

52-Week Study Finds ONGLYZA™ (saxagliptin) When Added To Metformin Was Non-Inferior To Titrated Glipizide When Added To Metformin In Reducing Glycosylated Hemoglobin (HbA1c) In Adults With Type 2 Diabetes Mellitus

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(ORLANDO, FL, June 26, 2010) -- [Bristol-Myers Squibb Company](#) (NYSE: BMY) and [AstraZeneca](#) (NYSE: AZN) today announced results from a 52-week Phase 3b study in adults with type 2 diabetes who had inadequate glycemic control on metformin therapy plus diet and exercise. This study found that the addition of [ONGLYZA™](#) (saxagliptin) 5 mg to existing metformin therapy achieved the primary objective of demonstrating non-inferiority compared to the addition of titrated glipizide (sulphonylurea) to existing metformin therapy in reducing glycosylated hemoglobin levels (HbA1c). Glipizide 5 mg was titrated as required to 20 mg (mean dose 14.7 mg). The final dose in two-thirds of glipizide-treated patients was 15 mg or greater, requiring two or more dosage titrations. Additionally, the study found that treatment with ONGLYZA 5 mg plus metformin resulted in a statistically significant lower proportion of subjects reporting hypoglycemic events and statistically significant weight loss compared to titrated glipizide plus metformin. ONGLYZA 5 mg plus metformin also resulted in a significantly smaller rise per week in HbA1c from week 24 to week 52 compared to titrated glipizide plus metformin. Overall adverse events excluding hypoglycemia were reported at a similar rate between the two treatment groups. Results were presented at the 70th American Diabetes Association (ADA) Annual Scientific Sessions.

“Many adult patients with type 2 diabetes need more than one therapy to help improve glycemic control, and the data presented today adds to the body of evidence for ONGLYZA,” said Burkhard Göke, MD, Professor of Internal Medicine, University Hospital Munich, Germany.

ONGLYZA has been submitted for regulatory review in more than 58 countries and is approved in 43 countries, including the United States, Canada, Mexico, 30 EU countries, Chile, India, Brazil, Argentina and Switzerland. ONGLYZA was approved by the FDA in July 2009 and is indicated as an adjunct to diet and exercise to improve blood sugar (glycemic) control in adults for the treatment of type 2 diabetes mellitus. ONGLYZA once daily can be used in combination with commonly prescribed oral anti-diabetic medications – metformin, glyburide (a sulphonylurea) or a thiazolidinedione (TZD) (pioglitazone or rosiglitazone), – or as a

monotherapy to significantly reduce HbA1c levels. ONGLYZA (saxagliptin) should not be used for the treatment of type 1 diabetes or for the treatment of diabetic ketoacidosis (high levels of certain acids, known as ketones, in the blood or urine). ONGLYZA has not been studied in combination with insulin.

About The Study: Saxagliptin Added to Metformin vs. Titrated Glipizide Added to Metformin

The study was a 52-week, international, multicenter, randomized, parallel-group, double-blind, active-controlled Phase 3b study of 858 patients with type 2 diabetes (aged ≥ 18) whose HbA1c was greater than 6.5% and less than or equal to 10% at baseline. The study was designed to assess the efficacy and safety of ONGLYZA 5 mg per day compared to glipizide 5 mg, titrated as required to 20 mg as added to a stable dose of metformin (greater than or equal to 1,500 mg per day) in adult patients with type 2 diabetes who did not achieve adequate glycemic control with metformin alone. Individuals were randomized to one of two treatment groups: ONGLYZA 5 mg once daily plus metformin (n=428) or glipizide 5 mg (titrated as required to 20 mg) plus metformin (n=430).

The primary endpoint of the study was to assess whether the change from baseline in HbA1c achieved with ONGLYZA 5 mg was non-inferior to titrated glipizide (defined in the study protocol as a treatment group numerical difference in the HbA1c reduction of less than 0.35% for the upper limit of the two-sided 95% confidence interval [CI]) when both were added to a stable dose of metformin. Key secondary endpoints included the proportion of patients reporting at least one episode of a hypoglycemic event at week 52, change from baseline in body weight at week 52 and durability of HbA1c effect based on change per week in HbA1c from week 24 to week 52.

Study Results

The mean dose of titrated glipizide was 14.7 mg and the median dose 20 mg. Using the per-protocol analysis, after 52 weeks, individuals taking ONGLYZA 5 mg plus metformin achieved an adjusted mean change from baseline in HbA1c of -0.74%, compared to -0.80% for titrated glipizide plus metformin. Results of the study demonstrated that therapy with ONGLYZA 5 mg was non-inferior to titrated glipizide when added to existing metformin

therapy (difference in adjusted mean change from baseline vs. titrated glipizide as added to existing metformin therapy was 0.06%, 95% CI -0.05 to 0.16). Non-inferiority of ONGLYZA (saxagliptin) 5 mg to titrated glipizide was also demonstrated in a confirmatory analysis of all individuals receiving study treatment for whom HbA1c data were available.

The number of individuals with any hypoglycemic event was significantly lower for patients treated with ONGLYZA 5 mg plus metformin as compared to those treated with titrated glipizide plus metformin (3 % for ONGLYZA plus metformin vs. 36.3 % for titrated glipizide plus metformin; p-value less than 0.0001) at week 52.

The study also demonstrated that patients treated with ONGLYZA 5 mg plus metformin experienced a statistically significant weight decrease when compared to those treated with titrated glipizide plus metformin (-1.1 kg for ONGLYZA 5 mg plus metformin vs. +1.1 kg for titrated glipizide plus metformin; p-value less than 0.0001) at week 52.

While both treatment groups exhibited slight increases in HbA1c from week 24 to week 52, the study demonstrated that patients treated with ONGLYZA had a smaller rise per week in HbA1c compared to those treated with titrated glipizide (0.001% for ONGLYZA plus metformin vs. 0.004% for titrated glipizide plus metformin; p-value equal to 0.04) at week 52.

The number of individuals experiencing adverse events or serious adverse events after 52 weeks between the two treatment groups were as follows (excluding hypoglycemia): adverse events: 60.0% for ONGLYZA 5 mg plus metformin, 56.7% for titrated glipizide plus metformin; serious adverse events: 9.1% for ONGLYZA 5 mg plus metformin, 7.4% for titrated glipizide plus metformin. The most common adverse events (greater than or equal to 5% and observed more frequently in the ONGLYZA 5 mg treatment group compared to the titrated glipizide treatment group) were nasopharyngitis (9.6% vs. 8.6%, respectively) and diarrhea (5.1% vs. 3.7%, respectively). Discontinuations due to adverse events were 4.2% for ONGLYZA 5 mg plus metformin groups vs. 4.4% for titrated glipizide plus metformin.

IMPORTANT INFORMATION ABOUT ONGLYZA

Indication and Important Limitations of Use

ONGLYZA (saxagliptin) is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

ONGLYZA should not be used for the treatment of type 1 diabetes mellitus or diabetic ketoacidosis.

ONGLYZA has not been studied in combination with insulin.

Important Safety Information

- **Use with Medications Known to Cause Hypoglycemia:** Insulin secretagogues, such as sulfonylureas, cause hypoglycemia. Therefore, a lower dose of the insulin secretagogue may be required to reduce the risk of hypoglycemia when used in combination with ONGLYZA.
- **Macrovascular Outcomes:** There have been no clinical studies establishing conclusive evidence of macrovascular risk reduction with ONGLYZA or any other antidiabetic drug.

Most common adverse reactions (regardless of investigator assessment of causality) reported in $\geq 5\%$ of patients treated with ONGLYZA and more commonly than in patients treated with control were upper respiratory tract infection (7.7%, 7.6%), headache (7.5%, 5.2%), nasopharyngitis (6.9%, 4.0%) and urinary tract infection (6.8%, 6.1%). When used as add-on combination therapy with a thiazolidinedione, the incidence of peripheral edema for ONGLYZA 2.5 mg, 5 mg, and placebo was 3.1%, 8.1% and 4.3%, respectively.

Laboratory Tests: There was a dose-related mean decrease in absolute lymphocyte count observed with ONGLYZA.

Drug Interactions: Because ketoconazole, a strong CYP3A4/5 inhibitor, increased saxagliptin exposure, the dose of ONGLYZA should be limited to 2.5 mg when coadministered with a

strong CYP3A4/5 inhibitor (e.g., atazanavir, clarithromycin, indinavir, itraconazole, ketoconazole, nefazodone, nelfinavir, ritonavir, saquinavir, and telithromycin).

Patients with Renal Impairment: The dose of ONGLYZA (saxagliptin) is 2.5 mg once daily for patients with moderate or severe renal impairment, or with end-stage renal disease requiring hemodialysis (creatinine clearance [CrCl] \leq 50 mL/min). ONGLYZA should be administered following hemodialysis. ONGLYZA has not been studied in patients undergoing peritoneal dialysis. Assessment of renal function is recommended prior to initiation of ONGLYZA and periodically thereafter.

Pregnant and Nursing Women: There are no adequate and well-controlled studies in pregnant women. ONGLYZA, like other antidiabetic medications, should be used during pregnancy only if clearly needed. It is not known whether saxagliptin is secreted in human milk. Because many drugs are secreted in human milk, caution should be exercised when ONGLYZA is administered to a nursing woman.

Pediatric Patients: Safety and effectiveness of ONGLYZA in pediatric patients have not been established.

U.S. Full Prescribing Information is available at www.bms.com.

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>.

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.

For more information about AstraZeneca in the US or our AZ&Me™ Prescription Savings programs, please visit: www.astrazeneca-us.com or call 1-800-AZandMe (292-6363).

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ONGLYZA is a trademark of the Bristol-Myers Squibb Company.

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