Boehringer Ingelheim and Lilly initiate first ever study to assess Jardiance® in people hospitalized for acute heart failure who have been stabilized

November 12, 2019

- EMPULSE is a superiority study that will assess the clinical benefit, safety and tolerability of 10 mg daily Jardiance® (empagliflozin) in acute heart failure

RIDGEFIELD, Conn. and INDIANAPOLIS, Nov. 12, 2019 /PRNewswire/ -- Boehringer Ingelheim and Eli Lilly and Company (NYSE: LLY) today announced the initiation of EMPULSE, the sixth phase III study in the Jardiance® (empagliflozin) heart failure program. The study will assess whether in-hospital administration of Jardiance 10 mg daily improves heart failure outcomes when initiated in people hospitalized for any type of acute heart failure event once they have been stabilized. The study will include participants both with and without type 2 diabetes.

Heart failure contributes to one in nine deaths and is a leading cause of hospitalization in the U.S., yet there are limited treatment options for people living with this debilitating disease. Outcomes for patients after they have been hospitalized for heart failure are poor, with a 15 percent mortality and 30 percent readmission rate within 60 to 90 days of discharge from the hospital. Initiating treatment in the hospital is one of the best predictors of long-term improved prognosis and patient treatment adherence. The EMPULSE study aims to understand whether Jardiance has the potential to improve outcomes in this population.

"Acute decompensated heart failure is one of the fastest-growing diseases in the world and a leading cause of hospital admissions worldwide with high short term mortality and rehospitalization. Unlike chronic heart failure, there is no established therapy available that improves clinical outcomes in acute heart failure," said Adriaan Voors, Professor of Cardiology, University Medical Center Groningen, Netherlands. "The beneficial effects of SGLT2 inhibitors, as seen in three large randomized trials in type 2 diabetes patients, are thought to be at least partly explained by the diuretic/natriuretic effects of SGLT2 inhibitors. The EMPULSE study will investigate whether Jardiance, due to its mode of action, can alleviate symptoms associated with heart failure and improve outcomes after discharge from the hospital."

The primary outcome of the study will be net clinical benefit, a composite of all-cause mortality, number of heart failure events (including hospitalizations, urgent heart failure visits and unplanned patient visits), time to first heart failure event and change from baseline in Kansas City Cardiomyopathy Questionnaire – Clinical Summary Score (KCCQ-CSS), an instrument for measuring disease-specific quality of life in heart failure.

"We are particularly delighted to announce the addition of EMPULSE as the first-ever study to assess the effects of Jardiance in people who have been hospitalized for acute heart failure," said Mohamed Eid, M.D., M.P.H., M.H.A., vice president, Clinical Development & Medical Affairs, Cardio-Metabolism & Respiratory Medicine, Boehringer Ingelheim Pharmaceuticals, Inc. "The study aims to address an unmet need and is an important addition to our broad and comprehensive heart failure program."

EMPULSE is part of the empagliflozin heart failure program, which also consists of the EMPEROR-Reduced and EMPEROR-Preserved, EMPERIAL-Preserved and EMPERIAL-Reduced, and EMPA-VISION studies. These studies are investigating the effects of empagliflozin on heart failure-related outcomes and functional capacity in more than 9,500 adults with heart failure, including those with and without diabetes.

About EMPULSE (NCT04157751)
The EMPULSE study is a multicenter, randomized, double-blind, 90-day superiority study to evaluate the effect on clinical benefit, safety and tolerability of once-daily oral EMPagliflozin 10 mg compared to placebo, initiated in patients hospitalized for acUte heart faiLure (de novo or decompensated chronic HF) who have been StabilizEd (EMPULSE).

- Primary endpoint: Net clinical benefit, a composite of all-cause mortality, number of heart failure events (including hospitalizations for heart failure, urgent heart failure visits and unplanned outpatient visits), time to first heart failure event and change from baseline in Kansas City Cardiomyopathy Questionnaire - Clinical Summary Score (KCCQ-CSS) after 90 days of treatment
- Anticipated number of patients: approx. 500

About Heart Failure
Heart failure is a progressive, debilitating and potentially fatal condition that occurs when the heart cannot supply adequate circulation to meet the body's demands for oxygenated blood or, to do so, requires increased blood volume leading to fluid accumulation (congestion) in the lungs and peripheral tissues. It is a widespread condition affecting 60 million people worldwide and expected to increase as the population ages. Heart failure is highly prevalent in people with diabetes; however, approximately half of all people with heart failure do not have diabetes.

Symptoms of heart failure include difficulty breathing, swelling – most commonly in feet, legs and ankles – and fatigue, among others. People with heart failure experience a substantial reduction in quality of life, approximately 76 percent of whom find it difficult to carry out usual activities. This is, in part, due to the limitation of physical activity.

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 U.S. and Europe.

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. A team approach to optimize patient care by coordinating treatment of related comorbidities, including the use of emerging therapies with broad cardiorenal metabolic effects, may 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. **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/medwatch or call 1-800-FDA-1088.

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

CL-JAR-100026 10.30.18

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 to help those living with heart failure or chronic kidney disease.

Currently, no Boehringer Ingelheim and Lilly products are approved for the treatment of 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 @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 health care 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 lilly.com and lilly.com/newsroom.

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 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.

Jardiance® is a registered trademark of Boehringer Ingelheim.

P-LLY
MPR-US-101007

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

Stephan Thalen
Global Business Communications
Lilly Diabetes and Lilly USA
Email: stephan.thalen@lilly.com
Phone: (317) 903-5640

View original content to download multimedia:http://www.prnewswire.com/news-releases/boehringer-ingelheim-and-lilly-initiate-first-ever-study-to-assess-jardiance-in-people-hospitalized-for-acute-heart-failure-who-have-been-stabilized-300956005.html

SOURCE Eli Lilly and Company