U.S. FDA Grants Fast Track Designation to Empagliflozin for the Treatment of Chronic Heart Failure

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- Fast Track designation facilitates development of new therapies that treat serious conditions and fulfill an unmet medical need

- FDA's Fast Track designation for empagliflozin underscores the urgent need for new potential treatment options for the 6.5 million people in the U.S. who have heart failure

RIDGEFIELD, Conn. and INDIANAPOLIS, June 26, 2019 /PRNewswire/ -- The U.S. Food and Drug Administration (FDA) has granted Fast Track designation to empagliflozin for the reduction of the risk of cardiovascular death and hospitalization for heart failure in people with chronic heart failure, Boehringer Ingelheim and Eli Lilly and Company (NYSE: LLY) announced. The Fast Track designation facilitates the development of new therapies that fill an unmet medical need for serious conditions in an effort to expedite the availability of new treatment options.

This designation is for the ongoing EMPEROR program, which consists of the EMPEROR-Reduced and EMPEROR-Preserved studies. These studies will evaluate the effect of empagliflozin on cardiovascular death and hospitalization for heart failure in adults with chronic heart failure with reduced or preserved ejection fraction, respectively.

"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," said Mohamed Eid, M.D., M.P.H., M.H.A, vice president, Clinical Development & Medical Affairs, Boehringer Ingelheim Pharmaceuticals, Inc. "The FDA Fast Track designation for empagliflozin is an important step forward in addressing this unmet need, and we look forward to working closely with the FDA as we explore the potential for empagliflozin to improve outcomes for adults with chronic heart failure."

Heart failure is a serious condition in which the heart is unable to supply enough blood to the body. About half of people who develop heart failure die within five years. Heart failure also leads to a substantial reduction in quality of life and a high symptom burden, in part due to limitation of physical activity and difficulty carrying out typical everyday activities. Already affecting 26 million people worldwide, including more than 6.5 million in the U.S., heart failure is expected to become even more prevalent.

"Boehringer Ingelheim and Lilly are committed to advancing treatments that address the public health challenges of cardiometabolic diseases, including chronic heart failure," said Jeff Emmick, M.D., Ph.D., vice president, Product Development, Lilly. "We eagerly anticipate results from the EMPEROR studies as we advance the development of empagliflozin in this setting."

The two EMPEROR phase III studies include more than 8,500 people with chronic heart failure and are designed to assess the effect of treatment with empagliflozin on cardiovascular death and hospitalization for chronic heart failure as primary endpoints. The EMPEROR studies are part of the empagliflozin chronic heart failure program.

Empagliflozin, marketed as Jardiance® in the U.S., is a once-daily tablet used along with diet and exercise to lower blood sugar in adults with type 2 diabetes and to reduce the risk of cardiovascular death in adults with type 2 diabetes and 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).

About the Empagliflozin Chronic Heart Failure Program
The empagliflozin chronic heart failure program consists of the EMPEROR-Reduced and EMPEROR-Preserved studies, the EMPERIAL-Reduced and EMPERIAL-Preserved studies and the EMPA-VISION study. These studies are evaluating the efficacy and safety of empagliflozin in more than 9,000 adults with chronic heart failure, including those with and without diabetes.

About the EMPEROR Chronic Heart Failure Studies
The EMPEROR (EMPagliflozin outcomE tRial in patients with chrOnic heaRt failure) chronic heart failure studies are two phase III, randomized, double-blind trials investigating once-daily empagliflozin compared with placebo in adults with chronic heart failure with preserved or reduced ejection fraction*, both with and without diabetes, who are receiving current standard of care:

- **EMPEROR-Preserved** [NCT03057951]: will investigate the safety and efficacy of empagliflozin in patients with chronic heart failure with **preserved ejection fraction** (HFpEF).
  - Primary endpoint: time to first event of adjudicated cardiovascular death or adjudicated hospitalization for heart failure (HHF) [Time Frame: up to 38 months]
  - Anticipated number of patients: approx. 5,250
  - Estimated completion: 2020
- **EMPEROR-Reduced** [NCT03057977]: will investigate the safety and efficacy of empagliflozin in patients with chronic heart failure with **reduced ejection fraction** (HFrEF).
  - Primary endpoint: time to first event of adjudicated cardiovascular death or adjudicated HHF [Time Frame: up to 38 months]

- Anticipated number of patients: approx. 3,600
- Estimated completion: 2020

***Ejection fraction** is a measurement of the percentage of blood the left ventricle pumps out with each contraction. When the heart relaxes, the ventricle refills with blood.
HFpEF occurs when the heart muscle contracts normally but the ventricle does not fill with enough blood, so less blood can enter the heart compared with a normally functioning heart.
HFrEF occurs when the heart muscle does not contract effectively and less blood is pumped out to the body compared with a normally functioning heart.

About Heart Failure
Heart failure is a progressive, debilitating and potentially fatal condition that occurs when the heart cannot supply 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 also leads to a substantial reduction in quality of life, due in part to difficulty carrying out typical everyday activities.

Affecting 26 million people worldwide, the prevalence of heart failure is expected to increase as the population ages. While heart failure is very common in people with diabetes, approximately half of people with heart failure do not have diabetes.

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.

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.

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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, 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 per cent 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 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 empagliflozin as a potential treatment for chronic heart failure and reflects Lilly's current beliefs. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of drug 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 a further discussion of these and other risks and uncertainties that could cause actual results to differ from Lilly's expectations, please see Lilly's most recent Forms 10-K and 10-Q filed with the U.S. Securities and Exchange Commission. Lilly undertakes no duty to update forward-looking statements.

Jardiance® is a registered trademark of Boehringer Ingelheim.

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