Jardiance® Recommended as Preferred SGLT2 Inhibitor for Adults with Type 2 Diabetes and Established Cardiovascular Disease in American College of Cardiology Expert Consensus Decision Pathway

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RIDGEFIELD, Conn. and INDIANAPOLIS, Nov. 26, 2018 /PRNewswire/ -- A new Expert Consensus Decision Pathway issued by the American College of Cardiology (ACC) recommends Jardiance® (empagliflozin) as the preferred SGLT2 inhibitor for its proven benefit in reducing the risk of cardiovascular death in adults with type 2 diabetes and established cardiovascular disease. The recommendation, part of the ACC's first Expert Consensus Decision Pathway on novel therapies for cardiovascular risk reduction in adults with type 2 diabetes and atherosclerotic cardiovascular disease, was released today and published online in the *Journal of the American College of Cardiology.* Jardiance is marketed by Boehringer Ingelheim and Eli Lilly and Company (NYSE: LLY).

The recommendation of Jardiance is based on evidence from the landmark EMPA-REG OUTCOME® trial, which investigated the effects of Jardiance compared with placebo when added to standard of care in adults with type 2 diabetes and established cardiovascular disease. In addition to the ACC Expert Consensus Decision Pathway, the American Diabetes Association (ADA) and European Association for the Study of Diabetes (EASD) recommend SGLT2 inhibitors such as Jardiance to help manage cardiovascular outcomes. Jardiance is also the only SGLT2 inhibitor recommended in the ADA 2018 Standards of Medical Care in Diabetes for reducing the risk of cardiovascular death in people with type 2 diabetes and established cardiovascular disease. Worldwide, more than 50 treatment guidelines have been updated to include findings from the EMPA-REG OUTCOME trial in their endorsement of type 2 diabetes treatments with proven cardiovascular benefits.

"People with type 2 diabetes are at an increased risk of serious cardiovascular complications and events even when their blood sugar is under control, which is why reducing cardiovascular risk in people with diabetes is critical," said Thomas Seck, M.D., senior vice president, Medicine and Regulatory Affairs, Boehringer Ingelheim Pharmaceuticals, Inc. "The ACC Expert Consensus Decision Pathway, along with the ADA and EASD, all now recommend a comprehensive cardiovascular program for adults with type 2 diabetes and established cardiovascular disease that includes a treatment such as Jardiance, shown to improve cardiovascular outcomes in this population. These recommendations reflect a fundamental change in the management of diabetes, moving beyond glucose control to a broader strategy of comprehensive cardiovascular risk reduction."

The 2018 ACC Expert Consensus statement emphasizes the need for a collaborative treatment approach by healthcare providers to reduce cardiovascular risk and improve survival in people with type 2 diabetes, a growing public health epidemic. People with diabetes are up to four times more likely to develop cardiovascular disease than those without diabetes, and cardiovascular disease ranks as the leading cause of death associated with diabetes.

The ACC Expert Consensus Decision Pathway's recommendation of Jardiance, along with those of the ADA and EASD, represents a shift toward a comprehensive and team-based approach for managing the overall health of people with type 2 diabetes. The ACC encourages cardiologists to work as part of a broad healthcare provider team including primary care, internal medicine and endocrinology physicians, as well as nurse practitioners, physician assistants, diabetes educators and pharmacists, to improve the care and outcomes of people with type 2 diabetes.

"The EMPA-REG OUTCOME trial ushered in a new era for managing type 2 diabetes. Now, cardiovascular risk reduction is prioritized as a primary goal of diabetes management," said Sherry Martin, M.D., vice president, Medical Affairs, Lilly. "With the adoption of the ACC's Expert Consensus Decision Pathway and ADA-EASD guidelines, the cardiology community will have an important role as part of the healthcare team managing cardiovascular risk in people with type 2 diabetes."

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 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 12 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 totalled more than $23 billion in 2012.

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

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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
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.

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