



**NEWS RELEASE**

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**Janssen Presents New Data Showing INVOKANA<sup>®</sup> (canagliflozin) is Associated with Greater Blood Glucose Control and Treatment Adherence Compared to DPP-4 Inhibitors**

*Other Presentations at American Diabetes Association Scientific Sessions<sup>®</sup> Show INVOKANA<sup>®</sup> Therapy also is Associated with Achieving Blood Glucose and Blood Pressure Treatment Goals*

**Note:** This release corresponds to American Diabetes Association Scientific Sessions abstracts 1155-P, 1161-P, 1174-P, 1194-P, 1224-P and 1248-P

**RARITAN, N.J., June 11, 2016** – Janssen Pharmaceuticals, Inc. (Janssen), today announced real-world and clinical findings showing that people with type 2 diabetes treated with INVOKANA<sup>®</sup> (canagliflozin) achieved greater blood glucose control and were more likely to stay on therapy than were those treated with dipeptidyl peptidase-4 (DPP-4) inhibitors, a common class of medicines for type 2 diabetes that includes Januvia<sup>®</sup> (sitagliptin). The results were from four presentations among a total of 18 related to INVOKANA<sup>®</sup>, presented at the American Diabetes Association's 76th Scientific Sessions on June 10-14 in New Orleans.

"These real-world findings provide valuable information for physicians in identifying therapeutic options with the best potential for success, which is especially important since up to half of patients with type 2 diabetes are not at treatment goals,<sup>1</sup>" said Paul Burton, M.D., Ph.D., Vice President, Medical Affairs, Janssen. "These findings show the use of INVOKANA<sup>®</sup> in people with type 2 diabetes leads to reduced A1C levels and, for many, achievement of treatment goals."

A1C, or hemoglobin 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.<sup>2</sup>

In one of the four comparative studies, patients taking INVOKANA<sup>®</sup>, a sodium glucose co-transporter 2 (SGLT2) inhibitor, were most likely to stay on therapy after nine months compared to those taking DPP-4 inhibitors, Farxiga (dapagliflozin) or glucagon-like peptide 1 (GLP-1) receptor agonists. Another analysis demonstrated INVOKANA<sup>®</sup> was associated with more time before patients needed to initiate insulin therapy compared to sitagliptin. Two other studies showed greater A1C and blood pressure control with INVOKANA<sup>®</sup> compared to sitagliptin.

“These results add to the growing body of evidence demonstrating INVOKANA<sup>®</sup> is an effective and generally well tolerated therapy in everyday clinical practice, and are in line with recent treatment guidelines that place SGLT2 inhibitors ahead of DPP-4 inhibitors for managing blood glucose control,<sup>3</sup>” said Dr. Burton. “We continue to realize the potential of INVOKANA<sup>®</sup> in supporting patients with type 2 diabetes through ongoing studies, and are excited to share these findings with physicians to optimize patient care.”

In addition to the four comparative studies, a *post-hoc* analysis of clinical trial data demonstrated use of INVOKANA<sup>®</sup> as an add-on therapy to sitagliptin and metformin helped patients achieve A1C and blood pressure treatment goals. Also, a real-world analysis showed INVOKANA<sup>®</sup> as a monotherapy was associated with reductions in A1C, good medication adherence and patients being able to reduce the number of other antihyperglycemic agents (including DPP-4 inhibitors) they take.

INVOKANA<sup>®</sup> is used along with diet and exercise to lower blood glucose in adults with type 2 diabetes. It is the number-one prescribed SGLT2 inhibitor available in the United States, with more than 8 million prescriptions written since launch. The most common side effects of INVOKANA<sup>®</sup> include genital yeast infections, urinary tract infection and changes in urination. These specific adverse events were generally mild to moderate in intensity in clinical studies.

## The Presentations

**Efficacy of Canagliflozin (CANA) Versus Dipeptidyl Peptidase-4 Inhibitors (DPP-4i) in Patients With Type 2 Diabetes Mellitus (T2DM): Results From Randomized Controlled Trials (RCTs) and a Real-World (RW) Study (Poster No. 1194-P):** William Canovatchel, M.D., Janssen Research & Development, presented findings comparing the A1C-lowering efficacy of INVOKANA<sup>®</sup> versus DPP-4 inhibitors in patients with type 2 diabetes, based on data from three randomized clinical trials (RCTs) and a retrospective RW analysis of health insurance claims and laboratory data.

The analysis showed:

- In RCTs, with patients starting with a baseline A1C of 8 percent, INVOKANA<sup>®</sup> 100 mg provided similar A1C reductions to sitagliptin 100 mg: 0.72-0.73 percent vs. 0.73-0.78 percent, respectively; INVOKANA<sup>®</sup> 300 mg provided greater reductions than sitagliptin 100 mg: 1.03 percent vs. 0.66 percent, respectively.
- In the RW study, with patients who had a baseline A1C of about 9.0 percent, greater A1C reductions were seen with INVOKANA<sup>®</sup> than with DPP-4 inhibitors: 1.07 percent vs. 0.79 percent, respectively.

The RCTs included 2,002 patients randomly assigned to add-on therapy with INVOKANA<sup>®</sup> 100 mg or 300 mg, or sitagliptin 100 mg. For the RW analysis, the investigators matched patients taking INVOKANA<sup>®</sup> (624 patients) with those taking a DPP-4 inhibitor (603 patients) based on demographics and initial clinical characteristics using a technique called propensity score matching.

**HbA1c Outcomes in Patients Treated with Canagliflozin vs. Sitagliptin in a US Health Plan (Poster No. 1224-P):** Sarah Thayer, M.A., Optum Corporation, presented an analysis of RW findings from a large US insurance claims database showing that patients taking INVOKANA<sup>®</sup> had greater reductions in A1C than those taking sitagliptin after nine months.

Specifically, the study showed that after nine months:

- INVOKANA<sup>®</sup> patients achieved significantly greater reductions in A1C than sitagliptin patients: 0.93 percent vs. 0.57 percent, respectively (p=0.004).
- In the subset of patients with baseline A1C of 7 percent or greater, the reduction with INVOKANA<sup>®</sup> was also significantly greater than with sitagliptin: 1.08 percent vs. 0.71 percent, respectively (p=0.010).

The data for the analysis were from a large US insurance claims database (Optum) and included commercial and Medicare Advantage members with type 2 diabetes and use of INVOKANA<sup>®</sup> or sitagliptin. Patients were 18 years of age or older, with six months of continuous health plan enrollment before the index date (baseline, the start of one of the two therapies), nine months after (follow-up), and had no claims for the drugs at baseline. Patients from the two therapy cohorts were matched based on demographics and initial clinical characteristics using a technique called propensity score matching.

**Comparative Persistence with Antihyperglycemic Agents (AHA) Used to Treat Type 2 Diabetes Mellitus (T2DM) in the Real World (Poster No. 1155-P):** Jennifer Cai, M.S., M.P.H., Janssen Scientific Affairs, presented an analysis of health claims data from 38,083 patients with type 2 diabetes showing persistence (staying on a therapy) in patients taking INVOKANA<sup>®</sup> was greater than in those taking dapagliflozin, DPP-4 inhibitors or glucagon-like peptide-1 (GLP-1) receptor agonists.

Specifically, the analysis showed that the following proportions of patients remained on therapy after nine months:

- INVOKANA<sup>®</sup>: Nearly 67 percent
- Dapagliflozin: 46 percent
- DPP-4 inhibitors: 47 percent to 53 percent
- GLP-1 receptor agonists: 26 percent to 50 percent

The analysis included patients with type 2 diabetes (average age 52 years) who received the first claim (index date) for the therapies analyzed from February 2014 to October 2014 in the Truven Health Analytics MarketScan<sup>®</sup> database (commercial). Continuous enrollment for six months before and nine months after the index date was required for inclusion in the analysis. Time to discontinuation and proportion of patients remaining on treatment were determined by Kaplan-Meier curves.

**Time Until Insulin Initiation for Canagliflozin (CANA) Versus Sitagliptin (SITA) in Dual Therapy and Triple Therapy for Type 2 Diabetes Mellitus (T2DM) in the UK (Poster No. 1248-P):** Melanie Schroeder, B.Sc., Janssen-Cilag Ltd, presented an analysis showing the time to insulin initiation was delayed for patients taking INVOKANA<sup>®</sup> or sitagliptin in dual and triple therapy in the UK health care setting, using economic modeling techniques.

Specifically, the modeling analysis showed INVOKANA<sup>®</sup> delayed insulin therapy initiation by 0.9 years compared to sitagliptin in dual therapy (5.7 years vs. 4.8 years, respectively), and by 1.2 years in triple therapy (5.1 years vs. 3.9 years, respectively). These delays were associated with fewer severe

hypoglycemic events with INVOKANA<sup>®</sup> (0.016 vs. 0.017 per patient-year in dual therapy and 0.048 vs. 0.057 per patient-year in triple therapy) and improved body weight profiles.

**Target Achievement and Quality Measure (QM) Attainment With Titrated Canagliflozin (CANA) in Patients With Type 2 Diabetes Mellitus (T2DM) as Add-on to Metformin (MET) + Sitagliptin (SITA) (Poster No. 1174-P):** Jochen Seufert, M.D., Ph.D., Department of Endocrinology and Diabetology, Freiburg University Hospital, presented a *post-hoc* analysis of data from a 26-week, randomized, double-blind study showing INVOKANA<sup>®</sup> add-on therapy increased the achievement of blood glucose and blood pressure treatment goals in 213 patients with type 2 diabetes inadequately controlled on metformin and sitagliptin.

At week 26, significantly more patients taking INVOKANA<sup>®</sup> vs. placebo as an add-on to metformin and sitagliptin achieved target treatment goals:

- A1C level less than 7 percent: 32.3 percent vs. 12.2 percent (p=0.001)
- A1C level less than 8 percent (a treatment goal used by Medicare and many health plans<sup>4</sup>): 70.8 percent vs. 39.0 percent (p<0.001)
- A1C levels greater than 9 percent: 11.5 percent vs. 23.2 percent (p=0.002)
- Blood pressure less than 140/90 mmHg: 86.5 percent vs. 78.3 percent (p=0.017)
- Blood pressure less than 130/80 mmHg: 54.2 percent vs. 32.5 percent (p=0.001)

In the study, patients were randomly assigned to receive add-on therapy with INVOKANA<sup>®</sup> 100 mg or placebo for six weeks. The dose of INVOKANA<sup>®</sup> (or matching placebo) was then increased (titrated up) to 300 mg/day in most patients (85.4 percent) based on criteria related to adequate kidney function, fasting blood glucose level and lack of adverse events related to volume depletion.

**Real World (RW) Glycemic Control and Medication Adherence among Patients with Type 2 Diabetes Mellitus (T2DM) Initiated on Canagliflozin (Poster No. 1161-P):** Rahul Jain, Ph.D., HealthCore, Inc., presented findings from an analysis of health claims data showing that patients with type 2 diabetes who started taking INVOKANA<sup>®</sup> achieved significant reductions in A1C over 12 months, and appeared to have good adherence (taking the medication as prescribed).

The analysis showed that, during 12 months of taking INVOKANA<sup>®</sup>:

- A1C was reduced by 0.8 percent after 12 months (baseline average A1C was 8.4 percent).
- Among patients with baseline A1C of 7 percent or greater (84 percent of patients), the reduction was 1.0 percent after 12 months.
- The mean and median proportion of days covered (PDC) by claims for INVOKANA<sup>®</sup>, used as an indicator of adherence, were 71 percent and 83 percent, respectively.
- The mean and median medication possession ratio (MPR), another indicator of adherence, were 76 percent and 88 percent, respectively.
- The mean and median number of other, background anti-hyperglycemic agents used at baseline was reduced from 2.5 at baseline to 2.3 in the follow up period.

The study included 881 adult patients with type 2 diabetes (average age: 55 years, 40 percent female) from the HealthCore Integrated Research Database.

Abstracts of all accepted presentations can be accessed on the American Diabetes Association's Scientific Sessions [website](#).

## About INVOKANA®

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<sup>5</sup> and the other studying glimepiride<sup>6</sup> – 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.<sup>7</sup> It is also the second most common branded therapy prescribed by primary care physicians when adding or switching therapies in patients.<sup>8</sup> Since its launch, more than 8 million prescriptions have been written for INVOKANA®.<sup>9</sup>

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 Aruba, Australia, 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

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 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.

## 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<sup>®</sup> 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<sup>®</sup> if you:**

- are allergic to canagliflozin or any of the ingredients in INVOKANA<sup>®</sup>. 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<sup>®</sup>, 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<sup>®</sup>; or have other medical conditions.

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

INVOKANA<sup>®</sup> may harm your unborn baby. If you become pregnant while taking INVOKANA<sup>®</sup>, tell your doctor right away. INVOKANA<sup>®</sup> may pass into your breast milk and may harm your baby. Do not breastfeed while taking INVOKANA<sup>®</sup>.

**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<sup>®</sup>, Kaletra<sup>®</sup> – used to treat HIV infection), or digoxin (Lanoxin<sup>®</sup> – used to treat heart problems).

**Possible Side Effects of INVOKANA<sup>®</sup>**

**INVOKANA<sup>®</sup> 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<sup>®</sup>. Ketoacidosis can be life-threatening and may need to be treated in a hospital. **Ketoacidosis can happen with INVOKANA<sup>®</sup> even if your blood sugar is less than 250 mg/dL. Stop taking INVOKANA<sup>®</sup> 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<sup>®</sup>. 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<sup>®</sup>. 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<sup>®</sup> 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<sup>®</sup>.

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<sup>®</sup> 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<sup>®</sup>. Talk to your doctor about factors that may increase your risk of bone fracture.

The most common side effects of INVOKANA<sup>®</sup> 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](http://www.janssen.com). Follow us at [@JanssenUS](https://twitter.com/JanssenUS).

*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 Pharmaceuticals, Inc. and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges and uncertainties inherent in product research, development and commercialization, 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 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](http://www.sec.gov), [www.jnj.com](http://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.*

## References

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- <sup>4</sup> National Committee for Quality Assurance. <http://www.ncqa.org/HEDISQualityMeasurement/HEDISMeasures.aspx>. Accessed 2015 May 7.
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- <sup>6</sup> 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.
- <sup>7</sup> Data on file. Based on NBRx data sourced from IMS NPA Market Dynamics Database, weekly data, showing INVOKANA<sup>®</sup> 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<sup>®</sup>.
- <sup>8</sup> Data on file. Based on NBRx data sourced from IMS NPA Market Dynamics Database, weekly data through January 2, 2015
- <sup>9</sup> Data on file. Janssen Pharmaceuticals, Inc. Based on IMS Health, NPA Weekly, Total Prescriptions, April 2013-April 8th 2016.