NEWS RELEASE

Janssen Submits INVOKAMET® XR (Canagliflozin / Metformin Hydrochloride Extended Release) for Approval by the U.S. FDA as an Adjunctive Treatment in Adults with Type 2 Diabetes

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RARITAN, NJ, November 20, 2015 – Janssen Research & Development, LLC (Janssen) announced today it has submitted to the U.S. Food and Drug Administration (FDA) a New Drug Application (NDA) for INVOKAMET® XR, a once-daily therapy combining fixed doses of canagliflozin and metformin hydrochloride extended release (XR) in two tablets. If approved, INVOKAMET® XR will provide a new treatment option for adults with type 2 diabetes mellitus as an adjunctive treatment to diet and exercise to improve glycemic control. INVOKAMET® XR would offer the combination of INVOKANA® (canagliflozin), the most prescribed sodium glucose co-transporter 2 (SGLT2) inhibitor in the United States, and extended release metformin, which is commonly prescribed as an initial therapy for the treatment of type 2 diabetes.

“This submission to the FDA is evidence of Janssen’s continued commitment to bringing forth new treatment options for people with type 2 diabetes,” said James List, M.D., Ph.D., Global Therapeutic Area Head, Cardiovascular & Metabolism, Janssen. “We look forward to working with the FDA to bring this combination therapy to adult patients with type 2 diabetes in need of new options.”

INVOKAMET®, the first fixed-dose combination tablet in the United States combining canagliflozin and immediate release metformin hydrochloride, received **approval** from the FDA in August 2014 for the treatment of adults with type 2 diabetes. The same formulation was approved by the European Commission (EC) in April 2014, under the

name VOKANAMET® for the treatment of adults with type 2 diabetes mellitus to improve glycemic control.

In **March 2013**, the FDA approved canagliflozin – INVOKANA® – as a single agent. In two studies comparing INVOKANA® plus metformin to current standard treatments plus metformin – one studying sitagliptin[1] and the other studying glimepiride[2] – INVOKANA® dosed at 300 mg provided greater reductions in A1C levels and body weight than either comparator. In the two studies, the overall incidence of adverse events was similar with INVOKANA® and the comparators. INVOKANA® is currently the number-one branded non-insulin type 2 diabetes medication prescribed by U.S. endocrinologists.[3] It is also the second most common branded therapy prescribed by primary care physicians when adding or switching therapies in patients.[4] Since its launch, more than six million prescriptions have been written for INVOKANA®.[5] Formulary coverage of INVOKANA® is expanding rapidly, with preferred access for 80 percent of Commercial and Medicare Part D lives in the U.S.

Janssen continues to study canagliflozin in several ongoing clinical trials. These include the CREDENCE study, evaluating the effects of canagliflozin on slowing the progression of diabetic nephropathy; the CANVAS study, evaluating the cardiovascular safety of canagliflozin; and the CANVAS-R study, evaluating the effect of canagliflozin on renal endpoints and the risk of cardiovascular events.

Janssen Pharmaceuticals, Inc. and its affiliates have rights to canagliflozin through a license agreement with Mitsubishi Tanabe Pharma Corporation. Janssen Pharmaceuticals, Inc. and its affiliates have marketing rights in Africa, parts of Asia, Australia, Europe, the Middle East, New Zealand, North America and South America.

INVOKANA® is approved as a single agent in Argentina, Aruba, Australia, Bolivia, Brazil, Canada, Chile, Colombia, Costa Rica, Curacao, Dominican Republic, El Salvador, the European Union (28 countries), Guatemala, Hong Kong, Iceland, India, Israel, Jamaica, Kazakhstan, Kuwait, Lebanon, Liechtenstein, Mexico, New Zealand, Nicaragua, Norway, Panama, Paraguay, Peru, Philippines, Qatar, Russia, Serbia, Singapore, South Korea, Switzerland, Thailand, United Arab Emirates, and the United States.

About Type 2 Diabetes

An estimated 387 million people worldwide are living with diabetes[6] and approximately 29 million people have diabetes in the United States.[7] Type 2 diabetes comprises 90 to 95 percent of cases of diabetes.[5] It is a chronic disease that affects the body's ability to metabolize sugar (glucose), and is characterized by insulin resistance and inadequate pancreatic beta cell function.

Nearly half of adults with type 2 diabetes do not achieve recommended levels of glucose control, and if left uncontrolled, type 2 diabetes can lead to serious complications.[8,9,10] Improved glycemic control has been demonstrated to reduce the onset and progression of these complications.[5]

WHAT IS INVOKAMET®?

INVOKAMET® contains two prescription medicines called canagliflozin (INVOKANA®) and metformin hydrochloride (GLUCOPHAGE®). It is used along with diet and exercise to improve blood sugar (glucose) control in adults with type 2 diabetes when treatment with either canagliflozin or metformin, or both medications, has not controlled your blood sugar. INVOKAMET® is not for people with type 1 diabetes or with diabetic ketoacidosis (increased ketones in blood or urine). It is not known if INVOKAMET® is safe and effective in children under 18 years of age.

IMPORTANT SAFETY INFORMATION

INVOKAMET® can cause serious side effects, including:

- Lactic Acidosis. Metformin, one of the medicines in INVOKAMET®, can cause a rare but serious condition called lactic acidosis (a build-up of lactic acid in the blood) that can cause death. Lactic acidosis is a medical emergency and must be treated in the hospital. Stop taking INVOKAMET® and call your doctor right away if you have any of the following symptoms which could be signs of lactic acidosis: feel very weak or tired; have unusual (not normal) muscle pain; have trouble breathing; have unusual sleepiness or sleep longer than usual; have stomach pains, nausea, or vomiting; feel dizzy or lightheaded; or have a slow/irregular heartbeat

You have a higher chance of getting lactic acidosis with INVOKAMET® if you have conditions such as: kidney problems, or your kidneys are affected by certain X-ray tests that use injectable dye; liver problems; congestive heart failure; drink alcohol very often, (or drink a lot of alcohol in short-term); get dehydrated; have surgery; have a heart attack, severe infection, or stroke; or are 80 years of age or older and have not had your kidneys tested.

Do not take INVOKAMET® if you:

- Have severe kidney problems or are on dialysis, have a condition called metabolic acidosis or diabetic ketoacidosis (increased ketones in the blood or urine). Are allergic to canagliflozin, metformin, or any of the ingredients in INVOKAMET®. See the end of the Medication Guide for a list of ingredients in INVOKAMET®. Symptoms of allergic reaction may include: rash; raised red patches on your skin (hives); swelling of the face, lips, tongue, and throat that may cause difficulty in breathing or swallowing

Before you take INVOKAMET®, tell your doctor if you: have kidney problems, have liver problems, are on a low sodium (salt) diet, have ever had an allergic reaction to INVOKAMET®, or are going to get an injection of dye or contrast agents for an X-ray procedure (INVOKAMET® will need to be stopped for a short time); have heart problems (including congestive heart failure); drink alcohol very often (or drink a lot of alcohol in short-term); or have any other medical conditions.

Tell your doctor if you are or plan to become pregnant, are breastfeeding or plan to

breastfeed. It is not known if INVOKAMET® will harm your unborn baby. It is also not known if INVOKAMET® passes into your breast milk.

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 INVOKAMET®

INVOKAMET® may cause serious side effects, including: dehydration- INVOKAMET® can cause some people to have dehydration (the loss of body water and salt), **kidney problems, a high amount of potassium in your blood (hyperkalemia), liver problems, or low blood sugar (hypoglycemia)**. If you take INVOKAMET® 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 INVOKAMET®.

Signs and symptoms of low blood sugar may include: headache, drowsiness, weakness, dizziness, confusion, irritability, hunger, fast heartbeat, sweating, shaking or feeling jittery.

Vaginal yeast infection: Women taking INVOKAMET® may get vaginal yeast infections. Symptoms include: vaginal odor, white or yellowish discharge, or vaginal itching.

Yeast infection of the penis (balanitis or balanoposthitis): Men taking INVOKAMET® may get a yeast infection of the skin around the penis. Symptoms include: redness, itching, or swelling of the penis; rash; foul smelling discharge; or pain in the skin around penis.

Serious allergic reaction: If you have any symptoms of a serious allergic reaction, stop taking INVOKAMET® 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.

Low vitamin B_{12} (vitamin B_{12} deficiency): Using metformin for long periods of time may cause a decrease in the amount of vitamin B12 in your blood. Your doctor may do blood tests to check your levels.

The most common side effects of INVOKAMET® include: urinary tract infection; changes in urination, including urgent need to urinate more often, in larger amounts, or at night; diarrhea, nausea and vomiting, gas, weakness,

indigestion, upset stomach, or headache.

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 the full **Product Information**, including Boxed Warning, and **Medication Guide**.

Canagliflozin is licensed from Mitsubishi Tanabe Pharma Corporation.

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:

- Dehydration (the loss of body water and salt), 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 kidney problems, liver problems, are on a low sodium (salt) diet, 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. It is not known if INVOKANA® will harm your unborn baby. It is also not known if INVOKANA® passes into your breast milk.

Tell your doctor about all the medicines you take, including prescription and nonprescription 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: kidney problems, a high amount of potassium in your blood (hyperkalemia), or 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®.

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The most common side effects of INVOKANA® include: vaginal yeast infections and yeast infections of the penis; urinary tract infection; or 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 the full **Prescribing Information** and **Medication Guide.**

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About Janssen Research & Development, LLC

At Janssen, we are dedicated to addressing and solving some of the most important unmet medical needs of our time in oncology, immunology, neuroscience, infectious diseases and vaccines, and cardiovascular and metabolic diseases. Driven by our commitment to patients, we develop innovative products, services and healthcare solutions to help people throughout the world. Please visit **http://www.janssen.com** for more information.

(This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding product development. 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 new product development, including the uncertainty of clinical success and of obtaining regulatory approvals; competition, including technological advances, new products and patents attained by competitors; challenges to patents; changes to applicable laws and regulations, including global health care reforms; and trends toward health care cost containment. A further list and description 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 28, 2014, including in Exhibit 99 thereto, 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 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] Lavalle-Gonzalez F, Januszewicz A, Davidson J, et al. Efficacy and safety of canagliflozin compared with placebo and sitagliptin in patients with type 2 diabetes on background metformin monotherapy: a randomised trial. Diabetologia. 2013 Dec;56(12):2582-92.

[2] Cefalu T, Leiter L, Yoon K-H, Arias P, Niskanen L, Xie J, Balis D, Canovatchel W, Meininger G. Efficacy and safety of canagliflozin versus glimepiride in patients with type 2 diabetes inadequately controlled with metformin (CANTATA-SU): 52 week results from a randomised, double-blind, phase 3 non-inferiority trial. Lancet. 2013 Sep

14;382(9896):941-50.

[3] Data on file. Based on NBRx data sourced from IMS NPA Market Dynamics Database, weekly data, showing INVOKANA® has been the leading branded non-insulin type 2 diabetes medication newly prescribed by U.S. endocrinologists for thirty one weeks, through January 2, 2015, the most recent data available at time of approval of INVOKAMET®

[4] Data on file. Based on NBRx data sourced from IMS NPA Market Dynamics Database, weekly data through January 2, 2015

[5] Data on file. Based on total prescription data sourced from IMS NPA National Database, weekly data through January 2, 2015.

[6] International Diabetes Federation, Diabetes Atlas 65th Edition 2014 Update. Available at: **http://www.idf.org/sites/default/files/Atlas-poster-2014_EN.pdf**.

[7] Centers for Disease Control and Prevention, National Diabetes Statistics Report: Estimates of Diabetes and Its Burden in the United States, 2014. Atlanta, GA: U.S. Department of Health and Human Services; 2014. Available at: **http://www.cdc.gov//diabetes/pubs/statsreport14/national-diabetes-report-web.pdf**

[8] Bailey CJ. Renal glucose reabsorption inhibitors to treat diabetes. Trends Pharmacol Sci. 2011;32(2):63-71.

[9] Casagrande SS, Fradkin JE, Saydah SH, Rust KF, Cowie CC. The prevalence of meeting A1C, blood pressure, and LDL goals among people with diabetes, 1988- 2010. Diabetes Care. 2013 Feb 15. Epub ahead of print.

[10] World Health Organization, Media Centre, Diabetes, Fact sheet Number 312. Available at: **http://www.who.int/mediacentre/factsheets/fs312/en/**. Accessed April 1, 2013.

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