News Release
Global Media Contact:
Christina Chan
Phone: (908) 927-5769
Mobile: (908) 635-2406
cchan20@its.jnj.com

Europe Middle-East & Africa Media Contact:
Brigitte Byl
Phone: +32014607172
Mobile: +32473839426
bbyl@its.jnj.com

Investor Contacts:
Stan Panasewicz
Phone: (732) 524-2524

Louise Mehrotra
Phone: (732) 524-6491

Latest Phase 3 Results Demonstrate Safety and Efficacy Profile of INVOKANA® (canagliflozin) as Add-On Therapy in the Treatment of Type 2 Diabetes in Adults

In patients inadequately controlled on metformin and a sulfonylurea, study results suggest canagliflozin improves glycemic control and was generally well tolerated, compared to placebo

Note: This press release corresponds to EASD abstract #934.

BARCELONA, SPAIN, September 24, 2013 – Janssen Research & Development, LLC (Janssen) today announced results from a new 52-week analysis of Phase 3 results showing INVOKANA® (canagliflozin) provided substantial improvements in glycemic control in patients with type 2 diabetes who are inadequately controlled on metformin and a sulfonylurea, two of the most commonly used antihyperglycemic therapies. These results are among a total of 12 abstracts for canagliflozin being presented at the 49th European Association for the Study of Diabetes (EASD) Annual Meeting in Barcelona, Spain.

“Patients can experience difficulty in attaining and maintaining the levels of blood glucose recommended by their physician, despite treatment with commonly-used and available agents. These results provide evidence that canagliflozin may be an effective and generally well-tolerated option that provides glycemic improvements when used with metformin and a sulfonylurea,” said Guillame Charpentier, MD, Head of the Department of Diabetes at the Sud-Francilien Hospital in France, and one of the authors for these results presented at EASD.

Results from the 52-week study (known as DIA3002) showed that canagliflozin, at both the 100 mg and 300 mg doses, lowered glucose levels and provided greater reductions in secondary endpoints of body weight and blood pressure compared to placebo.

“We are pleased to share the 52-week data from this pivotal Phase 3 trial which provide additional insight on the persistence of response seen in patients with type 2 diabetes, particularly in patients who are inadequately controlled,” said Norman Rosenthal, MD, FACE, FACP, Compound Development Team Leader for canagliflozin at Janssen. “These and other data presented at EASD support the emerging safety, efficacy and tolerability profile of canagliflozin.”

Canagliflozin is currently undergoing review with a number of regulatory authorities. The Committee for Medicinal Products for Human Use of the European Medicines Agency adopted a positive opinion recommending the use of canagliflozin for the treatment of adult patients with type 2 diabetes. In the United States, canagliflozin was approved with the brand name INVOKANA® in March 2013 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 U.S.

Study Details and Findings

DIA3002 is a 52-week randomized, double-blind, placebo-controlled Phase 3 study in 469 adult patients with inadequate glycemic control on maximally effective doses of metformin and a sulfonylurea. During a 26-week core period, patients randomized to one of the three study arms and were given once-daily doses of canagliflozin 100 mg, 300 mg, or placebo. A 26-week extension period followed, with patients continuing on assigned therapy.

Results on blood glucose levels were measured by changes in baseline hemoglobin A1c (A1C), an indicator of average blood glucose during the previous two to three months. Secondary efficacy endpoints include changes in fasting plasma glucose, systolic blood pressure, body weight and fasting plasma lipids, and the proportion of patients with A1C levels less than 7 percent.

Patients treated with canagliflozin 100 mg and 300 mg experienced a statistically significant and clinically important decrease in A1C levels compared to placebo after 52 weeks (percent changes, -0.74 and -0.96 vs. 0.01, respectively). Canagliflozin 100 mg and 300 mg also resulted in significant reductions compared to placebo in fasting plasma glucose (-1.1 and -1.5 mmol/L vs. 0.6 mmol/L, respectively) and body weight (percent changes, -2.2 and -3.2 vs. -0.9, respectively). Systolic blood pressure was reduced with canagliflozin 100 mg and 300 mg (-3.7 and -2.9 mmHg vs. 0.1 mmHg, respectively). Increases in high-density lipoprotein cholesterol (HDL-C) were seen with canagliflozin 100 mg and 300 mg relative to placebo (percent changes 6.6 and 8.2 vs. 3.3, respectively); increases in low-density lipoprotein cholesterol (LDL-C) were seen with canagliflozin 300 mg (percent change, 13.3) while the results with the 100 mg dose were similar to placebo (percent change, 4.8 vs. 5.4, respectively).
The overall incidence of treatment-emergent adverse events (AEs) was slightly lower with canagliflozin 100 mg (67.5 percent) than canagliflozin 300 mg and placebo (73.1 percent and 71.2 percent,

respectively). The incidence of serious AEs was lower with canagliflozin 100 mg and 300 mg than placebo (4.5 percent and 5.1 percent vs. 8.3 percent); discontinuations due to AEs were higher in the canagliflozin 100 mg and 300 mg groups than in the placebo group (7.0 percent and 7.7 percent vs. 4.5 percent, respectively).

The following AEs were more frequent in the canagliflozin 100 mg and 300 mg groups compared to placebo, respectively: AEs related to genital mycotic infections in men (7.9 percent and 5.7 percent vs. 1.3 percent) and women (18.5 percent and 18.8 percent vs. 5.0 percent); AEs related to osmotic diuresis (increased urination) 5.7 percent and 7.1 percent vs. 1.9 percent; and AEs related to reduced intravascular volume, 0.6 percent and 3.8 percent vs. 1.9 percent. 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. Rates of urinary tract infections were higher with canagliflozin 100 mg and 300 mg compared to placebo (8.3 percent for both compared to 7.7 percent). Rates of documented hypoglycemia for canagliflozin 100 mg, 300 mg and placebo were 33.8 percent, 36.5 percent and 17.9 percent, respectively.

To view the corresponding abstract, visit the EASD Virtual Meeting and search for abstract number 934.

Results from Phase 3 studies for canagliflozin have been published[1, 2, 3] and presented at the American Diabetes Association (ADA) Annual Scientific Sessions in June 2012 and June 2013, 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 canagliflozin through a license agreement with Mitsubishi Tanabe Pharma Corporation. 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, there are 371 million people worldwide living with diabetes.[4] An estimated 55 million people in Europe have diabetes, with 36.8 percent undiagnosed.[4] Approximately 25.8 million people - about 8.3 percent 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 cells 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]

About INVOKANA® (canagliflozin)

Canagliflozin is an investigational, oral medication for the treatment of adult patients with type 2 diabetes. The kidneys of people with type 2 diabetes reabsorb greater amounts of glucose back into the body compared to people without diabetes, which may contribute to elevated glucose levels in the blood.[16] Canagliflozin, a selective sodium glucose co-transporter 2 (SGLT2) inhibitor, blocks the reabsorption of glucose by the kidney, increasing glucose excretion and lowering blood glucose levels.[17]

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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