NEWS RELEASE

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U.S. FDA Approves INVOKAMET® XR (Canagliflozin / Metformin Hydrochloride Extended-Release) for the Treatment of Adults with Type 2 Diabetes

Newest INVOKANA® (canagliflozin) plus metformin treatment provides unique formulation option for first-line therapy

RARITAN, N.J., September 21, 2016 – Janssen Pharmaceuticals, Inc. (Janssen) announced today the U.S. Food and Drug Administration (FDA) has approved INVOKAMET® XR—a once-daily, fixed-dose combination therapy of canagliflozin and metformin hydrochloride extended-release (XR)—for first-line use as an adjunct to diet and exercise to improve blood glucose control in adults with type 2 diabetes when treatment with the two medications is appropriate.[1] INVOKAMET® XR combines INVOKANA® (canagliflozin), the most prescribed sodium glucose co-transporter 2 (SGLT2) inhibitor, with more than 9 million U.S. prescriptions since launch,[2] and an XR formulation of metformin. Metformin is commonly prescribed as an initial therapy for the treatment of type 2 diabetes.

"INVOKAMET® XR offers the convenience of once-daily dosing and provides physicians needed flexibility for tailoring treatment to the needs of type 2 diabetes patients, especially those with higher A1C levels," said John Anderson, M.D.,* Frist Clinic, Nashville, Tenn. "As with INVOKAMET®, physicians can prescribe the XR formulation to adults when they are first diagnosed with type 2 diabetes or as additional therapy for people whose A1C levels are not well controlled with either agent alone."

Phase 3 studies have shown the combination of INVOKANA® and metformin reduces A1C significantly more than metformin alone, sitagliptin plus metformin, or glimepiride plus metformin. Treatment with INVOKANA® as an add-on to metformin also demonstrated greater reductions in the secondary endpoints of body weight and systolic blood pressure.

The approved indication for INVOKAMET® XR aligns with current type 2 diabetes treatment guidelines from the American Association of Clinical Endocrinologists and American College of Endocrinology and from the American Diabetes Association, which recommend dual therapy for patients with higher A1C levels.[3,4] Specifically, guidelines recommend dual therapy for patients who have an initial A1C level of 7.5 percent or higher[3] and for those who have an initial level below 7.5 percent and do not achieve an A1C treatment goal after about three months on single therapy, often metformin.[4] In addition, dual or triple

therapy is recommended as first-line therapy in asymptomatic patients with an initial A1C level above 9 percent.[3]

A1C is a measure of average blood glucose over the past two to three months; the American Diabetes Association recommends most adults with type 2 diabetes maintain A1C levels of 7 percent or less.[5]

“The approval of INVOKAMET® XR is further evidence of our ongoing commitment to provide new treatment options for people with type 2 diabetes,” said Paul Burton, M.D., Ph.D., Vice President, Medical Affairs, Janssen. “Our INVOKANA® portfolio now offers physicians even more choices for helping patients improve control of A1C levels and other important health measures, with numerous dosing options for monotherapy and for combination therapy with both metformin and metformin XR.”

INVOKAMET® XR is available in four dosages, in tablets containing canagliflozin 50 milligrams (mg) or 150 mg, and metformin XR 500 mg or 1000 mg. The recommended dosing is two tablets once daily with the morning meal. The prescribing information for INVOKAMET® XR also contains a boxed warning for lactic acidosis, a rare but serious complication that can occur due to metformin accumulation.[1]

Studies in healthy adults have demonstrated that administration of INVOKAMET® XR results in the same levels of canagliflozin and metformin XR in the body as when corresponding dosages of the two medicines are administered as separate tablets. Canagliflozin works with the kidneys to help adults with type 2 diabetes lose some sugar through the process of urination, and metformin decreases the production of glucose in the liver and improves the body's response to insulin. INVOKAMET® XR should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis.[1]

INVOKAMET®, the first combination of an SGLT2 inhibitor and an immediate-release formulation of metformin available in the United States, was initially approved by FDA in August 2014 as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes not adequately controlled with metformin or canagliflozin, or who are already being treated with both medications separately. In May 2016, FDA expanded the INVOKAMET® indication to include adults with type 2 diabetes who are not already being treated with canagliflozin or metformin and may benefit from dual therapy.[6]

Phase 3 Studies of Canagliflozin-Metformin Therapy

The co-administration of canagliflozin—INVOKANA®—and metformin has been evaluated in seven Phase 3 studies. One study included 1,186 adults with type 2 diabetes inadequately controlled with diet and exercise, and who had not been treated previously with any glucose-lowering medications; the six other studies included 4,732 patients with type 2 diabetes who were already taking glucose-lowering medications. Collectively, the Phase 3 studies showed that the combination of INVOKANA® and metformin lowered blood sugar and, in pre-specified secondary endpoints, was associated with greater reductions in body weight and systolic blood pressure.

The Phase 3 studies also showed that INVOKANA® is generally well-tolerated, and the most common adverse events include genital yeast infections, urinary tract infections, and changes in urination. The most common adverse reactions due to initiation of metformin, as noted in the prescribing information for that medication, are diarrhea, nausea, vomiting, flatulence, asthenia, indigestion, abdominal discomfort, and headache. Hypoglycemia does not occur in patients receiving metformin alone under usual circumstances of use. INVOKANA® can increase the risk of hypoglycemia when combined with insulin or a medication that increases insulin levels (e.g., a sulfonylurea). Therefore, a lower dose of insulin or

insulin-raising medication may be required to minimize the risk of hypoglycemia when used in combination with INVOKAMET® XR.

About Type 2 Diabetes
Of the approximately 29 million people who have diabetes in the United States, 90 to 95 percent of them have type 2 diabetes, which is chronic, affects the body's ability to metabolize sugar (glucose), and is characterized by the inability of pancreatic beta cell function to keep up with the body's demand for insulin.

WHAT IS INVOKAMET®/INVOKAMET® XR?

INVOKAMET® contains two prescription medicines called canagliflozin (INVOKANA®) and metformin hydrochloride (GLUCOPHAGE®). INVOKAMET® XR contains two prescription medicines called canagliflozin (INVOKANA®) and metformin hydrochloride extended-release (GLUMETZA®). They are used along with diet and exercise to improve blood sugar (glucose) control in adults with type 2 diabetes when treatment with both canagliflozin and metformin is appropriate. INVOKAMET®/INVOKAMET® XR is not for people with diabetic ketoacidosis (increased ketones in blood or urine). It is not known if INVOKAMET® or INVOKAMET® XR is safe and effective in children under 18 years of age.

IMPORTANT SAFETY INFORMATION

INVOKAMET®/INVOKAMET® XR can cause serious side effects, including:

- **Lactic Acidosis.** Metformin, one of the medicines in INVOKAMET®/INVOKAMET® XR, 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. **Call your doctor right away if you have any of the following symptoms, which could be signs of lactic acidosis:** feel cold in your hands or feet; 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®/INVOKAMET® XR if you have conditions such as: severe kidney problems, or your kidneys are affected by certain X-ray tests that use injectable dye; liver problems; 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.

Do not take INVOKAMET®/INVOKAMET® XR if you:

- Have moderate to severe kidney problems or are on dialysis, have conditions 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®/INVOKAMET® XR. See the end of the Medication Guide for a list of ingredients in INVOKAMET®/INVOKAMET® XR. 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®/INVOKAMET® XR, tell your doctor if you: have moderate to severe kidney problems; liver problems; have a history of urinary tract infections or problems with urination; are on a low sodium (salt) diet; have ever had an allergic reaction to INVOKAMET®/INVOKAMET® XR; are going to get an injection of dye or contrast agents for an X-ray procedure (INVOKAMET®/INVOKAMET® XR will need to be stopped for a short time); have heart problems (including congestive heart failure); 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; 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. INVOKAMET®/INVOKAMET® XR may harm your unborn baby. If you become pregnant while taking INVOKAMET®/INVOKAMET® XR, tell your doctor as soon as possible. If you are a premenopausal woman (before the "change of life"), who does not have periods regularly or at all, INVOKAMET®/INVOKAMET® XR may increase your chance of becoming pregnant. Talk to your doctor about birth control choices while taking INVOKAMET®/INVOKAMET® XR, if not planning to become pregnant. Tell your doctor right away if you become pregnant. INVOKAMET®/INVOKAMET® XR may pass into your breast milk and harm your baby. Do not breastfeed while taking INVOKAMET®/INVOKAMET® XR.

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: 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® XR

INVOKAMET®/INVOKAMET® XR may cause serious side effects, including:

- **Dehydration:** INVOKAMET®/INVOKAMET® XR can cause some people to become dehydrated (the loss of too much body water). This may cause you to feel dizzy, faint, lightheaded, or weak, especially when you stand up (orthostatic hypotension). You may be at higher risk if you have low blood pressure, take medicines to lower blood pressure, are on a low sodium (salt) diet, have kidney problems, or are 65 years of age or older. Talk to your doctor about ways to prevent dehydration
- **Ketoacidosis (increased ketones in your blood or urine)** has happened in people who have **type 1 or type 2 diabetes**, during treatment with canagliflozin. Ketoacidosis is a serious condition, which may need to be treated in a hospital. Ketoacidosis may lead to death. **Ketoacidosis can happen with INVOKAMET®/INVOKAMET® XR, even if your blood sugar is less than 250 mg/dL. Stop taking INVOKAMET®/INVOKAMET® XR 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 INVOKAMET®/INVOKAMET® XR. 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 canagliflozin, one of the medicines in INVOKAMET®/INVOKAMET® XR. 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 fever, back pain, nausea, or vomiting
- **Low blood sugar (hypoglycemia)**. If you take INVOKAMET®/INVOKAMET® XR 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 taking INVOKAMET®/INVOKAMET® XR.

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®/INVOKAMET® XR 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®/INVOKAMET® XR 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®/INVOKAMET® XR 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 INVOKAMET®/INVOKAMET® XR. 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 B_{12} in your blood. Your doctor may do blood tests to check your levels.

Other common side effects of INVOKAMET®/INVOKAMET® XR include: 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 full Product Information for INVOKAMET® and INVOKAMET® XR, including Boxed Warning, and Medication Guides for INVOKAMET® and INVOKAMET® XR.

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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. 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 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 and Medication Guide.

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About the Janssen Pharmaceutical Companies
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 @JanssenUS.

**Dr. Anderson was not compensated for any media work. He has been a paid consultant to Janssen Pharmaceuticals, Inc.*

Cautions Concerning Forward-Looking Statements

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding treatment options for people with type 2 diabetes. 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 Pharmaceuticals, Inc. 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 obtaining regulatory approvals; uncertainty of commercial success; manufacturing difficulties and delays; competition, including new products and patents attained by competitors; challenges to patents; product efficacy or safety concerns resulting in product recalls or regulatory action; 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 January 3, 2016, 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] INVOKAMET® XR (canagliflozin and metformin hydrochloride extended release) tablets, for oral use. Prescribing information, 09/2016. Janssen Pharmaceuticals, Inc., Titusville, NJ, 08560.

[2] Data on file. Janssen Pharmaceuticals, Inc. Based on IMS Health, NPA Weekly, Total Prescriptions, April 2013-July 1 2016.

[3] Garber AJ, Abrahamson MJ, Barzilay JI, et al. CONSENSUS STATEMENT BY THE AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS AND AMERICAN COLLEGE OF ENDOCRINOLOGY ON THE COMPREHENSIVE TYPE 2 DIABETES MANAGEMENT ALGORITHM - 2016 EXECUTIVE SUMMARY. Endocr Pract. 2016 Jan;22(1):84-113.

[4] American Diabetes Association. Approaches to glycemic treatment. Sec. 7. In Standards of Medical Care in Diabetesd2016. Diabetes Care 2016;39(Suppl. 1):S52–S59.

[5] American Diabetes Association. Glycemic targets. Sec. 5. In Standards of Medical Care in Diabetes – 2016. Diabetes Care 2016;39(Suppl. 1):S39–S46.

[6] INVOKAMET® (canagliflozin and metformin hydrochloride) tablets, for oral use. Prescribing information, updated 08/2016. Janssen Pharmaceuticals, Inc., Titusville, NJ, 08560.