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Studies Reinforce INVOKANA™ (canagliflozin) (300mg) Provides Greater Improvements in Blood Glucose than Sitagliptin (100 mg) or Glimepiride (6 or 8 mg) in Adults with Type 2 Diabetes

Phase 3 Results for INVOKANA™ Demonstrate Novel Type 2 Diabetes Medicine Also Provided Greater Secondary Endpoint Reductions in Weight and Systolic Blood Pressure

Note: This release corresponds to ADA abstracts 238-OR and 65-LB.

CHICAGO, JUNE 23, 2013 - Janssen Research & Development, LLC (Janssen) today announced results from a new 52-week Phase 3 clinical study, showing 300 milligrams (mg) of INVOKANA™ (canagliflozin) provided greater improvements in blood glucose control compared to a commonly prescribed therapy, sitagliptin, in adult patients with type 2 diabetes taking background metformin. The study also showed that 100 mg of INVOKANA™ provided similar improvements in blood glucose control to sitagliptin, and both doses of INVOKANA™ resulted in greater secondary endpoint reductions in body weight and blood pressure.

Results of a second Phase 3 study, also in adult patients taking metformin, showed greater improvements in blood glucose control with 300 mg INVOKANA™ and similar improvements with 100 mg INVOKANA™ compared to another commonly prescribed therapy, glimepiride, over a period of 104 weeks. Both doses of INVOKANA™ provided greater secondary endpoir reductions in body weight and blood pressure than glimepiride.

Both studies showed INVOKANA™ was generally well tolerated, with similar rates of discontinuation due to adverse events in the INVOKANA™ and comparator treatment groups. The results of the two trials were presented today and are among a total 17 presentations on INVOKANA™ at the American Diabetes Association (ADA) 73rd Annual Scientific Sessions.

"Although a variety of type 2 diabetes medications have long been available, blood glucose levels remain above recognized goals for many patients, increasing their risks for complications associated with this devastating disease," said Fernando Lavalle Gonzalez, M.D., from the Endocrinology Department, University Hospital at Universidad Autónoma de Nuevo León in Mexico, lead investigator on the sitagliptin comparison study. "These results suggest INVOKANA™ is a viable treatment optior when metformin alone or other therapies do not provide adequate glycemic control."

INVOKANA™ was approved in March of this year by the U.S. Food and Drug Administration for the treatment of adult patients with type 2 diabetes, and is the first in a new class of medications called sodium glucose co-transporter 2 (SGLT2) inhibitors available in the United States. It is also the only oral, once-daily medication available in the United States offering improved glycemic control while also showing reduced body weight and systolic blood pressure in clinical trials.

INVOKANA™ acts on the kidneys, which make an important contribution to balancing blood glucose. As glucose is filtered fror the blood into the kidneys, it is reabsorbed back into the bloodstream; SGLT2 is an important carrier responsible for this reabsorption. INVOKANA™ selectively inhibits SGLT2, promoting the loss of glucose in the urine and lowering blood glucose levels in adults with type 2 diabetes.

The INVOKANA™ recommended starting dose is 100 mg once daily. In patients tolerating the starting dose, who have an eGF of 60 mL/min/1.73 m2 or greater, and require additional glycemic control, the dose can be increased to 300 mg once daily.

Studies and Findings
In both Phase 3 studies, the change in hemoglobin A1c (A1C) was the primary efficacy endpoint. A1C is the percent of red blood cell hemoglobin with glucose attached to it and an indicator of average blood glucose over the previous two to three months. Changes in body weight and systolic blood pressure were secondary efficacy endpoints.

Results from the 52-week Phase 3 clinical study DIA3006 showed INVOKANA™ 300 mg reduced A1C levels compared to sitagliptin, one of the most commonly prescribed medications for type 2 diabetes, in adult patients with type 2 diabetes who had inadequate glycemic control on metformin therapy. Patients treated with INVOKANA™ 300 mg had statistically greater A1C lowering after 52 weeks (-0.88%) than those treated with sitagliptin (-0.73%); the decrease in A1C with INVOKANA™ 100 mg was similar to sitagliptin (-0.73% for both). INVOKANA™ 100 mg and 300 mg also resulted in significantly greater reductions ir fasting plasma glucose compared to sitagliptin (-26.2 and -35.2 vs. -17.7 mg/dL, respectively). Patients treated with INVOKANA™ 100 mg and 300 mg also had statistically greater reductions compared to sitagliptin in body weight (percent

changes of -3.8 and -4.2 vs. -1.3, respectively) and systolic blood pressure (-3.5 and -4.7 vs. -0.7 mmHg, respectively). INVOKANA™ raised HDL-C relative to sitagliptin (percent change, 11.2 and 13.3 vs. 6.0, respectively), and was associated with an increase in LDL-C (percent change, 7.7 and 8.7 vs. 6.0, respectively).

Results from the study DIA3009, the 104-week head-to-head Phase 3 comparison trial of INVOKANA™ with glimepiride, also i adult patients taking metformin, showed that INVOKANA™ 100 mg and 300 mg resulted in greater reductions than glimepiride in the primary A1C endpoint (-0.65% and -0.74% vs. -0.55%, respectively), fasting plasma glucose (-19.3 and -22.5 vs. -10.6 mg/dL, respectively), body weight (percent changes of -4.1 and -4.2 vs. +0.9, respectively), and systolic blood pressure (-2.0 and -3.1 vs. +1.7 mmHg, respectively). INVOKANA™ raised HDL-C relative to glimepiride (percent change, 9.4 and 10.1 vs. 0.8, respectively), and was associated with increases in LDL-C (percent change, 11.1 and 14.2 vs. 6.3, respectively).

In both studies, the incidence of discontinuation due to adverse events (AEs) was generally similar across treatment groups. AEs related to genital mycotic infections in men and women and AEs related to an osmotic diuresis (increased urination) were more frequent in patients taking INVOKANA™ than the other two comparators. The genital infections and osmotic diuresis-related AEs were generally mild to moderate in intensity and infrequently led to discontinuation; most genital infections responded to topical or oral antifungal therapy.

In DIA3006, the overall incidences of treatment-emergent AEs in the INVOKANA™ 100 mg, INVOKANA™ 300 mg and sitagli groups were 72%, 63% and 65%, respectively. For the pooled INVOKANA™ groups and sitagliptin group, respectively, rates c specific AEs were: genital mycotic infections, 11% and 3% (women) and 4% and 1% (men); documented hypoglycemia, 7% and 4%; AEs related to osmotic diuresis, 6% vs. 2%; urinary tract infections, 6% for both groups; AEs related to reduced renal function, 3% for both groups; and AEs related to reduced intravascular volume, 1% and 2%.

In DIA3009, the overall incidences of AEs for the INVOKANA™ 100 mg, 300 mg and glimepiride groups were 73%, 78% and 78%, respectively. The rates of specific AEs for these three groups, respectively, were: urinary tract infections, 11%, 9% and 7%; and hypoglycemia, 7%, 8% and 41%. The rates of genital mycotic infections for the pooled INVOKANA™ groups and the glimepiride group, respectively, were 15% and 3% (women) and 9% and 2% (men).

"The results presented today build on the strong evidence that supported the approval of INVOKANA™ in the United States," said Kirk Ways, M.D., Ph.D., Development Head, Cardiovascular & Metabolism and Compound Development Team Leader, Canagliflozin, Janssen Research & Development, LLC. "We are very pleased with the recent successful launch of INVOKANA™, because it reflects a rapid and wide adoption of a much-needed new therapeutic approach for adults with type 2 diabetes."

In addition to DIA3006 and DIA3009, 15 other presentations on INVOKANA™ are on the ADA Scientific Sessions program, based on data from other Phase 3 clinical trials, a health economic analysis, Phase 1 trials, and preclinical studies.

About the Studies

DIA3006 is a 52-week randomized, double-blind, active-controlled Phase 3 study in 1,284 adult patients with inadequate glycemic control on maximally effective doses of metformin. For a 26-week placebo-controlled period, patients were given once-daily doses of INVOKANA™ (100 mg or 300 mg), sitagliptin (100 mg) or placebo; in the 26-week, active-controlled period, patients taking placebo switched to sitagliptin.

To access the abstract, visit http://jnssn.us/15HsH6x and search for abstract number 238-OR.

DIA3009 is a 104-week randomized, double-blind, active-controlled Phase 3 study in 1,450 adult patients with inadequate glycemic control on maximally effective doses of metformin. Patients were given once-daily doses of INVOKANA™ (100 mg or 300 mg) or glimepiride (up to 6 or 8 mg) during a 52-week core period followed by a 52-week extension (n=1050 patients who did not require hyperglycemia rescue in the 52-week core period).

To access the abstract, visit http://jnssn.us/15HsH6x and search for abstract number 65-LB.

Results from Phase 3 studies for INVOKANA™ have been published[1, 2, 3] and presented at the American Diabetes Association (ADA) Annual Scientific Sessions in June 2012, at the European Association for the Study of Diabetes (EASD) Annual Meeting in October 2012, and at the World Congress on Controversies to Consensus in Diabetes, Obesity, and Hypertension (CODHy) in November 2012.

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

About Type 2 Diabetes

According to the International Diabetes Federation, 371 million worldwide are living with diabetes.[4] Approximately 25.8 million

people - about 8.3% of the population - have diabetes in the United States, where the disease is estimated to be the seventh leading cause of death.[5] The World Health Organization projects diabetes will be the seventh leading cause of death worldwide by 2030.[6]

The central defect of diabetes is high levels of blood glucose. Blood glucose levels are the result of orchestrated actions by a number of hormones, including insulin, incretins, glucagon, and others; and organs including the pancreas, liver, kidneys, and muscle and fat tissue.[7] The role of the kidneys in blood glucose regulation is often overlooked but is unique because, unlike any other organ, the kidneys can synthesize glucose, utilize it for fuel, return it to the bloodstream, and excrete it.[8]

Type 2 diabetes comprises 90 percent of people with diabetes[9] which is chronic and 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.

The World Health Organization estimates that 44 percent of the global diabetes burden is attributable to overweight and obesity.[10] Worldwide, an estimated one billion adults are considered overweight and another 475 million are obese.[11] In most people at risk for type 2 diabetes, obesity causes the body to resist the action of insulin, and if the pancreatic beta cell cannot produce enough insulin, hyperglycemia and type 2 diabetes ensue.

Nearly half of adults with type 2 diabetes do not achieve recommended levels of glucose control.[12,13] If left uncontrolled, type 2 diabetes can lead to serious complications.[14] Improved glycemic control has been demonstrated to reduce the onset and progression of these complications.[15]

INDICATION STATEMENT
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.
- INVOKANA™ is not for people 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

WHAT IS THE MOST IMPORTANT INFORMATION I SHOULD KNOW ABOUT INVOKANA™?
INVOKANA™ can cause important side effects, including:

- **Dehydration. INVOKANA™ can cause some people to have dehydration (the loss of body water and salt). Dehydration 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 pill)
  - are on low sodium (salt) diet
  - have kidney problems
  - are 65 years of age or older

- **Vaginal yeast infection.** Women who take INVOKANA™ may get vaginal yeast infections.

  Symptoms of a vaginal yeast infection include:
  - vaginal odor
  - white or yellowish vaginal discharge (discharge may be lumpy or look like cottage cheese)
  - vaginal itching

- **Yeast infection of the penis (balanitis or balanoposthitis).** Men who take INVOKANA™ may get a yeast infection o the skin around the penis. Certain men who are not circumcised may have swelling of the penis that makes it difficult to pull back the skin around the tip of the penis. Other symptoms of yeast infection of the penis include:
  - redness, itching, or swelling of the penis
  - rash of the penis
  - foul smelling discharge from the penis

- 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. Your doctor may suggest you use an over-the-counter antifungal medicine. Talk to your doctor right away if you use an over-the-counter antifungal medication and your symptoms do not go away.

WHO SHOULD NOT TAKE INVOKANA™?

Do not take INVOKANA™ if you:

- are allergic to canagliflozin or any of the ingredients in INVOKANA™. See the end of the Medication Guide for a list of ingredients in INVOKANA™. Symptoms of allergic reaction to INVOKANA™ 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
- have severe kidney problems or are on dialysis

WHAT SHOULD I TELL MY DOCTOR BEFORE TAKING INVOKANA™?
Before you take INVOKANA™, tell your doctor if you:

- have kidney problems
- have liver problems
- are on a low sodium (salt) diet. Your doctor may change your diet or your dose of INVOKANA™.
- have ever had an allergic reaction to INVOKANA™
- have other medical conditions
- are pregnant or plan to become pregnant. It is not known if INVOKANA™ will harm your unborn baby. If you are pregnant, talk with your doctor about the best way to control your blood sugar while you are pregnant.
- are breastfeeding or plan to breastfeed. It is not known if INVOKANA™ passes into your breast milk. Talk with your doctor about the best way to feed your baby if you are taking INVOKANA™.

Tell your doctor about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements.

INVOKANA™ may affect the way other medicines work, and other medicines may affect how INVOKANA™ works. Especially 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®, Lopinavir®) (used to treat HIV infection)
- digoxin (Lanoxin®) (used to treat heart problems)

Ask your doctor or pharmacist for a list of these medicines if you are not sure if your medicine is listed above.

Know the medicines you take. Keep a list of them and show it to your doctor and pharmacist when you get a new medicine.

HOW SHOULD I TAKE INVOKANA™?

- Take INVOKANA™ by mouth 1 time each day exactly as your doctor tells you to take it.
- Your doctor will tell you how much INVOKANA™ to take and when to take it. Your doctor may change your dose if needed.
- It is best to take INVOKANA™ before the first meal of the day.
- Your doctor may tell you to take INVOKANA™ along with other diabetes medicines. Low blood sugar can happen more often when INVOKANA™ is taken with certain other diabetes medicines. See **"What are the possible side effects of INVOKANA™?"**
- If you miss a dose, take it as soon as you remember. If it is almost time for your next dose, skip the missed dose and take the medicine at the next regularly scheduled time. Do not take two doses of INVOKANA™ at the same time. Talk to your doctor if you have questions about a missed dose.
- If you take too much INVOKANA™, call your doctor or go to the nearest hospital emergency room right away. When your body is under some types of stress, such as fever, trauma (such as a car accident), infection, or surgery, the amount of diabetes medicine you need may change. Tell your doctor right away if you have any of these conditions and follow your doctor's instructions.
- Stay on your prescribed diet and exercise program while taking INVOKANA™.

- Check your blood sugar as your doctor tells you to.
- INVOKANA™ will cause your urine to test positive for glucose.
- Your doctor may do certain blood tests before you start INVOKANA™ and during treatment as needed. Your doctor ma change your dose of INVOKANA™ based on the results of your blood tests.
- Your doctor will check your diabetes with regular blood tests, including your blood sugar levels and your hemoglobin A1C.

WHAT ARE THE POSSIBLE SIDE EFFECTS OF INVOKANA™?
INVOKANA™ may cause serious side effects, including:
See **"What is the most important information I should know about INVOKANA™?"**

- **kidney problems**
- **a high amount of potassium in your blood (hyperkalemia)**
- **low blood sugar (hypoglycemia).** If you take INVOKANA™ with another medicine that can cause low blood sugar, suc 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. See **"Who should not take INVOKANA™?"** Your doctor may give you a medicine for your allergic reaction and prescribe a different medicine for your diabetes.

The most common side effects of INVOKANA™ include:
- vaginal yeast infections and yeast infections of the penis (See **"What is the most important information I should know about INVOKANA™?"**
- urinary tract infection
- 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. These are not all the possible side effects of INVOKANA™. For more information, ask your doctor or pharmacist.

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.

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. Janssen Research & Development, LLC and Janssen Pharmaceuticals, Inc. are part of the Janssen Pharmaceutical Companies of Johnson & Johnson. Please visit http://www.janssenrnd.com for more information.

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