

Dapagliflozin As Add On Therapy To Insulin Demonstrated Improved Glycemic Control in Patients With Type 2 Diabetes Inadequately Controlled With Insulin

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(ORLANDO, FL, June 26, 2010) - Results from a 24-week Phase 3 clinical study demonstrated that the addition of the investigational drug dapagliflozin achieved reductions in the primary endpoint, glycosylated hemoglobin level (HbA1c), in inadequately controlled type 2 diabetes patients who were treated with insulin (with or without oral anti-diabetes medications (OADs)), compared to placebo plus insulin (with or without OADs). The study also demonstrated that dapagliflozin achieved reductions in the secondary endpoints that evaluated the change in total body weight from baseline, change from baseline in mean daily insulin dose, and change from baseline in fasting plasma glucose (FPG). Generally, adverse events, serious adverse events and study discontinuations were similar across all treatment groups. Signs, symptoms and other reports suggestive of urinary tract and genital infections were more frequently noted in the dapagliflozin treatment arms compared to placebo and rarely led to discontinuation. Results from the 24-week study were presented at the 70th American Diabetes Association (ADA) Annual Scientific Sessions.

Dapagliflozin, an investigational compound, is a potential first-in-class sodium-glucose cotransporter-2 (SGLT2) inhibitor currently in Phase 3 trials under joint development by [Bristol-Myers Squibb Company](#) (NYSE: BMY) and [AstraZeneca](#) (LSN, NYSE: AZN) as a once-daily oral therapy for the treatment of adult patients with type 2 diabetes. SGLT2 inhibitors facilitate the elimination of glucose by the kidney, which should result in lowering serum glucose levels.

“Many type 2 diabetes patients who are treated with insulin are not able to achieve their blood sugar goals,” said John Wilding, DM, FRCP, Professor of Medicine and Honorary Consultant Physician, Head of Diabetes and Endocrinology Clinical Research Unit, University Hospital Aintree (UK). “The Phase 3 data on glycemic and weight parameters presented today suggest that further study of dapagliflozin in this patient population is warranted.”

Data from the 48 week follow-up of the same study will be presented as a late breaker at the ADA Scientific Sessions.

About the Study

The study was a randomized, double-blind, placebo-controlled study of 800 individuals

with type 2 diabetes (ages 18 – 80) and inadequate glycemic control whose HbA1c level was greater than or equal to 7.5% and less than or equal to 10.5% at baseline, with a mean baseline HbA1c level of 8.5%. The study was designed to assess the efficacy and safety of dapagliflozin in patients with inadequately controlled type 2 diabetes receiving treatment with a mean insulin dose of greater than or equal to 30 IU for at least 8 weeks (mean baseline dose: 77 IU per day) with or without concomitant OADs. Individuals were equally randomized to one of four separate treatment groups: dapagliflozin 2.5 mg (n= 202), dapagliflozin 5 mg (n= 211), dapagliflozin 10 mg (n= 194), or placebo (n= 193).

The primary endpoint of the study compared mean HbA1c change from baseline for each dapagliflozin treatment arm compared to placebo after 24 weeks. Secondary endpoints included change in body weight from baseline, change from baseline in mean daily insulin dose, and change from baseline in fasting plasma glucose (FPG).

Study Results

After 24 weeks, individuals receiving dapagliflozin 2.5 mg, 5 mg and 10 mg demonstrated a statistically significant adjusted mean change in HbA1c from baseline of -0.75%, -0.82% and -0.90%, respectively, compared to -0.30% for placebo (p-value less than or equal to 0.0001 for all treatment groups).

The study also evaluated the potential impact of dapagliflozin on total body weight at week 24. At week 24, the study found that individuals treated with dapagliflozin demonstrated an adjusted mean change in total body weight: -0.98 kg for dapagliflozin 2.5 mg, -0.98 kg for dapagliflozin 5 mg and -1.67 kg for dapagliflozin 10 mg, compared to a weight gain of 0.02 kg for placebo (p-value less than or equal to 0.0001 for all treatment groups).

Individuals treated with dapagliflozin also demonstrated a reduction in daily insulin dose at week 24: -1.80 IU/d for dapagliflozin 2.5 mg, -0.61 IU/d for dapagliflozin 5 mg and -1.16 IU/d for dapagliflozin 10 mg, compared to an increase of 5.08 IU/d for placebo (p-value less than or equal to 0.0001 for all treatment groups).

Individuals treated with dapagliflozin demonstrated a reduction in FPG, a secondary endpoint, from baseline at week 24: -12.5 mg/dL for dapagliflozin 2.5 mg, -18.8 mg/dL for dapagliflozin 5 mg and -21.7 mg/dL for dapagliflozin 10 mg, compared to an increase of 3.3 mg/dL for placebo (p-value equal to 0.0008 for dapagliflozin 2.5 mg; p-value less than or

equal to 0.0001 for dapagliflozin 10 mg. (Note that due to the study testing procedure, the p-value for dapagliflozin 5 mg could not be assessed).

Generally, adverse events, serious adverse events and study discontinuations were similar across all treatment groups. The percentage of patients experiencing the most common adverse events (greater than or equal to 5 %) for dapagliflozin 2.5 mg, 5 mg 10 mg, and placebo, respectively are as follows: nasopharyngitis: 13.9%, 13.7%, 8.7%, 11.2%; hypertension: 5.4%, 6.1%, 3.6%, 7.6%; headache: 4.0%, 4.2%, 1.0%, 7.1%; back pain: 4.5%, 1.9%, 4.6%, 5.1%; upper respiratory tract infection: 2.5%, 2.8%, 3.1%, 5.1%.

The percentage of patients with signs, symptoms and other reports suggestive of urinary tract and genital infections were higher for the dapagliflozin treatment arms compared to placebo. Events suggestive of urinary tract infections were as follows: 5.9%, 7.5%, 7.7% with dapagliflozin 2.5 mg, 5 mg and 10 mg respectively, versus 2.0% with placebo. Events suggestive of genital infections were as follows: 5.4%, 8.0%, 9.2% with dapagliflozin 2.5 mg, 5 mg and 10 mg respectively, versus 2.0% with placebo.

Reports of hypoglycemia observed in the dapagliflozin treatment groups compared to placebo were 55% for dapagliflozin 2.5 mg, 47.6% for dapagliflozin 5 mg, 44.9% for dapagliflozin 10 mg and 42.1% for placebo. Of these hypoglycemic events, 1% were major and were equally distributed across groups.

Reductions in blood pressure were observed without associated signs of orthostatic hypotension.

About Type 2 Diabetes

Type 2 diabetes (diabetes mellitus) is a complex, progressive disease characterized by elevated glucose which is frequently associated with other co-morbidities such as obesity, hypertension and dyslipidemia. Significant unmet needs exist as nearly half of the patients remain uncontrolled on their current treatment regimen.

The kidneys play a key but underappreciated role in the overall regulation of blood glucose levels in the body. Normally, in healthy individuals, the kidneys filter a large volume of glucose and actively reabsorb virtually all of it. Glucose reabsorption is necessary to retain calories, but becomes counterproductive in type 2 diabetes. In patients with type 2 diabetes who have hyperglycemia, a greater amount of glucose is filtered and reabsorbed by the kidneys, which contributes to sustained hyperglycemia in diabetes.

Over time, sustained hyperglycemia worsens insulin resistance and contributes to dysfunction in the beta cells of the pancreas further undermining control of the disease. Sustained hyperglycemia is also directly related to diabetic microvascular complications such as blindness and may also contribute to macrovascular complications.

About SGLT2 Inhibition

The kidney continuously filters glucose through the glomerulus; however, nearly all of this glucose is reabsorbed. A protein called SGLT2 is responsible for the majority of glucose reabsorption and helps the body retain glucose for its energy requirements. For patients with diabetes, retention of excess glucose by this pathway contributes to persistent hyperglycemia. Suppressing the activity of SGLT2 inhibits renal-glucose reabsorption in the body, thereby leading to the excretion of glucose in the urine.

Bristol-Myers Squibb and AstraZeneca Collaboration

Bristol-Myers Squibb and AstraZeneca entered into a collaboration in January 2007 to enable the companies to research, develop and commercialize select investigational drugs for type 2 diabetes. The Bristol-Myers Squibb/AstraZeneca Diabetes collaboration is dedicated to global patient care, improving patient outcomes and creating a new vision for the treatment of type 2 diabetes.

About Bristol-Myers Squibb

Bristol-Myers Squibb is a global biopharmaceutical company whose mission is to discover, develop and deliver innovative medicines that help patients prevail over serious diseases. For more information about Bristol-Myers Squibb, visit www.bms.com or follow us on Twitter at <http://twitter.com/bmsnews>.

This press release contains "forward-looking statements" as that term is defined in the Private Securities Litigation Reform Act of 1995 regarding product development. Such forward-looking statements are based on current expectations and involve inherent risks and uncertainties, including factors that could delay, divert or change any of them, and could cause actual outcomes and results to differ materially from current expectations. No forward-looking statement can be guaranteed. Among other risks, there can be no guarantee that dapagliflozin

will receive regulatory approval or, if approved, that it will become a commercially successful product. Forward-looking statements in this press release should be evaluated together with the many uncertainties that affect Bristol-Myers Squibb's business, particularly those identified in the cautionary factors discussion in Bristol-Myers Squibb's Annual Report on Form 10-K for the year ended December 31, 2009, in our Quarterly Reports on Form 10-Q and our Current Reports on Form 8-K. Bristol-Myers Squibb undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise.

About AstraZeneca

AstraZeneca is a global, innovation-driven biopharmaceutical business with a primary focus on the discovery, development and commercialization of prescription medicines. As a leader in gastrointestinal, cardiovascular, neuroscience, respiratory and inflammation, oncology and infectious disease medicines, AstraZeneca generated global revenues of \$32.8 billion in 2009. In the United States, AstraZeneca is a \$14.8 billion healthcare business.

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