4 years) and consisted primarily of people without established CV disease. The study had a more balanced ratio of women (46.3 percent) to men (53.7 percent) and one of the lowest median baseline A1Cs of any diabetes CV outcome trial to date (7.2 percent).

This decision is now referred for final action to the European Commission, which grants approval in the European Union.

About the REWIND Study
REWIND (Researching cardiovascular Events with a Weekly INcretin in Diabetes) was a multicenter, randomized, double-blind, placebo-controlled trial designed to assess the effect of Trulicity 1.5 mg, a weekly GLP-1 RA, compared to placebo, both added to standard of care (according to local standard of care guidelines), on CV events in adults with type 2 diabetes. The primary endpoint was the first occurrence of MACE (the composite of CV death or non-fatal myocardial infarction or non-fatal stroke). Secondary endpoints included each component of the primary composite endpoint, a composite clinical microvascular endpoint comprising retinal or renal disease, hospitalization for unstable angina, heart failure requiring hospitalization or an urgent heart failure visit, and all-cause mortality. The 9,901 participants from 24 countries had a mean duration of diabetes of 10.5 years and a median baseline HbA1c of 7.2 percent. While all participants had CV risk factors, only 31 percent of the study participants had established CV disease. Prior (or established) CV disease in REWIND was defined as prior myocardial infarction, prior ischemic stroke, prior unstable angina, prior revascularization (coronary, carotid, or peripheral), prior hospitalization for ischemia-related events (unstable angina or myocardial ischemia on imaging, or need for percutaneous coronary intervention), or prior documented myocardial ischemia.

The REWIND trial's international scope, high proportion of women, high proportion of people without established CV disease and inclusion of participants with a lower mean baseline HbA1c suggest that the findings will be directly relevant to the typical patient with type 2 diabetes seen in general practice throughout the world.

Indication and Limitations of Use for Trulicity
Trulicity is a once-weekly injectable prescription medicine to improve blood sugar (glucose) in adults with type 2 diabetes (mellitus). It should be used along with diet and exercise.

Trulicity is not recommended as the first medication to treat diabetes. It has not been studied in people who have had inflammation of the pancreas (pancreatitis). Trulicity should not be used by people with type 1 diabetes, people with diabetic ketoacidosis, or people with a history of severe gastrointestinal (GI) disease. It is not a substitute for insulin. It has not been studied in children under 18 years of age.

Important Safety Information for Trulicity®
Patients should tell their healthcare provider if they get a lump or swelling in their neck, have hoarseness, trouble swallowing, or shortness of breath while taking Trulicity. These may be symptoms of thyroid cancer. In studies with rats or mice, Trulicity and medicines that work like Trulicity caused thyroid tumors, including thyroid cancer. It is not known if Trulicity will cause thyroid tumors or a type of thyroid cancer called medullary thyroid carcinoma (MTC) in people. Patients should not take Trulicity if they or any of their family members have ever had MTC or if they have Multiple Endocrine Neoplasia syndrome type 2 (MEN 2).

Patients should not take Trulicity if they have had an allergic reaction to dulaglutide or any of the other ingredients in Trulicity.

Trulicity should not be used in children under 18 years of age.

Trulicity may cause serious side effects, including:

- **Inflammation of the pancreas (pancreatitis).** If a patient has pain in their stomach area (abdomen) that is severe and will not go away, they should stop taking Trulicity and call their healthcare provider right away. The pain may happen with or without vomiting. It may be felt going from the abdomen through to the back.

- **Low blood sugar (hypoglycemia).** If patients are using another medicine that can cause low blood sugar (such as insulin or a sulfonylurea) while taking Trulicity, their risk for getting low blood sugar (hypoglycemia) may be higher. Signs and symptoms of low blood sugar may include dizziness, blurred vision, anxiety, irritability, mood changes, sweating, slurred speech, hunger, confusion or drowsiness, shakiness, weakness, headache, fast heartbeat, or feeling jittery. Patients should talk to their healthcare provider about low blood sugar and how to manage it.

- **Serious allergic reactions**. Patients should stop taking Trulicity and get medical help right away if they have symptoms of a serious allergic reaction including: swelling of the 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.

Patients should tell their healthcare provider if they:

- *have or have had problems with their pancreas, kidneys, or liver.*
- *have severe problems with their stomach, such as slowed emptying of the stomach (gastroparesis) or problems with digesting food.*
- *have any other medical conditions.*
- *are pregnant or plan to become pregnant, or if they become pregnant while taking Trulicity. It is not known if Trulicity will harm their unborn baby.*
- *are breastfeeding or plan to breastfeed. It is not known if Trulicity passes into breast milk. Patients should not use Trulicity while breastfeeding without first talking to their healthcare provider.*
- *are taking other medicines including prescription and over-the-counter medicines, vitamins, and herbal supplements. Trulicity may affect the way some medicines work and some medicines may affect the way Trulicity works.*
- *are taking other medicines to treat diabetes, including insulin or sulfonylureas.*

If patients take too much Trulicity, they should call their healthcare provider or go to the nearest emergency room right away.

The most common side effects with Trulicity may include: *nausea, diarrhea, vomiting, abdominal pain and decreased appetite. Patients should talk to their healthcare provider about any side effect that bothers them or does not go away. These are not all the possible side effects of Trulicity. Patients should call their doctor for medical advice about side effects.*

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

Please click to access Prescribing Information, including Boxed Warning about possible thyroid tumors including thyroid cancer, and Medication Guide.

Please see Instructions for Use included with the pen.

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About Diabetes

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

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 and collaboration, a broad and growing product portfolio and a continued determination to provide real solutions—from medicines to support programs and more—we strive to make life better for all those affected by diabetes around the world. For more information, visit www.lillydiabetes.com or follow us on Twitter: @LillyDiabetes.

About Eli Lilly and Company

Lilly is a global healthcare leader that unites caring with discovery to create medicines that 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 http://newsroom.lilly.com/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 Trulicity (dulaglutide) as a treatment for type 2 diabetes and the reduction of cardiovascular events and reflects Lilly's current belief. 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 the results to date, that Trulicity will receive additional regulatory approvals or that

Trulicity will continue 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.

1. International Diabetes Federation. *IDF Diabetes Atlas*, 8th edn. Brussels, Belgium: International Diabetes Federation, 2017. http://www.diabetesatlas.org.
2. 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.

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View original content to download multimedia:http://www.prnewswire.com/news-releases/chmp-issues-positive-opinion-to-expand-trulicity-dulaglutide-label-to-include-results-from-rewind-cardiovascular-outcomes-trial-300922307.html

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