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Jardiance® (empagliflozin) tablets to be studied in chronic kidney disease

- **New outcome study to evaluate the effect of JARDIANCE for the treatment of people with chronic kidney disease**
- **Approximately 15 percent of adults in the U.S. are affected by chronic kidney disease**
- **The study is based on cardiovascular and renal insights from the landmark EMPA-REG OUTCOME® trial**

RIDGEFIELD, Conn. and INDIANAPOLIS, June 12, 2017 /PRNewswire/ -- Boehringer Ingelheim and Eli Lilly and Company (NYSE: LLY) today announced plans to conduct a new, large clinical outcomes trial investigating Jardiance® (empagliflozin) tablets for the treatment of people with chronic kidney disease. The trial will enroll people with chronic kidney disease both with and without type 2 diabetes.

"Our plans for this new trial are yet another example of our ongoing commitment to improving patient health, especially in areas where unmet needs exist," said Prof. Hans-Juergen Woerle, global vice president medicine, Boehringer Ingelheim. "We look forward to exploring the potential that empagliflozin may offer for people with chronic kidney disease."

JARDIANCE is the first and only type 2 diabetes medicine approved to reduce the risk of cardiovascular death in patients with type 2 diabetes and established cardiovascular disease. The landmark EMPA-REG OUTCOME® trial demonstrated that JARDIANCE reduced the risk of cardiovascular death by 38 percent versus placebo in people with type 2 diabetes and established cardiovascular disease when added to standard of care (including glucose-lowering agents and cardiovascular drugs). As one of the secondary endpoints, the trial also showed that JARDIANCE reduced the risk for new-onset or worsening of kidney disease by 39 percent versus placebo when added to standard of care in adults with type 2 diabetes and established cardiovascular disease. Based on these results, BI and Lilly decided to formally investigate the potential of JARDIANCE in people with chronic kidney disease. This and other ongoing mechanistic studies will allow the companies to further explore the potential mechanisms - including the reduction in glomerular pressure - by which empagliflozin may impact renal outcomes in those with chronic kidney disease.

"Based on the cardiovascular and renal results of the EMPA-REG OUTCOME trial, we, along with Boehringer Ingelheim, look forward to starting this new trial to gather evidence in support of a potential new indication for empagliflozin in people with chronic kidney disease," said Jeff Emmick, M.D., Ph.D., vice president, Product Development, Lilly Diabetes.

About Chronic Kidney Disease

Chronic kidney disease is defined as a progressive decline of kidney function over time. About two thirds of chronic kidney disease cases are attributable to metabolic diseases such as diabetes, hypertension and obesity. Notably, chronic kidney disease is associated with increased morbidity and mortality. The majority of deaths among people with chronic kidney disease occur as a result of cardiovascular complications, often before reaching end stage renal disease. Chronic kidney disease affects approximately 15 percent of adults in the U.S. and treatment costs are estimated to exceed \$48 billion annually. Since there are currently only few treatment options, the overarching unmet medical need for new treatment options in chronic kidney disease is evident.

About the EMPA-REG OUTCOME Trial (NCT01131676)

EMPA-REG OUTCOME was a long-term, multicenter, randomized, double-blind, placebo-controlled trial of more than 7,000 patients from 42 countries with type 2 diabetes and established cardiovascular disease.

The study assessed the effect of JARDIANCE (10 mg or 25 mg once daily) added to standard of care compared with placebo added to standard of care. Standard of care was comprised of glucose-lowering agents and cardiovascular drugs (including for blood pressure and cholesterol). The primary endpoint was defined as time to first occurrence of cardiovascular death, non-fatal heart attack or non-fatal stroke.

Although the EMPA-REG OUTCOME trial was not designed to assess the potential mechanisms behind the effect of empagliflozin on kidney outcomes, the kidney assessment was part of a pre-specified exploratory analysis plan of additional endpoints.

The overall safety profile of JARDIANCE was consistent with that of previous trials.

What is JARDIANCE? (www.jardiance.com)

JARDIANCE is a prescription medicine used along with diet and exercise to lower blood sugar in adults with type 2 diabetes.

JARDIANCE is also used to reduce the risk of cardiovascular death in adults with type 2 diabetes who have known cardiovascular disease.

JARDIANCE is not for people with type 1 diabetes or for people with diabetic ketoacidosis (increased ketones in the blood or urine).

IMPORTANT SAFETY INFORMATION

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

JARDIANCE can cause serious side effects, including:

- | **Dehydration.** JARDIANCE can cause some people to have dehydration (the loss of body water and salt). Dehydration may cause you to feel dizzy, faint, light-headed, or weak, especially when you stand up.

You may be at a higher risk of dehydration if you:

- | have low blood pressure
- | take medicines to lower your blood pressure including water pills (diuretics)
- | are on a low salt diet
- | have kidney problems
- | are 65 years of age or older.

- | **Ketoacidosis (increased ketones in your blood or urine).** Ketoacidosis is a serious condition and may need to be treated in the hospital. Ketoacidosis may lead to death. Ketoacidosis occurs in people with type 1 diabetes and can also occur in people with type 2 diabetes taking JARDIANCE, even if blood sugar is less than 250 mg/dL. **Stop taking JARDIANCE and call your doctor right away if you get any of the following symptoms**, and if possible, check for ketones in your urine:

- | nausea
- | vomiting
- | stomach-area (abdominal) pain
- | tiredness
- | trouble breathing

- | **Serious urinary tract infections.** Serious urinary tract infections can occur in people taking JARDIANCE and may lead to hospitalization. Tell your doctor if you have symptoms of a urinary tract infection such as a burning feeling when passing urine, a need to urinate often or right away, pain in the lower part of your stomach or pelvis, or blood in the urine. Sometimes people also may have a fever, back pain, nausea or vomiting.
- | **Vaginal yeast infection.** Women who take JARDIANCE may get vaginal yeast infections. Talk to your doctor if you experience vaginal odor, white or yellowish vaginal discharge (discharge may be lumpy or look like cottage cheese), and/or vaginal itching.
- | **Yeast infection of the penis.** Men who take JARDIANCE may get a yeast infection of the skin around the penis, especially uncircumcised males and those with chronic infections. Talk to your doctor if you experience redness, itching or swelling of the penis, rash of the penis, foul smelling discharge from the penis, and /or pain in the skin around penis.

Who should not take JARDIANCE?

Do not take JARDIANCE if you are allergic to empagliflozin or any of the ingredients in JARDIANCE. Symptoms of serious allergic reactions to JARDIANCE may include:

- | skin rash
- | raised red patches on your skin (hives)
- | swelling of the face, lips, tongue, and throat that may cause difficulty breathing or swallowing.

If you have any of these symptoms, stop taking JARDIANCE and contact your doctor or go to the nearest emergency room right away.

Do not take JARDIANCE if you have severe kidney problems or are on dialysis.

What should I tell my doctor before using JARDIANCE?

Tell your doctor if you:

- | have kidney problems. Your doctor may do blood tests to check your kidneys before and during your treatment with JARDIANCE
- | have liver problems
- | have a history of urinary tract infections or problems with urination
- | are going to have surgery
- | are eating less due to illness, surgery, or a change in your diet
- | have or have had problems with your pancreas, including pancreatitis or surgery on your pancreas
- | drink alcohol very often, or drink a lot of alcohol in the short term ("binge" drinking)
- | have any other medical conditions
- | are pregnant or planning to become pregnant. It is unknown if JARDIANCE will harm your unborn baby
- | are breastfeeding, or plan to breastfeed. It is unknown if JARDIANCE passes into your breast milk.

Tell your doctor about all the medicines you take including prescription and over-the-counter medicines, vitamins, and herbal supplements. Especially tell your doctor if you take water pills (diuretics) or medicines that can lower your blood sugar such as insulin.

What are other possible side effects of JARDIANCE?

- | **Low blood sugar** (hypoglycemia): if you take JARDIANCE with another medicine that can cause low blood sugar, such as sulfonylurea or insulin, your risk of low blood sugar is higher. The dose of your sulfonylurea or insulin may need to be lowered. Symptoms of low blood sugar may include:
 - | Headache
 - | Drowsiness
 - | Weakness
 - | Dizziness
 - | Confusion
 - | Irritability
 - | Hunger
 - | Fast heartbeat
 - | Sweating
 - | Shaking or feeling jittery
- | **Kidney Problems.** Sudden kidney injury has happened in people taking JARDIANCE. Talk to your doctor right away if you reduce the amount you eat or drink, or if you lose liquids; for example, from vomiting, diarrhea, or being in the sun too long.
- | **Increased fats in your blood (cholesterol).**

The most common side effects of JARDIANCE include urinary tract infections, and yeast infections in females.

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.

For more information, please see [full Prescribing Information](#) and [Patient Information](#).

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Boehringer Ingelheim and Eli Lilly and Company

In January 2011, Boehringer Ingelheim and Eli Lilly and Company announced an alliance in diabetes that centers on compounds representing several of the largest diabetes treatment classes. This alliance leverages the strengths of two of the world's leading pharmaceutical companies. By joining forces, the companies demonstrate commitment in the care of patients with diabetes and stand together to focus on patient needs. Find out more about the alliance at www.boehringer-ingelheim.com or www.lilly.com.

About Boehringer Ingelheim

Boehringer Ingelheim Pharmaceuticals, Inc., based in Ridgefield, CT, is the largest U.S. subsidiary of Boehringer Ingelheim Corporation.

Boehringer Ingelheim is one of the world's top 20 pharmaceutical companies. Headquartered in Ingelheim, Germany, the company operates globally with approximately 50,000 employees. Since its founding in 1885, the company has remained family-owned and today creates value through innovation for three business areas including human pharmaceuticals, animal health and biopharmaceutical contract manufacturing.

Boehringer Ingelheim is committed to improving lives and providing valuable services and support to patients and their families. Our employees create and engage in programs that strengthen our communities. Please visit our [website](#) to learn more about how we make more health for more people through our Corporate Social Responsibility initiatives.

In 2016, Boehringer Ingelheim achieved net sales of about \$17.6 billion (15.9 billion euros). R&D expenditure corresponds to 19.6 percent of its net sales.

For more information please visit www.boehringer-ingelheim.us, or follow us on Twitter @BoehringerUS.

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 wide range of therapies 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.

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.

This press release contains forward-looking statements (as that term is defined in the Private Securities Litigation Reform Act of 1995) about empagliflozin as a potential treatment of people with chronic kidney disease, 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 or that empagliflozin will receive additional regulatory approvals. 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.

Jardiance[®] and EMPA-REG OUTCOME[®] are registered trademarks of Boehringer Ingelheim.

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To view the original version on PR Newswire, visit:<http://www.prnewswire.com/news-releases/jardiance-empagliflozin-tablets-to-be-studied-in-chronic-kidney-disease-300471971.html>

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