US FDA grants Fast Track designation to Jardiance® for the treatment of chronic kidney disease

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-- FDA Fast Track designation is for the investigation of potential new therapies that treat serious conditions and fulfill an unmet medical need

RIDGEFIELD, Conn. and INDIANAPOLIS, March 12, 2020 /PRNewswire/ -- The U.S. Food and Drug Administration (FDA) has granted Fast Track designation for the investigation of Jardiance® (empagliflozin) to reduce the risk of kidney disease progression and cardiovascular death in adults with chronic kidney disease, Boehringer Ingelheim and Eli Lilly and Company (NYSE: LLY) announced. This Fast Track designation for Jardiance underscores the urgent need for additional treatment options for the over 30 million Americans living with chronic kidney disease, many of whom are at risk of progressing to end-stage kidney disease.

"Chronic kidney disease can have a devastating impact on people's lives. Not only does it cause damage to the kidneys that can eventually lead to the need for dialysis or transplant, but it could also increase the risk of cardiovascular death," said Mohamed Eid, M.D., M.P.H., M.H.A, vice president, Clinical Development & Medical Affairs, Boehringer Ingelheim Pharmaceuticals, Inc. "Chronic kidney disease is a common and deadly condition, and there are still only limited treatment options, which is what motivates us to explore the potential role Jardiance may play in improving outcomes."

Chronic kidney disease is associated with an increased risk of premature death from cardiovascular causes and is the ninth leading cause of death in the U.S. About two-thirds of cases are attributed to metabolic conditions such as diabetes (known as diabetic kidney disease), hypertension and obesity.

"We recognize the close link between the health of the heart, kidneys and metabolic system, and we have committed to a broad clinical development program assessing the cardiorenal metabolic benefits of Jardiance," said Jeff Emmick, M.D., Ph.D., vice president, Product Development, Lilly. "The Fast Track designation from the FDA is an important step in evaluating the potential of Jardiance to enhance care for those with chronic kidney disease."

The ongoing EMPA-KIDNEY clinical study is evaluating the effect of Jardiance on the progression of kidney disease and the occurrence of cardiovascular death in adults with established chronic kidney disease with and without diabetes. The EMPA-KIDNEY study was initiated based on promising exploratory results from the landmark EMPA-REG OUTCOME® trial, which found that treatment with Jardiance reduced the risk of new-onset and worsening kidney disease by 39 percent in adults with type 2 diabetes and established cardiovascular disease compared with placebo.

EMPA-KIDNEY is being independently conducted, analyzed and reported by the Medical Research Council Population Health Research Unit at the University of Oxford (MRC PHRU), which is based in the Clinical Trial Service Unit and Epidemiological Studies Unit (CTSU), in partnership with the Duke Clinical Research Institute. Boehringer Ingelheim and Lilly are providing the funding for the study.

Jardiance is a once-daily tablet used along with diet and exercise to lower blood sugar in adults with type 2 diabetes and to reduce the risk of cardiovascular death in adults with type 2 diabetes and 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).

In June 2019, the FDA granted Fast Track designation to the clinical investigation of Jardiance to reduce the risk of cardiovascular death and hospitalization for heart failure in people with chronic heart failure.

About EMPA-KIDNEY [NCT03594110]

EMPA-KIDNEY is a multinational randomized, double-blind, placebo-controlled clinical trial. It is designed to evaluate the effect of Jardiance on kidney disease progression and cardiovascular mortality risk. The primary outcome is defined as time to a first event of either cardiovascular death or kidney disease progression, defined as end-stage kidney disease (the need for kidney replacement therapy such as dialysis or kidney transplantation), a sustained decline in eGFR to <10 mL/min/1.73 m^2, renal death, or a sustained decline of ≥40% in eGFR from randomization. EMPA-KIDNEY includes adults with established chronic kidney disease both with and without diabetes.

The study is a global trial aiming to randomize about 6,000 participants to receive either Jardiance 10 mg once daily or placebo, each on top of standard of care.

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 (known as diabetic kidney disease), 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 United States and treatment costs are estimated to exceed $48 billion annually. Since there are currently only few treatment options, the overarching unmet medical need for additional treatment options in chronic kidney disease is evident.

About Cardiorenal Metabolic Conditions

Cardiorenal metabolic conditions are a group of interconnected disorders affecting the heart, kidneys and endocrine system. In aggregate, these

conditions are the leading cause of deaths worldwide, accounting for up to 20 million deaths annually. Conditions within this group include coronary artery disease, heart failure, chronic kidney disease and type 2 diabetes, among many others.

Emerging science on the link between the cardiorenal and metabolic systems supports taking a multidisciplinary approach toward diagnostic, preventive and therapeutic strategies for people living with these conditions. We remain committed to developing treatments with broad cardiorenal metabolic effects, which may help improve outcomes for people with serious chronic conditions such as these.

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

Do not take JARDIANCE if you are allergic to empagliflozin or any of the ingredients in JARDIANCE.

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

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.

- **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.

- **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. Ketoacidosis has also happened in people with diabetes who were sick or who had surgery during treatment with JARDIANCE. **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

- **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.

- **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.

- **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

- **Necrotizing fasciitis. A rare but serious bacterial infection that causes damage to the tissue under the skin in the area between and around your anus and genitals (perineum).** This bacterial infection has happened in women and men who take JARDIANCE, and may lead to hospitalization, multiple surgeries, and death. **Seek medical attention immediately if you have fever or are feeling very weak, tired or uncomfortable (malaise), and you develop any of the following symptoms in the area between and around your anus and genitals: pain or tenderness, swelling, and redness of skin (erythema).**

- **Allergic (hypersensitivity) reactions.** Symptoms of serious allergic reactions to JARDIANCE may include:
  - swelling of your face, lips, throat and other areas of your skin
  - difficulty with swallowing or breathing
  - raised, red areas on your skin (hives)

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

- **Increased fats in your blood (cholesterol).**

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

These are not all the possible side effects of JARDIANCE. For more information, ask your doctor or pharmacist.

Before taking 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. Your doctor may stop your JARDIANCE before you have surgery. Talk to your doctor if you are having surgery about when to stop taking JARDIANCE and when to start it again
- are eating less or there is 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 plan to become pregnant. JARDIANCE may harm your unborn baby. Tell your doctor right away if you become pregnant during treatment with JARDIANCE
- are breastfeeding or are planning to breastfeed. JARDIANCE may pass into your breast milk and may harm your baby. Do not breastfeed while taking JARDIANCE

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.

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 Prescribing Information and Medication Guide.

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Boehringer Ingelheim and Eli Lilly and Company
In January 2011, Boehringer Ingelheim and Eli Lilly and Company announced an alliance that centers on compounds representing several of the largest diabetes treatment classes. Depending on geographies, the companies either co-promote or separately promote the respective molecules each contributing to the alliance. The alliance leverages the strengths of two of the world's leading pharmaceutical companies to focus on patient needs. By joining forces, the companies demonstrate their commitment, not only to the care of people with diabetes, but also to investigating the potential to address areas of unmet medical need. Clinical trials have been initiated to evaluate the impact of Jardiance on people living with heart failure or chronic kidney disease.

About Boehringer Ingelheim Pharmaceuticals, Inc.
Boehringer Ingelheim Pharmaceuticals, Inc., based in Ridgefield, Conn., 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 our goal is to improve the lives

of humans and animals through its three business areas: human pharmaceuticals, animal health and biopharmaceutical contract manufacturing.

Boehringer Ingelheim concentrates on developing innovative therapies that can improve and extend patients' lives. As a research-driven pharmaceutical company, it plans in generations for long-term success. Its research efforts are focused on diseases with high, unmet medical need. In animal health, the company stands for advanced prevention.

In 2018, Boehringer Ingelheim achieved net sales of around $20.7 billion (17.5 billion euros). R&D expenditure of almost $3.7 billion (3.2 billion euros) corresponded to 18.1 percent of net sales.

Boehringer Ingelheim is committed to improving lives and strengthening our communities. Please visit www.boehringer-ingelheim.us/csr to learn more about Corporate Social Responsibility initiatives.

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

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 newsroom.lilly.com/social-channels.

This press release contains forward-looking statements (as that term is defined in the Private Securities Litigation Reform Act of 1995) about Jardiance and reflects Lilly's current belief. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of drug 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 Jardiance will receive additional regulatory approvals. For a further discussion of these and other risks and uncertainties that could cause actual results to differ from Lilly's expectations, please see Lilly's most recent Forms 10-K and 10-Q filed with the U.S. Securities and Exchange Commission. Lilly undertakes no duty to update forward-looking statements.

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