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U.S. FDA Approves INVOKANA® (canagliflozin) to Treat Diabetic Kidney Disease (DKD) and Reduce the Risk of Hospitalization for Heart Failure in Patients with Type 2 Diabetes (T2D) and DKD

INVOKANA® is the only diabetes medicine indicated to slow the progression of diabetic nephropathy (also known as DKD) and reduce the risk of hospitalization for heart failure in patients with T2D and DKD

Approval is based on the landmark Phase 3 CREDENCE renal outcomes study – the only completed renal outcomes study of a diabetes medicine

RARITAN, N.J. (September 30, 2019) – The Janssen Pharmaceutical Companies of Johnson & Johnson announced today that the U.S. Food and Drug Administration (FDA) approved a new indication for INVOKANA® (canagliflozin) to reduce the risk of end-stage kidney disease (ESKD), worsening of kidney function, cardiovascular (CV) death, and hospitalization for heart failure in adults with type 2 diabetes and diabetic kidney disease (nephropathy) with a certain amount of protein in the urine. INVOKANA® is now the only type 2 diabetes medicine indicated to both treat diabetic kidney disease and reduce the risk of hospitalization for heart failure in patients with T2D and DKD.

T2D is the leading cause of kidney disease in the United States [1] and the fifth fastest-growing cause of death around the world. [2]

"With the approval of these new uses, INVOKANA® is now the only diabetes medicine indicated to help type 2 diabetes patients reduce the risks associated with diabetic kidney disease, including hospitalization for heart failure," said James List, M.D., Ph.D., Global Therapeutic Area Head, Cardiovascular & Metabolism, Janssen Research & Development, LLC. "This significant advancement addresses serious unmet needs and could change the trajectory of care for the many millions of patients living with type 2 diabetes and diabetic kidney disease."

Click to Tweet: #BREAKING: Only type 2 diabetes medicine now approved by FDA to slow the progression of diabetic kidney disease and reduce the risk of hospitalization for heart failure in patients with type 2 #diabetes #T2D and #DKD. Read more here: https://ctt.ec/Pa0cz+

In the United States, one in three people with T2D has DKD,[1] which multiplies the risk of cardiovascular complications including heart failure and CV death, and puts patients on a trajectory to dialysis and kidney transplant.[1,2] Additionally, heart failure is one of the leading causes of hospitalization,[3] with a high unmet need for effective treatment options. With this approval, INVOKANA® is the only type 2 diabetes medicine indicated to reduce the risk of hospitalization for heart failure in

patients with T2D and DKD, and is the first new treatment option in nearly 20 years indicated to slow the progression of DKD in these patients.[4,5,6]

"Given the nation's heightened focus on kidney health at the highest levels of government, this approval couldn't have come at a better time and offers real hope for patients with type 2 diabetes and diabetic kidney disease," said LaVerne A. Burton, President and Chief Executive Officer, American Kidney Fund.[*] "We know that the real battle to turn the tide on kidney disease is in early detection and slowing its progression so that patients stay healthier and fewer patients reach kidney failure. We are so grateful that advances in kidney disease research are producing treatment options that help to slow the progression of diabetic kidney disease and reduce the risk of hospitalization for heart failure."

Click to Tweet: .@KidneyFund talks importance of FDA's approval of the first new treatment option in nearly 2 decades to slow the progression of diabetic #kidneydisease and reduce the risk of hospitalization for heart failure in patients with type 2 #diabetes #T2D and #DKD. See here for details: https://ctt.ec/7R071+

The new indication is based on results from the landmark Phase 3 CREDENCE study in patients with T2D and DKD, which was stopped early because it met the prespecified criteria for efficacy. In CREDENCE, INVOKANA® 100 mg demonstrated a 30 percent reduction in the risk of the primary composite endpoint, comprising end-stage kidney disease (ESKD), doubling of serum creatinine and renal or CV death.[†] Results also showed INVOKANA® reduced the risk of secondary CV endpoints, including a 39 percent reduction in the risk of hospitalization for heart failure. Overall, adverse events and serious adverse events were similar but numerically lower in the INVOKANA® group compared to placebo. The rates of diabetic ketoacidosis and genital mycotic infections were numerically higher in the

[*] Janssen Pharmaceuticals, Inc. is a corporate sponsor for the American Kidney Fund.
[†] There were too few events to evaluate the risk of renal death. INVOKANA® is not indicated to reduce the risk of renal death.

INVOKANA® group, as observed in other clinical trials. Additionally, there was no imbalance in lower limb amputation or bone fracture in this trial and no new safety signals were identified.

"Millions of T2D patients around the world have DKD and almost half of them aren't even aware of it. By the time they are referred to a nephrologist, it is often too late because their disease has progressed to the point where dialysis is inevitable," said CREDENCE study investigator George Bakris, M.D., Professor of Medicine and Director, Comprehensive Hypertension Center, University of Chicago.[‡] "For nearly two decades, we've been searching for a treatment that can help us intervene earlier to slow kidney disease progression. With the approval for this new indication for INVOKANA®, physicians will not only be able to help reduce the risks associated with diabetic kidney disease, but also reduce the risk of hospitalization for heart failure in patients with T2D and DKD."

About CREDENCE

CREDENCE (**C**anagliflozin and **R**enal **E**vents in **D**iabetes with **E**stablished **N**ephropathy **C**linical **E**valuation) is the first dedicated renal outcomes study of any sodium-glucose co-transporter 2 (SGLT2) inhibitor in patients with T2D and DKD in addition to standard of care. The study is a randomized, double-blind, event-driven, placebo-controlled, parallel-group, 2-arm, multicenter study, which evaluated 4,401 patients with T2D, Stage 2 or 3 DKD (defined as an estimated glomerular filtration rate [eGFR] of ≥30 to <90 mL/min/1.73 m^2) and macroalbuminuria (defined as urinary albumin-to-creatinine ratio [ACR] >300 to ≤5,000 mg/g) who were receiving standard of care, including a maximum tolerated labeled daily dose of an angiotensin-converting enzyme (ACE) inhibitor or angiotensin II receptor blocker (ARB). The primary efficacy outcome for these analyses was the composite of end-stage kidney disease (dialysis, transplant, or eGFR <15), doubling of serum creatinine, and renal death or cardiovascular (CV) death. Specified secondary outcomes included a composite of heart attack, stroke, or CV death and a composite of CV death or hospitalization for heart failure.

[‡] Dr. George Bakris was compensated for his work on the CREDENCE study.

WHAT IS INVOKANA®?

INVOKANA® is a prescription medicine used:

- along with diet and exercise to lower blood sugar (glucose) in adults with type 2 diabetes
- to reduce the risk of major cardiovascular events such as heart attack, stroke, or death in adults with type 2 diabetes who have known cardiovascular disease
- to reduce the risk of end-stage kidney disease (ESKD), worsening of kidney function, cardiovascular death, and hospitalization for heart failure in adults with type 2 diabetes mellitus and diabetic kidney disease (nephropathy) with a certain amount of protein in the urine

INVOKANA® is not for people with type 1 diabetes or with diabetic ketoacidosis (increased ketones in blood or urine). It is not known if INVOKANA® is safe and effective in children under 18 years of age.

IMPORTANT SAFETY INFORMATION

INVOKANA® can cause important side effects, including:

- **Amputations. INVOKANA® may increase your risk of lower-limb amputations. Amputations mainly involve removal of the toe or part of the foot; however, amputations involving the leg, below and above the knee, have also occurred. Some people had more than one amputation, some on both sides of the body.** You may be at a higher risk of lower-limb amputation if you: have a history of amputation, have heart disease or are at risk for heart disease, have had blocked or narrowed blood vessels (usually in leg), have damage to the nerves (neuropathy) in the leg, or have had diabetic foot ulcers or sores**. Call your doctor right away if you have new pain or tenderness, any sores, ulcers, or infections in your leg or foot.** Your doctor may decide to stop your INVOKANA® for a while if you have any of these signs or symptoms. Talk to your doctor about proper foot care
- **Dehydration. INVOKANA® can cause some people to become dehydrated (the loss of too much body water), which may cause you to feel dizzy,**

faint, lightheaded, or weak, especially when you stand up (orthostatic hypotension). You may be at higher risk of dehydration if you have low blood pressure, take medicines to lower your blood pressure (including diuretics [water pills]), are on a low sodium (salt) diet, have kidney problems, or are 65 years of age or older

- **Vaginal yeast infection.** Women who take INVOKANA® may get vaginal yeast infections. Symptoms include: vaginal odor, white or yellowish vaginal discharge (discharge may be lumpy or look like cottage cheese), or vaginal itching
- **Yeast infection of the penis (balanitis or balanoposthitis).** Men who take INVOKANA® may get a yeast infection of the skin around the penis. Symptoms include: redness, itching, or swelling of the penis; rash of the penis; foul-smelling discharge from the penis; or pain in the skin around penis

Talk to your doctor about what to do if you get symptoms of a yeast infection of the vagina or penis.

Do not take INVOKANA® if you:

- are allergic to canagliflozin or any of the ingredients in INVOKANA®. Symptoms of allergic reaction may include: rash; raised red patches on your skin (hives); or swelling of the face, lips, mouth, tongue, and throat that may cause difficulty in breathing or swallowing
- have severe kidney problems and are taking INVOKANA® to lower your blood sugar
- are on kidney dialysis

Before you take INVOKANA®, tell your doctor if you have a history of amputation; heart disease or are at risk for heart disease; blocked or narrowed blood vessels (usually in leg); damage to the nerves (neuropathy) of your leg; diabetic foot ulcers or sores; kidney problems; liver problems; history of urinary tract infections or problems with urination; are on a low sodium (salt) diet; are going to have surgery; are eating less due to illness, surgery, or change in diet; pancreas problems; drink alcohol very often (or drink a lot of alcohol in short-

term); ever had an allergic reaction to INVOKANA®; or have other medical conditions.

Tell your doctor if you are or plan to become pregnant, are breastfeeding, or plan to breastfeed. INVOKANA® may harm your unborn baby. If you become pregnant while taking INVOKANA®, tell your doctor right away. INVOKANA® may pass into your breast milk and may harm your baby. Do not breastfeed while taking INVOKANA®.

Tell your doctor about all the medicines you take, **including prescription and non-prescription medicines, vitamins, and herbal supplements**. Especially tell your doctor if you take diuretics (water pills), rifampin (used to treat or prevent tuberculosis), phenytoin or phenobarbital (used to control seizures), ritonavir (Norvir®, Kaletra® – used to treat HIV infection), or digoxin (Lanoxin®– used to treat heart problems).

Possible Side Effects of INVOKANA®

INVOKANA® may cause serious side effects, including:

- **Ketoacidosis** (increased ketones in your blood or urine). **Ketoacidosis has happened in people who have type 1 or type 2 diabetes**, during treatment with INVOKANA®. Ketoacidosis is a serious condition, which may need to be treated in a hospital. Ketoacidosis may lead to death. **Ketoacidosis can happen with INVOKANA® even if your blood sugar is less than 250 mg/dL. Stop taking INVOKANA® and call your doctor right away if you get any of the following symptoms: nausea, vomiting, stomach-area pain, tiredness, or trouble breathing**
- **Kidney problems.** Sudden kidney injury has happened to people taking INVOKANA®. Talk to your doctor right away if you: 1) reduce the amount of food or liquid you drink, if you are sick, or cannot eat or 2) you start to lose liquids from your body from vomiting, diarrhea, or being in the sun too long
- **Serious Urinary Tract Infections:** may lead to hospitalization and have happened in people taking INVOKANA®. Tell your doctor if you have signs or

symptoms of a urinary tract infection such as: burning feeling while urinating, need to urinate often or right away, pain in the lower part of your stomach (pelvis), or blood in the urine. Some people may also have high fever, back pain, nausea, or vomiting

- **Low blood sugar (hypoglycemia).** If you take INVOKANA® with another medicine that can cause low blood sugar, such as a sulfonylurea or insulin, your risk of getting low blood sugar is higher. The dose of your sulfonylurea medicine or insulin may need to be lowered while you take INVOKANA®. Signs and symptoms of low blood sugar may include: headache, drowsiness, weakness, dizziness, confusion, irritability, hunger, fast heartbeat, sweating, shaking, or feeling jittery
- **A rare but serious bacterial infection that destroys the tissue under the skin (necrotizing fasciitis) in the area between and around the anus and genitals (perineum).** Necrotizing fasciitis of the perineum has happened in women and men who take INVOKANA®. Necrotizing fasciitis of the perineum may lead to hospitalization, may require multiple surgeries, and may lead to death. **Seek medical attention immediately if you have fever or you 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, or redness of the skin (erythema)
- **Serious allergic reaction.** If you have any symptoms of a serious allergic reaction, stop taking INVOKANA® and call your doctor right away or go to the nearest hospital emergency room
- **Broken Bones (fractures):** Bone fractures have been seen in patients taking INVOKANA®. Talk to your doctor about factors that may increase your risk of bone fracture

The most common side effects of INVOKANA® include: vaginal yeast infections and yeast infections of the penis; changes in urination, including urgent need to urinate more often, in larger amounts, or at night.

Tell your doctor if you have any side effect that bothers you or that does not go away. **Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.** You may also report side effects to Janssen Scientific Affairs, LLC at 1-800-526-7736.

Please read the full Product Information, including Boxed Warning, and Medication Guide for INVOKANA®.

Canagliflozin is licensed from Mitsubishi Tanabe Pharma Corporation.

About Janssen Cardiovascular & Metabolism

In Cardiovascular & Metabolism (CVM), we take on the most pervasive diseases that burden hundreds of millions of people and healthcare systems around the world. As part of this long-standing commitment and propelled by our successes in treating T2D and thrombosis, we advance highly differentiated therapies that prevent and treat life-threatening cardiovascular, metabolic and retinal diseases. Uncovering new therapies that can improve the quality of life for this large segment of the population is an important endeavor – one which Janssen CVM will continue to lead in the years to come. Our mission is global, local and personal. Together, we can reshape the future of cardiovascular, metabolic and retinal disease prevention and treatment. Please visit www.janssen.com/cardiovascular-and-metabolism.

About the Janssen Pharmaceutical Companies of Johnson & Johnson

At Janssen, we're creating a future where disease is a thing of the past. We're the Pharmaceutical Companies of Johnson & Johnson, working tirelessly to make that future a reality for patients everywhere by fighting sickness with science, improving access with ingenuity, and healing hopelessness with heart. We focus on areas of medicine where we can make the biggest difference: Cardiovascular & Metabolism, Immunology, Infectious Diseases & Vaccines, Neuroscience, Oncology, and Pulmonary Hypertension.

Learn more at www.janssen.com. Follow us at www.twitter.com/JanssenGlobal. Janssen Research & Development, LLC is part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

Cautions Concerning Forward-Looking Statements

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding the potential benefits and further development of canagliflozin. The reader is cautioned not to rely on these forward-looking statements. These statements are based on current expectations of future events. If underlying assumptions prove inaccurate or known or unknown risks or uncertainties materialize, actual results could vary materially from the expectations and projections of Janssen Research & Development, LLC, any of the other Janssen Pharmaceutical Companies and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges and uncertainties inherent in product research and development, including the uncertainty of clinical success and of obtaining regulatory approvals; uncertainty of commercial success; manufacturing difficulties and delays; competition, including technological advances, new products and patents attained by competitors; challenges to patents; product efficacy or safety concerns resulting in product recalls or regulatory action; changes in behavior and spending patterns of purchasers of health care products and services; changes to applicable laws and regulations, including global health care reforms; and trends toward health care cost containment. A further list and descriptions of these risks, uncertainties and other factors can be found in Johnson & Johnson's Annual Report on Form 10-K for the fiscal year ended December 30, 2018, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in the company's most recently filed Quarterly Report on Form 10-Q, and the company's subsequent filings with the Securities and Exchange Commission. Copies of these filings are available online at www.sec.gov, www.jnj.com or on request from Johnson & Johnson. None of the Janssen Pharmaceutical Companies nor Johnson & Johnson undertakes to update

any forward-looking statement as a result of new information or future events or developments.

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