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## **Canagliflozin Provided Substantial and Sustained Glycemic Improvements as Monotherapy and in Add-On Combinations in Adults with Type 2 Diabetes in Five Phase 3 Studies**

### **Canagliflozin Provides Greater Reduction of A1C Levels in Adults with Type 2 Diabetes in 52-Week Head-to-Head Studies Compared to Sitagliptin and Glimepiride**

**PHILADELPHIA, JUNE 9, 2012** - Janssen Research & Development, LLC (Janssen) presented results from five Phase 3 clinical studies evaluating canagliflozin in monotherapy and in add-on combination use showing that canagliflozin provided substantial and sustained glycemic improvements in adult patients with type 2 diabetes, and was generally well tolerated. In two of these studies comparing canagliflozin to current standard treatments, sitagliptin and glimepiride, canagliflozin dosed once-daily at 300 mg provided significantly greater reductions in A1C levels relative to both comparators with similar overall incidence of adverse events. These studies were presented today as late-breaking poster presentations at the 72<sup>nd</sup> American Diabetes Association (ADA) Annual Scientific Sessions.

Canagliflozin is an investigational sodium glucose co-transporter 2 (SGLT2) inhibitor for the treatment of patients with type 2 diabetes. The kidneys of people with type 2 diabetes reabsorb greater amounts of glucose back into the body compared to non-diabetic people, which may contribute to elevated glucose levels. Canagliflozin blocks the reabsorption of glucose by the kidney, increasing glucose excretion and lowering blood glucose levels.

"Type 2 diabetes is a chronic condition that over time may require the use of combinations of antihyperglycemic agents, including insulin, to maintain optimal glycemic control which is a primary goal of treatment," said William T. Cefalu, M.D., Chief of the Joint Program on Diabetes, Endocrinology and Metabolism of the Pennington Biomedical Research Center and Louisiana State University Health Sciences Center School of Medicine, and lead investigator on the DIA3009 study. "The sustained glucose control and low rate of occurrence of hypoglycemia shown with canagliflozin, an SGLT2 inhibitor, as compared to glimepiride when evaluated over a 52-week period in this comparative study are very promising. When combined with the other clinical benefits, the data suggests that this class of agents may provide an additional and valuable treatment option for people with type 2 diabetes."

The global Phase 3 canagliflozin clinical program enrolled more than 10,300 patients in nine studies, and is the largest late-stage development program for an investigational pharmacologic product for the treatment of type 2 diabetes submitted to health authorities to date. The Phase 3 clinical program evaluated the safety and efficacy of canagliflozin across the spectrum of type 2 diabetes management, from adult patients treated only with diet and exercise to those requiring insulin injections to maintain glycemic control. The program also included three large studies in special populations: older patients with type 2 diabetes, patients with type 2 diabetes who had moderate renal impairment, and patients with type 2 diabetes who have or were considered to be at high risk for cardiovascular disease. On May 31, 2012, Janssen submitted a New Drug Application to the U.S. Food and Drug Administration seeking approval for the use of canagliflozin as a treatment for adult patients with type 2 diabetes.

"The results in each of these studies suggest that canagliflozin could provide an effective therapeutic option for adults with type 2 diabetes in a range of clinical settings," said Kirk Ways, M.D., Ph.D., Vice President and Compound Development Team Leader for canagliflozin at Janssen. "Canagliflozin has the potential to be administered as monotherapy in patients who are inadequately controlled with diet and exercise alone, as an add-on therapy in patients being treated with metformin alone or in combination with sulfonylureas, and in patients with moderate renal impairment. As part of our commitment to develop new therapeutic options for unmet patient needs in the treatment of type 2 diabetes, we look forward to presenting data from the remaining Phase 3 canagliflozin clinical trials in the near future."

#### **About the Studies**

**DIA3015** is a 52-week randomized, double-blind, active-controlled Phase 3 study in 755 adult patients with inadequate glycemic control on maximally effective doses of metformin and sulfonylurea. Patients were given once-daily doses of canagliflozin (300 mg) or sitagliptin (100 mg). Patients treated with canagliflozin had a substantial and sustained decrease in A1C levels, with a significantly greater reduction relative to sitagliptin after 52 weeks (-0.37, 95% CI -0.50; -0.25). Based on protocol-specified withdrawal criteria, more subjects discontinued from the study due to loss of glycemic control in the sitagliptin treatment arm (22.5%) than the canagliflozin arm (10.6%). In the key secondary endpoint measures, patients treated with canagliflozin 300 mg also had greater weight loss compared to sitagliptin (percent changes of -2.5 and 0.3, respectively); reductions in fasting plasma glucose changes were consistent with the primary A1C endpoint (-29.9 and -5.9 mg/dL, respectively); systolic blood pressure was reduced with canagliflozin (-5.1 and 0.9 mmHg, respectively). Canagliflozin raised HDL-C relative to sitagliptin (% change, 7.6 and 0.6, respectively), and also LDL-C (% change 11.7 and 5.2, respectively).

The overall incidence of treatment-emergent adverse events (AEs) was similar in the canagliflozin (76.7%) and sitagliptin (77.5%) groups. The incidence of serious AEs were low and similar in both groups (6.4% and 5.6%, and respectively, in the canagliflozin and sitagliptin groups); discontinuations due to AEs were low in both groups but higher in the canagliflozin than in the sitagliptin group (5.3%, and 2.9%, respectively). AEs related to genital mycotic infections in men and women, and AEs related to an osmotic diuresis such as increased urination, were more frequent in patients treated with canagliflozin than sitagliptin; a similar incidence of urinary tract infections was seen in the two treatment groups. 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. A similar incidence of hypoglycemic episodes was reported with canagliflozin and sitagliptin.

To access the abstract, visit <http://www.abstractsonline.com/plan/start.aspx?mkey=%7B0F70410F-8DF3-49F5-A63D-3165359F5371%7D> and search for abstract number 50-LB.

**DIA3009** is a 52-week randomized, double-blind, active-controlled Phase 3 trial in 1,450 adult patients with inadequate glycemic control on maximally effective doses of metformin. Patients were randomized and treated once daily with either canagliflozin (100 mg or 300 mg) or glimepiride (with up-titration of glimepiride allowed throughout the 52-week period). Patients treated with canagliflozin had a sustained decrease in A1C, with statistically greater A1C-lowering for canagliflozin 300 mg after 52 weeks when compared to glimepiride (-0.93% and -0.81%, respectively, with the between group difference of -0.12%, 95% CI -0.22; -0.02); the decrease in A1C with canagliflozin 100 mg (-0.82%) was similar to that for glimepiride (between group difference of -0.01%, 95% CI -0.11; 0.09). In the key secondary endpoint measures, both the 300 mg and 100 mg canagliflozin dose groups provided reductions in body weight, with no notable change in the glimepiride group (body weight % change, -4.7 and -4.2 and 1.0, respectively). Hypoglycemia episodes occurred at a low incidence with canagliflozin 300 mg and 100 mg, and at a higher incidence with glimepiride (% of patients with 1 or more episodes: 4.9 and 5.6 and 34.2, respectively). Reductions in fasting plasma glucose were consistent with the primary endpoint for canagliflozin 300 mg and 100 mg and glimepiride (-27.5 and -24.3 and -18.3 mg/dL, respectively); other secondary endpoints included reductions in systolic blood pressure with both doses of canagliflozin and no notable change with glimepiride (-4.6 and -3.3 and 0.2 mmHg, respectively); HDL-C increased with both 300 mg and 100 mg doses of canagliflozin, with no notable change with glimepiride (% change, 9.0 and 7.9 and 0.3, respectively); LDL-C rose with both doses of canagliflozin more than with glimepiride (% change, 14.1 and 9.6 and 5.0, respectively).

The incidence of AEs and discontinuations due to AEs were generally similar across all treatment arms. AEs were mild to moderate and the overall incidence was balanced across treatment arms. Adverse events related to osmotic diuresis such as increased urination, genital mycotic infections in men and women, and urinary tract infections were more frequent in patients treated with canagliflozin than glimepiride; these specific adverse events were generally mild or moderate in intensity and infrequently led to discontinuation.

To access the abstract, visit <http://www.abstractsonline.com/plan/start.aspx?mkey=%7B0F70410F-8DF3-49F5-A63D-3165359F5371%7D> and search for abstract number 38-LB.

Janssen presented results from three additional Phase 3 studies at this year's ADA meeting, which also demonstrate the potential value of canagliflozin across the spectrum of type 2 diabetes management including use in monotherapy, in add-on combination, and in patients with moderate renal impairment.

- "Canagliflozin, a Sodium Glucose Co-Transporter 2 Inhibitor, Improves Glycemia and is Well Tolerated in Type 2 Diabetes Mellitus Subjects with Moderate Renal Impairment" on June 10 (<http://www.abstractsonline.com/plan/start.aspx?mkey=%7B0F70410F-8DF3-49F5-A63D-3165359F5371%7D>, abstract 41-LB).
- "Canagliflozin, a Sodium Glucose Co-Transporter 2 Inhibitor, Improves Glycemic Control and Lowers Body Weight in Subjects With Type 2 Diabetes Inadequately Controlled With Diet and Exercise" on June 9 (<http://www.abstractsonline.com/plan/start.aspx?mkey=%7B0F70410F-8DF3-49F5-A63D-3165359F5371%7D>, abstract 81-OR).
- "Canagliflozin, a Sodium Glucose Co-Transporter 2 Inhibitor, Improves Glycemic Control and Reduces Body Weight in Subjects with Type 2 Diabetes Inadequately Controlled With Metformin and Sulfonylurea" on June 9 (<http://www.abstractsonline.com/plan/start.aspx?mkey=%7B0F70410F-8DF3-49F5-A63D-3165359F5371%7D>, abstract 1022-P).

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#### **About Janssen Research & Development, LLC**

Janssen Research & Development, LLC is headquartered in Raritan, N.J. and has affiliated facilities in Europe, the United States and Asia. Janssen Research & Development is leveraging a combination of internal and external innovation to discover and develop novel medicines and solutions in five distinct therapeutic areas: Neuroscience, Oncology, Immunology, Infectious Diseases and Vaccines, and Cardiovascular and Metabolism. For more information about Janssen Research & Development,

LLC, visit [www.janssenrnd.com](http://www.janssenrnd.com).

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