INVOKANA® (canagliflozin) Demonstrated Significant Renal Protective Benefits in Patients with Type 2 Diabetes Mellitus and Chronic Kidney Disease

April 12, 2018

New analysis further supports the potential renal protective effects of INVOKANA®

Austin, TX, April 12, 2018 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced an additional analysis from the landmark CANVAS Program showing INVOKANA® (canagliflozin) improved renal outcomes in people with type 2 diabetes mellitus (T2DM) with or at high risk for cardiovascular (CV) disease. This benefit was observed in people with both preserved and reduced kidney function, as measured by estimated glomerular filtration rate (eGFR) above or below 60 mL/min/1.73 m^2. These data were presented at the 2018 National Kidney Foundation's Spring Clinical Meetings (abstract #253) in Austin, TX.

In the new analysis, canagliflozin reduced the urinary albumin to creatinine ratio (UACR), a key biomarker for chronic kidney disease, from baseline eGFR in patients with preserved and reduced eGFR by 17 percent and 23 percent, respectively (P-heterogeneity=0.01).[1] Canagliflozin also resulted in a relative risk reduction of the pre-specified composite endpoint (40 percent decline in eGFR, end-stage kidney disease or renal death) by 47 percent (HR, 0.53; 95% CI, 0.39 to 0.73, P-heterogeneity=0.28) in patients with preserved eGFR and 24 percent (HR, 0.76; 95% CI, 0.49 to 1.17, P-heterogeneity=0.28) in patients with reduced eGFR. Findings were similar when doubling of serum creatinine was substituted for 40 percent decline in eGFR in the renal composite (P-heterogeneity=0.21). There was no difference in risk of serious adverse events with canagliflozin in the two patient subgroups and no new adverse events were observed during this additional analysis beyond those previously reported from the CANVAS Program.

"Diabetic kidney disease remains the most common cause of end-stage renal disease worldwide, which underscores the need to further explore the potential renal protective effects of SGLT2 inhibitors," said George Bakris, M.D., Professor of Medicine and Director, Comprehensive Hypertension Center, University of Chicago Medicine. "The new analysis adds to the body of evidence, which suggests canagliflozin could potentially improve renal outcomes for millions of people with type 2 diabetes and suggests this benefit can be observed in people who have preserved and reduced kidney function."

"Although roughly one in three adults with diabetes develops diabetic kidney disease, there have been no significant advances in treatment for patients," said James F. List, M.D., Ph.D., Global Therapeutic Area Head, Cardiovascular & Metabolism, Janssen Research & Development, LLC. "We are encouraged that canagliflozin could potentially provide much-needed benefit for those with diabetic kidney disease, and look forward to building further on this insight in CREDENCE, the fully recruited and first dedicated SGLT2 inhibitor trial evaluating renal and cardiovascular outcomes in people with type 2 diabetes and kidney disease."

The CANVAS Program is the longest, largest and broadest completed clinical research program evaluating CV outcomes of any sodium glucose cotransporter 2 (SGLT2) inhibitor in people with T2DM to date. The CANVAS Program assessed the efficacy, safety and durability of canagliflozin in more than 10,000 patients with T2DM who had either a prior history of CV disease or at least two CV risk factors. Data from the integrated analysis of the CANVAS and CANVAS-R trials were presented last year in a special symposium at the American Diabetes Association 77th Scientific Sessions and simultaneously published in *The New England Journal of Medicine*.

WHAT IS INVOKANA®?

INVOKANA® is a prescription medicine used along with diet and exercise to lower blood sugar in adults with type 2 diabetes. 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®. 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, tongue, and throat that may cause difficulty in breathing or swallowing
- have severe kidney problems or are on 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
- **A high amount of potassium in your blood (hyperkalemia)**
- **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.

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 see full Product Information, including Boxed Warning, and Medication Guide for INVOKANA®.

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About the Janssen Pharmaceutical Companies of Johnson & Johnson

At the Janssen Pharmaceutical Companies of Johnson & Johnson, we are working to create a world without disease. Transforming lives by finding new and better ways to prevent, intercept, treat and cure disease inspires us. We bring together the best minds and pursue the most promising science.

We are Janssen. We collaborate with the world for the health of everyone in it. Learn more at www.janssen.com. Follow us at www.twitter.com/JanssenGlobal and www.twitter.com/JanssenUS. 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 31, 2017, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in the company's subsequent Quarterly Reports on Form 10-Q, and other 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 or Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

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[1] Davey P, Tully V, Willison A. All patients with diabetes should have annual UACR tests. why is that so hard? *BMJ Open Quality.* 2016 Sept. 5(1): u209185.w3747.

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