



**ONGLYZA™ (saxagliptin) With Metformin as Initial Combination Therapy Provided 76-Week Long-Term Glycemic Control in Treatment-Naïve Adults With Type 2 Diabetes**

*EMBARGOED: 9:30AM EST*

(ORLANDO, FL, June 26, 2010) – [Bristol-Myers Squibb Company](#) (NYSE: BMY) and [AstraZeneca](#) (NYSE: AZN) today announced results up to 76-weeks from a Phase 3 study of ONGLYZA™ (saxagliptin) as initial combination therapy with metformin, which produced long-term glycemic improvement [as measured by glycosylated hemoglobin level (HbA1c)] in treatment-naïve adults with type 2 diabetes mellitus inadequately controlled on diet and exercise compared to treatment with an investigational 10 mg dose of saxagliptin or metformin alone. The study results also demonstrated that a higher number of patients were able to achieve the American Diabetes Association recommended HbA1c target of less than 7% with ONGLYZA and metformin as initial combination therapy, compared to monotherapy of either treatment at week 76. The initial combination of ONGLYZA and metformin, with or without pioglitazone rescue therapy, had similar adverse event (AE) rates compared to treatment with investigational saxagliptin or metformin alone. Results were presented at the 70th American Diabetes Association (ADA) Annual Scientific Sessions.

“As type 2 diabetes is a disease that needs to be actively managed, effective treatment options are needed to help improve blood sugar levels,” said Andreas Pfützner, MD, Chief Executive Officer, Institute for Clinical Research and Development, Mainz, Germany. “These data show that at 76 weeks, ONGLYZA and metformin when given as an initial treatment provided improved HbA1c levels for adult patients with type 2 diabetes.”

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 used in combination with commonly prescribed oral anti-diabetic medications – metformin, glyburide (a sulfonylurea) or a thiazolidinedione (TZD), (pioglitazone or rosiglitazone) – or as a monotherapy statistically significantly reduced HbA1c levels. ONGLYZA 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 (saxagliptin) has not been studied in combination with insulin.

### **About the Study: Saxagliptin In Combination with Metformin up to 76 Weeks**

The objectives of the study were to assess the long-term efficacy and tolerability of ONGLYZA plus metformin and an investigational dose of saxagliptin plus metformin as initial combination therapy compared to an investigational dose of saxagliptin or metformin alone. The study assessed the change from baseline in HbA1c and the proportion of individuals achieving the American Diabetes Association recommended HbA1c target of less than 7%.

The study was a multicenter, randomized, double-blind, active-controlled, 24 week short-term study of 1,306 patients followed by a 52 week long-term extension period, which included 1,103 patients with type 2 diabetes (ages 18-77). Patients were required to be treatment naïve and have screening HbA1c levels of greater than or equal to 8% and less than or equal to 12% to enter the study. After a one-week placebo lead-in phase, individuals were randomized to one of four separate treatment groups: ONGLYZA 5 mg + metformin 500 mg (n=320), an investigational dose of saxagliptin 10 mg + metformin 500 mg (n=323) or saxagliptin 10 mg + placebo (n=335), or metformin 500 mg + placebo (n=328), given daily. In the treatment groups which included metformin, the daily metformin dose could be increased to a maximum of 2,000 mg based on pre-specified glycemic criteria. Patients whose HbA1c exceeded predetermined levels during the study period received pioglitazone therapy and were eligible to enter directly into the long-term extension period.

### **Study Results**

A total of 1,240 patients, including 612 who remained in the study without requiring rescue therapy through week 76, were included in a repeated measures analysis of HbA1c change from baseline. After 76 weeks, individuals in the ONGLYZA + metformin treatment groups demonstrated a greater adjusted mean change in HbA1c from baseline: -2.31% for ONGLYZA 5 mg + metformin group (n=303; baseline HbA1c 9.41%) and -2.33% for investigational saxagliptin 10 mg + metformin group (n= 313; baseline HbA1c 9.54%), compared to -1.55% for saxagliptin 10 mg + placebo (n= 316; baseline HbA1c 9.61%) and -1.79% for metformin + placebo (n= 308; baseline HbA1c 9.42%).

A greater percentage of individuals treated with ONGLYZA (saxagliptin) in combination with metformin achieved HbA1c of less than 7% after 76 weeks: 51.1% for ONGLYZA 5 mg + metformin and 50.8% in the investigational saxagliptin 10 mg + metformin, compared to 25.0% for saxagliptin 10 mg + placebo and 34.7% for metformin + placebo.

No attenuation of the reduction in three-hour postprandial glucose OGTT (oral glucose tolerance test) as measured by the area under the curve was apparent between weeks 24 and 76 for the ONGLYZA + metformin groups; partial attenuation did occur in both monotherapy groups. The overall proportion of individuals requiring rescue or discontinuation for lack of efficacy by week 76 was lower in the ONGLYZA 5 mg + metformin group (23.1%) and investigational saxagliptin 10 mg + metformin group (26.0%) versus the saxagliptin 10 mg + placebo (47.2%) and metformin + placebo (34.1%) groups of the study.

The percentage of patients with reported adverse events was similar across all treatment groups. Adverse event rates were as follows: 65.9% for ONGLYZA 5 mg + metformin, 68.4% for investigational saxagliptin 10 mg + metformin, 66.3% for saxagliptin 10 mg + placebo, 68.3% for metformin + placebo.

The occurrence of confirmed hypoglycemia (symptoms of hypoglycemia with a fingerstick glucose less than or equal to 50 mg/dL) was: three cases (0.9 %) in the investigational saxagliptin 10 mg + metformin group and two cases (0.6%) in the metformin + placebo group, with no cases of confirmed hypoglycemia in the ONGLYZA 5 mg + metformin or the saxagliptin 10 mg + placebo groups.

## **IMPORTANT INFORMATION ABOUT ONGLYZA**

### **Indication and Important Limitations of Use**

ONGLYZA 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 (saxagliptin) 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 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 (saxagliptin) 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](http://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](http://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](http://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.

### **Contacts:**

**Media:** Ken Dominski, Bristol-Myers Squibb, 609-252-5251, [ken.dominski@bms.com](mailto:ken.dominski@bms.com)  
Corey Windett, AstraZeneca, 302-885-0034, [corey.windett@astrazeneca.com](mailto:corey.windett@astrazeneca.com)

**Investors:** John Elicker, Bristol-Myers Squibb, 609-252-4611, [john.elicker@bms.com](mailto:john.elicker@bms.com)  
Karl Hard, AstraZeneca, +44-20-7304-5322, [karl.j.hard@astrazeneca.com](mailto:karl.j.hard@astrazeneca.com)  
Clive Morris, AstraZeneca, +44-207-304-5084, [clive.morris@astrazeneca.com](mailto:clive.morris@astrazeneca.com)