Results announced from EMPACT-MI phase III trial investigating the effect of Jardiance® (empagliflozin) on risk of heart failure hospitalization and death in adults following a heart attack

RIDGEFIELD, Conn. and INDIANAPOLIS, April 6, 2024 – The EMPACT-MI phase III clinical trial showed a 10% relative risk reduction in the primary composite endpoint of time to first hospitalization due to heart failure or all-cause mortality for Jardiance® (empagliflozin) versus placebo, which did not reach statistical significance. Jardiance was initiated in adults within 14 days of an acute myocardial infarction, commonly known as a heart attack, and demonstrated a reassuring safety profile in this population. Additional pre-specified exploratory analyses revealed relative risk reductions of 23% for time to first hospitalization due to heart failure and 33% for total hospitalizations due to heart failure with Jardiance over placebo. Detailed results from Boehringer Ingelheim and Eli Lilly and Company's (NYSE: LLY) phase III EMPACT-MI trial were announced today at the American College of Cardiology's 2024 Scientific Session & Expo. Results were announced in collaboration with Duke Clinical Research Institute (DCRI) and simultaneously published in *The New England Journal of Medicine*.

"These results add to our understanding of SGLT2 inhibitors and contribute to the body of evidence across six clinical studies examining the potential for Jardiance to impact major outcomes in a broad population of adults with heart failure, chronic kidney disease or type 2 diabetes," said Mohamed Eid, M.D., M.Sc., M.H.A., vice president, Clinical Development & Medical Affairs, Cardio-Renal-Metabolic Medicine, Boehringer Ingelheim Pharmaceuticals, Inc. "Building on this strong foundation, we remain committed to leading efforts aimed at increasing awareness, generating real-world evidence and advancing care for people affected by interconnected cardiovascular, renal and metabolic diseases."

The EMPACT-MI phase III trial investigated Jardiance 10 mg compared with placebo, given once daily on top of standard of care, in more than 6,500 adults within 14 days of hospital admission for heart attack. The primary endpoint of the study was the composite of time to first hospitalization due to heart failure or all-cause mortality up to 26 months. Participants had no history of chronic heart failure and were eligible regardless of type 2 diabetes and chronic kidney disease status.

"Despite remarkable advances in treatment, heart attack remains the most common cause of heart failure," said Jeff Emmick, M.D., Ph.D., senior vice president, Product Development, Lilly. "There is still an unmet need to reduce the risk of new onset heart failure and other common complications after a heart attack. However, in adults who have chronic heart failure, Jardiance has proven to be an important therapy for reducing the risk of cardiovascular death and heart failure hospitalizations, and has the potential to meet the needs of millions of people worldwide."

EMPACT-MI is part of the EMPOWER program, launched by the Boehringer Ingelheim and Lilly Alliance to explore the impact of Jardiance on major patient outcomes across the spectrum of cardiovascular, renal and metabolic conditions including type 2 diabetes, chronic heart failure, heart attack and chronic kidney disease. Globally, more than 1 billion people live with these interconnected disorders, which are a leading cause of death worldwide.

About EMPACT-MI

EMPACT-MI (EMPAgliflozin for the prevention of Chronic heart failure and morTality after an acute Myocardial Infarction) is a multicenter, randomized, parallel group, double-blind, placebo-controlled superiority trial investigating the effect of Jardiance on all-cause mortality and hospitalization due to heart failure in adults who have had a heart attack. Participants had no history of chronic heart failure and were eligible regardless of type 2 diabetes and chronic kidney disease status. EMPACT-MI included more than 6,500 adults from 22 countries. Study participants were randomized to receive either Jardiance 10 mg or placebo, once daily, both on top of standard of care within 14 days of hospital admission for heart attack. The EMPACT-MI clinical trial is being conducted, analyzed, and reported in partnership with the Duke Clinical Research Institute (DCRI), with Boehringer Ingelheim and Lilly providing funding.

About the EMPOWER program

The Alliance has developed the EMPOWER program to explore the impact of Jardiance on major clinical cardiovascular and renal outcomes in a spectrum of cardiovascular, renal and metabolic conditions. Cardiovascular, renal and metabolic conditions are the leading cause of mortality worldwide and account for up to 20 million deaths annually. Through the EMPOWER program, Boehringer Ingelheim and Lilly are working to advance knowledge of these interconnected systems and create care which offers integrated, multi-organ benefits. Comprised of nine clinical trials and two real-world evidence studies, EMPOWER reinforces the long-term commitment of the Alliance to improve outcomes for people living with cardiovascular, renal and metabolic conditions. With more than 700,000 adults enrolled worldwide in studies, it is one of the broadest and most comprehensive clinical programs for an SGLT2 inhibitor to date.

What is JARDIANCE?

JARDIANCE is a prescription medicine used to:

- reduce the risk of cardiovascular death and hospitalization for heart failure in adults with heart failure, when the heart cannot pump enough blood to the rest of your body
- reduce the risk of further worsening of kidney disease, end-stage kidney disease (ESKD), death due to cardiovascular disease, and hospitalization in adults with chronic kidney disease
- reduce the risk of cardiovascular death in adults with type 2 diabetes who also have known cardiovascular disease
- lower blood sugar along with diet and exercise in adults and children who are 10 years of age and older with type 2 diabetes

JARDIANCE is not for use to lower blood sugar in people with type 1 diabetes. It may increase their risk of diabetic ketoacidosis (increased ketones in the blood or urine).

JARDIANCE is not for use to lower blood sugar in people with type 2 diabetes who have severe kidney problems, because it may not work.

JARDIANCE is not for people with polycystic kidney disease, or who are taking or have recently received certain types of immunosuppressive therapy to treat kidney disease. JARDIANCE is not expected to work if you have these conditions.

IMPORTANT SAFETY INFORMATION

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

- rash
- raised, red areas on your skin (hives)
- swelling of your face, lips, mouth, and throat that may cause difficulty in breathing or swallowing

If you have any of these symptoms, stop taking JARDIANCE and call your healthcare provider right away or go to the nearest hospital emergency room.

JARDIANCE can cause serious side effects, including:

- **Diabetic ketoacidosis (increased ketones in your blood or urine) in people with type 1 and other ketoacidosis.** JARDIANCE can cause ketoacidosis that can be life-threatening and may lead to death. Ketoacidosis is a serious condition which needs to be treated in a hospital. People with type 1 diabetes have a high risk of getting ketoacidosis. People with type 2 diabetes or pancreas problems also have an increased risk of getting ketoacidosis. Ketoacidosis can also happen in people who are sick, cannot eat or drink as usual, skip meals, and are on a diet high in fat and low in carbohydrates (ketogenic diet), take less than the usual amount of insulin or miss insulin doses, drink too much alcohol, have a loss of too much fluid from the body (volume depletion), or who have surgery. Ketoacidosis can happen even if your blood sugar is less than 250 mg/dL. Your healthcare provider may ask you to periodically check ketones in your urine or blood. **Stop taking JARDIANCE and call your healthcare provider or get medical help right away if you get any of the following symptoms. If possible, check for ketones in your urine or blood, even if your blood sugar is less than 250 mg/dL: nausea, vomiting, stomach-area (abdominal) pain, tiredness, trouble breathing, ketones in your urine or blood.**

- **Dehydration. JARDIANCE can cause some people to become dehydrated (the loss of body water and salt). Dehydration may cause you to feel dizzy, faint, light-headed, or weak, especially when you stand up. Sudden worsening of kidney function has happened in people who are taking JARDIANCE.** You may be at a higher risk of dehydration if you: take medicines to lower your blood pressure, including water pills (diuretics), are on a low salt diet, have kidney problems, or are 65 years of age or older. Talk to your healthcare provider about what you can do to prevent dehydration, including how much fluid you should drink on a daily basis. Call your healthcare provider right away if you reduce the amount of food or liquid you drink, if you are sick or cannot eat, or start to lose liquids from your body from vomiting, diarrhea, or being in the sun too long.

- **Vaginal yeast infection.** Talk to your healthcare provider if you have vaginal odor, white or yellowish vaginal discharge

(discharge may be lumpy or look like cottage cheese), and/or vaginal itching.

- **Yeast infection of the skin around the penis.** Swelling of an uncircumcised penis may develop that makes it difficult to pull back the skin around the tip of the penis. Talk to your healthcare provider if you have redness, itching or swelling of the penis, rash of the penis, foul smelling discharge from the penis, and/or pain in the skin around the penis.

  Talk to your healthcare provider about what to do if you get symptoms of a yeast infection of the vagina or penis. Your healthcare provider may suggest you use an over-the-counter antifungal medicine. Talk to your healthcare provider right away if you use an over-the-counter antifungal medication and your symptoms do not go away.

- **Serious urinary tract infections.** Serious urinary tract infections can occur in people taking JARDIANCE and may lead to hospitalization. Tell your healthcare provider 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). In adults, 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. In children 10 years of age and older, the risk for low blood sugar is higher with JARDIANCE regardless of use with another medicine that can also lower blood sugar. 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 people who take JARDIANCE, and may lead to hospitalization, multiple surgeries, and death. **Seek medical attention immediately if you have a 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).**

- **Amputations. SGLT2 inhibitors may increase your risk of lower limb amputations.** You may be at a higher risk of lower limb amputation if you have a history of amputation; have had blocked or narrowed blood vessels, usually in your leg; have had diabetic foot infection, ulcers or sores. **Call your healthcare provider right away if you have new pain or tenderness, any sores, ulcers, or infections in your leg or foot.** Talk to your healthcare provider about proper foot care.
- **Serious allergic reactions.** If you have any symptoms of a serious allergic reaction stop taking JARDIANCE and call your healthcare provider right away or go to the nearest hospital emergency room.

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 healthcare provider or pharmacist.

Before you take JARDIANCE, tell your healthcare provider about all of your medical conditions, including if you have type 1 diabetes or have had diabetic ketoacidosis, have a decrease in your insulin dose, have a serious infection, have a history of infection of the vagina or penis, have a history of amputation, or have kidney or liver problems. Also tell your healthcare provider if you have a history of urinary tract infections or problems with urination. Tell your healthcare provider if you are on a low sodium (salt) diet because your healthcare provider may change your diet or dose. Tell your healthcare provider if you are going to have surgery because your healthcare provider may stop JARDIANCE before you have surgery. Talk to your healthcare provider if you are having surgery about when to stop taking JARDIANCE and when to start it again. Also tell your healthcare provider if you are eating less or there is a change in your diet; are dehydrated; 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 ever had an allergic reaction to JARDIANCE; are pregnant or plan to become pregnant. JARDIANCE may harm your unborn baby. If you become pregnant while taking JARDIANCE, tell your healthcare provider as soon as possible. Tell your healthcare provider if you 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 healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

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
The Boehringer Ingelheim and Lilly Alliance leverages the strengths of two of the world's leading pharmaceutical companies. By joining forces, the companies demonstrate their commitment, not only to the care of people with type 2 diabetes, but also to address areas of unmet medical need like heart failure and chronic kidney disease.

About Boehringer Ingelheim
Boehringer Ingelheim is working on breakthrough therapies that transform lives, today and for generations to come. As a leading research-driven biopharmaceutical company, the company creates value through innovation in areas of high unmet medical need. Founded in 1885 and family-owned ever since, Boehringer Ingelheim takes a long-term, sustainable perspective. More than 53,000 employees serve over 130 markets in the two business units, Human Pharma and Animal Health. Learn more at boehringer-ingelheim.com/us/.

About Lilly
Lilly is a medicine company turning science into healing to make life better for people around the world. We've been pioneering life-changing discoveries for nearly 150 years, and today our medicines help more than 51 million people across the globe. Harnessing the power of biotechnology, chemistry and genetic medicine, our scientists are urgently advancing new discoveries to solve some of the world's most significant health challenges: redefining diabetes care; treating obesity and curtailing its most devastating long-term effects; advancing the fight against Alzheimer's disease; providing solutions to some of the most debilitating immune system disorders; and transforming the most difficult-to-treat cancers into manageable diseases. With each step toward a healthier world, we're motivated by one thing: making life better for millions more people. That includes delivering innovative clinical trials that reflect the diversity of our world and working to ensure our medicines are accessible and affordable. To learn more, visit Lilly.com and Lilly.com/news, or follow us on Facebook, Instagram and LinkedIn.

About the Duke Clinical Research Institute
The DCRI, part of the Duke University School of Medicine, is the largest academic clinical research organization in the world. Its mission is to develop and share knowledge that improves the care of patients through innovative research. The institute conducts groundbreaking multinational clinical trials, manages major national patient registries, and performs landmark outcomes research. DCRI research spans multiple disciplines, from pediatrics to geriatrics, primary care to subspecialty medicine, and genomics to proteomics. The DCRI also is home to the Duke Databank for Cardiovascular Diseases, the largest and oldest institutional cardiovascular database in the world, which continues to inform clinical decision-making 40 years after its founding.

Cautionary Statement Regarding Forward-Looking Statements
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 beliefs and expectations. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of drug research, development and commercialization. Among other things, there is no guarantee that planned or ongoing studies will be completed as planned, that future study results will be consistent with study results to date or that Jardiance® will receive additional regulatory approvals. For further discussion of these and other risks and uncertainties that could cause actual results to differ from Lilly's expectations, see Lilly's 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.

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CONTACTS:

Jennifer Forsyth
Boehringer Ingelheim
Email: jennifer.forsyth@boehringer-ingelheim.com
Phone: +1 (203) 791-5889

Niki Smithers
Eli Lilly and Company
Email: smithers_niki@lilly.com
Phone: +1 317-358-9074