Initial results from EMPRISE real-world evidence study show Jardiance® was associated with reduced risk for hospitalization for heart failure compared with DPP-4 inhibitors in people with type 2 diabetes with and without cardiovascular disease

November 5, 2018

- Jardiance (empagliflozin) was associated with a 44 percent reduction in relative risk of hospitalization for heart failure (HHF) compared with commonly used dipeptidyl peptidase-4 inhibitors

- Effect of Jardiance on HHF was consistent in patients with and without established cardiovascular disease

- Findings support data from the landmark EMPA-REG OUTCOME® trial, in which Jardiance reduced the relative risk of HHF by 35 percent in people with type 2 diabetes and established cardiovascular disease

- These early findings from EMPRISE, which will assess the first five years of Jardiance use in the U.S. through 2019, represent data collected between August 2014 and September 2016

RIDGEFIELD, Conn. and INDIANAPOLIS, Nov. 5, 2018 /PRNewswire/ -- Initial results from the real-world EMPagliflozin compaRative effectIveness and SafEty (EMPRISE) study showed Jardiance® was associated with a 44 percent relative risk reduction in hospitalization for heart failure (HHF) compared with dipeptidyl peptidase-4 (DPP-4) inhibitors in routine clinical practice in the U.S. The EMPRISE analysis of data from approximately 35,000 people with type 2 diabetes between August 2014 and September 2016 will be presented at the American Heart Association® (AHA) Scientific Sessions 2018 in Chicago, Boehringer Ingelheim and Eli Lilly and Company (NYSE: LLY) announced.

These results support findings from the EMPA-REG OUTCOME® trial, which showed a 35 percent relative risk reduction in HHF (a secondary endpoint) with Jardiance compared with placebo, when added to standard of care, in people with type 2 diabetes and established cardiovascular disease.

"With more than a million hospital admissions for heart failure in the U.S. every year, it's important to understand whether the relative risk reduction in hospitalization for heart failure seen in the EMPA-REG OUTCOME trial translates into routine clinical care," said Elisabetta Patorno, M.D., DrPH, Division of Pharmacoepidemiology and Pharmacoeconomics, Brigham and Women's Hospital and assistant professor of medicine, Harvard Medical School, and study co-investigator. "These first results from the EMPRISE study show that empagliflozin is associated with a reduction in hospitalization for heart failure, and the effect is consistent in people with type 2 diabetes with and without history of cardiovascular disease."

The full EMPRISE real-world evidence study will provide a clinical picture of Jardiance in routine clinical care including comparative effectiveness, safety and healthcare resource utilization and cost outcomes compared with commonly used DPP-4 inhibitors between 2014 and 2019. Early findings from EMPRISE, which at completion will assess the first five years of Jardiance use in the U.S. through 2019, represent data collected between August 2014 and September 2016. The effectiveness findings will be updated as more data are gathered. Safety data from EMPRISE are not yet available and will be presented at a future time. EMPRISE was initiated, and is being led, by academic partners from the Division of Pharmacoepidemiology at Brigham and Women's Hospital and Harvard Medical School. The study is part of an academic collaboration between Brigham and Women's Hospital and Boehringer Ingelheim.

"Boehringer Ingelheim and Lilly are committed to helping to reduce the burden of cardiovascular disease in people with type 2 diabetes," said Thomas Seck, M.D., senior vice president, Medicine and Regulatory Affairs, Boehringer Ingelheim Pharmaceuticals, Inc. "These real-world analyses build upon the clinical findings from the landmark EMPA-REG OUTCOME trial that have paved the way for further research of Jardiance in heart failure, including our ongoing studies."

By study completion, EMPRISE is expected to have analyzed health records of more than 200,000 people with type 2 diabetes from two commercial U.S. healthcare providers and Medicare. Further results from EMPRISE will be presented in 2019.

"The Boehringer Ingelheim and Lilly Diabetes Alliance is committed to building a comprehensive clinical picture of Jardiance across the cardiovascular risk continuum in type 2 diabetes," stated Sherry Martin, M.D., vice president, Medical Affairs, Lilly Diabetes. "Physicians need better options to help their patients avoid hospitalization for heart failure, and we are encouraged that these findings from EMPRISE complement cardiovascular results from the EMPA-REG OUTCOME trial. We are committed to further understanding whether Jardiance may have potential in this area and look forward to sharing the future results of the EMPRISE study."

As part of their efforts to help address unmet needs, Boehringer Ingelheim and Lilly have initiated two large clinical trial programs focused on improving outcomes and reducing morbidity and mortality for people with heart failure. EMPEROR HF comprises two Phase III outcome trials investigating Jardiance for the treatment of adults with chronic heart failure. The trials include not only adults with type 2 diabetes who have heart failure, but also people with heart failure who do not have diabetes. EMPERIAL comprises two Phase III studies evaluating the effect of Jardiance on exercise ability and heart failure symptoms in people with chronic heart failure with or without type 2 diabetes.

About EMPRISE (NCT03363464)

EMPRISE was initiated in 2016 to complement the EMPA-REG OUTCOME trial results by providing data on the comparative effectiveness, safety,

healthcare resource utilization and costs in routine clinical care compared with DPP-4 inhibitors in people with type 2 diabetes with and without cardiovascular disease.

The study will assess the first five years of Jardiance use in the U.S. from 2014 to 2019. Over 200,000 people with type 2 diabetes from two commercial U.S. healthcare providers and Medicare are projected to be included by study completion.

The EMPRISE study was initiated, and is being led, by academic partners from the Division of Pharmacoepidemiology at Brigham and Women's Hospital and Harvard Medical School. The study is part of an academic collaboration between Brigham and Women's Hospital and Boehringer Ingelheim.

About EMPA-REG OUTCOME (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.

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

About Heart Failure
Heart failure is a progressive, debilitating and potentially fatal condition that occurs when the heart cannot pump enough blood around the body. Symptoms of heart failure include difficulty breathing, swelling – most commonly in feet, legs and ankles – and fatigue, among others. Heart failure is a prevalent disease; 26 million people around the world have chronic heart failure. There is a high unmet need in the treatment of heart failure, as approximately 50 percent of people diagnosed with heart failure will die within five years. Additionally, heart failure represents the most common cause of hospitalization among individuals aged 65 years and over in the United States and Europe. Heart failure is highly prevalent in people with diabetes, but approximately half of all people with heart failure do not have diabetes.

About Diabetes and Cardiovascular Disease
Approximately 30 million Americans and an estimated 425 million people worldwide have diabetes, and nearly 24 percent of Americans with diabetes—or more than 7 million people—are undiagnosed. In the U.S., approximately nine percent of those aged 18 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 does not properly produce or use the hormone insulin.

Due to the complications associated with diabetes, such as high blood sugar, high blood pressure and obesity, cardiovascular disease is a major complication and the leading cause of death associated with diabetes. People with diabetes are up to four times more likely to develop cardiovascular disease than people without diabetes. Approximately 50 percent of deaths in people with type 2 diabetes worldwide and approximately two-thirds of deaths in people with type 2 diabetes in the U.S. are caused by cardiovascular disease. In the U.S., healthcare costs for managing cardiovascular conditions in patients with diabetes totaled more than $23 billion in 2012.

Having a history of diabetes at age 60 can shorten a person's life span by as much as six years compared with someone without diabetes. And having both diabetes and a history of heart attack or stroke by age 60 can shorten a person's life span by as much as 12 years compared with someone without these conditions.

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. **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
- 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 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/medwatchor call 1-800-FDA-1088.

For more information, please see Prescribing Information and Medication Guide.

About 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. The alliance leverages the strengths of two of the world's leading pharmaceutical companies. By joining forces, the companies demonstrate commitment in the care of people 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, 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 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 www.boehringer-ingelheim.us/csr to learn more about how we make more health through our Corporate Social Responsibility initiatives.

In 2017, Boehringer Ingelheim achieved net sales of about $20.4 billion (18.1 billion euros). R&D expenditure corresponds to approximately $3.4 billion (three billion euros), or 17.0 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 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 (empagliflozin), 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 Jardiance 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.

P-LLY

MPR-US-100577

CONTACT:
Jennifer Forsyth
Director, Public Relations
Boehringer Ingelheim Pharmaceuticals, Inc.
Email: jennifer.forsyth@boehringer-ingelheim.com
Phone: (203) 791-5889

Greg Kueterman
Director of Communications
Lilly Diabetes and Lilly USA
Email: kueterman_gregory_andrew@lilly.com
Phone: (317) 432-5195

View original content to download multimedia:http://www.prnewswire.com/news-releases/initial-results-from-emprise-real-world-evidence-study-show-jardiance-was-associated-with-reduced-risk-for-hospitalization-for-heart-failure-compared-with-dpp-4-inhibitors-in-people-with-type-2-diabetes-with-and-without-cardiovas-300743329.html

SOURCE Eli Lilly and Company