January 25, 2016

U.S. FDA Accepts Filing of Cardiovascular Outcomes Data for Jardiance® (empagliflozin)

RIDGEFIELD, Conn. and INDIANAPOLIS, Jan. 25, 2016 /PRNewswire/ -- The U.S. Food and Drug Administration (FDA) accepted a supplemental New Drug Application for Jardiance® (empagliflozin) based on cardiovascular risk reduction data from the landmark EMPA-REG OUTCOME® trial. Boehringer Ingelheim and Eli Lilly and Company (NYSE: LLY) expect to receive a decision from the FDA within the standard review time frame.

Cardiovascular complications can have a significant impact on the health and life expectancy of people with type 2 diabetes. Approximately 50 percent of deaths in people with type 2 diabetes worldwide are caused by cardiovascular disease.

"We're proud of this acceptance as we are now one step closer to helping address one of the most prevalent clinical needs of the type 2 diabetes community — reducing the risk of cardiovascular death," said Paul Fonteyne, president and CEO, Boehringer Ingelheim Pharmaceuticals, Inc. "We look forward to working with the FDA as it reviews the data from the EMPA-REG OUTCOME trial."

JARDIANCE was approved by the FDA in August 2014 as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes. JARDIANCE is not for people with type 1 diabetes or for people with diabetic ketoacidosis (increased ketones in the blood or urine).

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 (T2D) at high risk for cardiovascular (CV) events.

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 CV drugs (including for blood pressure and cholesterol). The primary endpoint was defined as time to first occurrence of CV death, non-fatal heart attack or non-fatal stroke.

Over a median of 3.1 years, JARDIANCE significantly reduced the risk of CV death, non-fatal heart attack or non-fatal stroke by 14 percent versus placebo. Risk of CV death was reduced by 38 percent, with no significant difference in the risk of non-fatal heart attack or non-fatal stroke. Treatment with JARDIANCE also resulted in a 32 percent reduction in all-cause mortality and a 35 percent reduction in hospitalization for heart failure. The overall safety profile of JARDIANCE was consistent with that of previous trials.

About Diabetes
Approximately 29 million Americans and an estimated 415 million people worldwide have type 1 or type 2 diabetes, and nearly 28 percent of Americans with diabetes—totaling 8 million people—are undiagnosed. In the U.S., approximately 12 percent of those aged 20 and older have diabetes. Type 2 diabetes is the most common type, accounting for an estimated 90 to 95 percent of all diagnosed adult diabetes cases in the U.S. Diabetes is a chronic condition that occurs when the body either does not properly produce, or use, the hormone insulin.

What is JARDIANCE?
JARDIANCE is a prescription medicine used along with diet and exercise to lower blood sugar in adults with type 2 diabetes. 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.** JARDIANCEÂ 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 can be life threatening and may need to be treated in the hospital. 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.Â **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:
  - nauseaÂ Â Â Â Â Â Â Â Â Â Â Â Â Â Â Â Â Â Â Â Â Â
  - 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.Â 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.Â 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 heart beat
    - Sweating
    - Shaking or feeling jittery

- **Kidney Problems,** especially in people 75 years of age or older and people who already have kidney problems

- **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, including 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 Pharmaceuticals, Inc.
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 20 leading pharmaceutical companies. Headquartered in Ingelheim, Germany, the company operates globally with 146 affiliates and more than 47,000 employees. Since its founding in 1885, the family-owned company has been committed to researching, developing, manufacturing and marketing novel treatments for human and veterinary medicine.

Boehringer Ingelheim is committed to improving lives and providing valuable services and support to patients and families.Â Our employees create and engage in programs that strengthen our communities. To learn more about how we make more health for more people, visit ourÂ Corporate Social Responsibility Report.

In 2014, Boehringer Ingelheim achieved net sales of about $16.96 billion dollars (13.3 billion euros). R&D expenditure corresponds to 19.9 percent of its net sales.

For more information please visitÂ www.us.boehringer-ingelheim.com, 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 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 @LillyDiabetes.

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. Â

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 treatment for patients with type 2 diabetes along with diet and exercise 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® is a registered trademark of Boehringer Ingelheim

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SOURCE Eli Lilly and Company; Boehringer Ingelheim