ONGLYZA™ (saxagliptin) With Metformin as Initial Combination Therapy Significantly Lowered A1C and Demonstrated Significant Improvements Across Key Measures of Glucose Control in Treatment Naive People With Type 2 Diabetes

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ROME--(BUSINESS WIRE)--Results from a 24-week Phase III study presented at the 44th European Association for the Study of Diabetes Annual Meeting demonstrated that ONGLYZA™ (saxagliptin), an investigational selective inhibitor with extended binding to the dipeptidyl peptidase-4 (DPP-4) enzyme in development by Bristol-Myers Squibb Company (NYSE: BMY) and AstraZeneca (NYSE: AZN), when used in combination with metformin as an initial therapy, produced significant reductions across all key measures of glucose control studied (glycosylated hemoglobin level (A1C), fasting plasma glucose (FPG) and postprandial glucose (PPG)) in treatment naive people with inadequately controlled type 2 diabetes, compared to monotherapy with saxagliptin or metformin. The initial combination of saxagliptin and metformin was well tolerated over the course of the study, and significantly more people were able to achieve target A1C of less than 7 percent, compared to monotherapy with saxagliptin or metformin.

The companies submitted a New Drug Application to the U.S. Food & Drug Administration (FDA) on June 30, which has been officially filed by the FDA, and a Marketing Authorization Application to the European Medicines Agency (EMEA) on July 1, which has been accepted for review by the Agency. The submissions are based on data from a comprehensive clinical trial program conducted in addition to standard therapies, as well as in treatment naive patients as a monotherapy. The clinical trial program included studies that evaluated the drug at up to 80 times the proposed usual clinical dose of 5 mg, once daily. The six core Phase III trials assessing the safety and efficacy of saxagliptin involved more than 4,000 patients, including 3,000 who were treated with saxagliptin. The companies have proposed the name ONGLYZA which, if approved by the FDA and the EMEA, will serve as the trade name for saxagliptin.

About the Study

The study was designed to assess saxagliptin as an initial combination therapy with metformin vs. each agent alone. The data represent findings from a 24-week, randomized, double-blind, active-controlled study of 1,306 people with type 2 diabetes (ages 18-77) who were treatment naive and whose A1C level was greater than or equal to 8 percent and less than or equal to 12 percent. After a one-week placebo lead-in phase, individuals were randomized to one of four separate treatment arms: saxagliptin 5 mg + metformin 500 mg (n=320), saxagliptin 10 mg + metformin 500 mg (n=323), saxagliptin 10 mg + placebo (n=335) or metformin 500 mg + placebo (n=328), given daily. From Week 1 to Week 5, in the saxagliptin 5 mg + metformin, saxagliptin 10 mg + metformin and metformin + placebo treatment arms, metformin was up-titrated weekly in 500 mg increments, as tolerated, to a maximum total daily dose of 2,000 mg, based on levels of FPG (a measure of a person's blood glucose after at least eight hours of fasting).

The primary endpoint of the study was the change from baseline to Week 24 in A1C. The secondary endpoints included the proportion of individuals achieving the American Diabetes Association recommended A1C target of less than 7 percent, the proportion of individuals achieving the International Diabetes Federation recommended A1C target of less than or equal to 6.5 percent and changes from baseline in FPG and PPG, measured during an oral glucose tolerance test (OGTT).

Study Results

After 24 weeks, individuals in the saxagliptin + metformin treatment arms demonstrated a significant adjusted mean change in A1C from baseline of -2.5 percent for saxagliptin 5 mg + metformin and -2.5 percent for saxagliptin 10 mg + metformin, compared to -1.7 percent for saxagliptin 10 mg + placebo and -2.0 percent for metformin + placebo (p-value less than 0.0001 for both treatment arms).

A greater percentage of individuals treated with saxagliptin in combination with metformin achieved A1C of less than 7 percent: 60.3 percent for saxagliptin 5 mg + metformin and 59.7 percent for saxagliptin 10 mg + metformin, compared to 32.2 percent for saxagliptin 10 mg + placebo and 41.1 percent for metformin + placebo (p-value less than 0.0001 for both treatment arms). A greater percentage of individuals treated with saxagliptin in combination with metformin also achieved A1C of less than or equal to 6.5 percent: 45.3 percent for saxagliptin 5 mg + metformin and 40.6 percent for saxagliptin 10 mg + metformin, compared to 20.3 percent for saxagliptin 10 mg + placebo and 29.0 percent for metformin + placebo (p-value less than or equal to 0.0026 for both treatment arms).

Individuals treated with saxagliptin in combination with metformin demonstrated a significant adjusted mean change in FPG from baseline: -60 mg/dL for saxagliptin 5 mg + metformin and -62 mg/dL for saxagliptin 10 mg + metformin, compared to -
31 mg/dL for saxagliptin 10 mg + placebo and -47 mg/dL for metformin + placebo (p-value less than or equal to 0.0002 for both treatment arms). The two saxagliptin + metformin treatment arms also demonstrated significant adjusted mean decreases in PPG from baseline, compared to either monotherapy.

Over 24 weeks, the incidence of adverse events was: 55.3 percent for saxagliptin 5 mg + metformin, 57.3 percent for saxagliptin 10 mg + metformin, 53.4 percent for saxagliptin 10 mg + placebo and 58.5 percent for metformin + placebo. The percentages of the most commonly reported (greater than or equal to 5 percent) adverse events for saxagliptin from the saxagliptin 5 mg + metformin, saxagliptin 10 mg + metformin, saxagliptin 10 mg + placebo and metformin + placebo treatment arms, respectively, were: nasopharyngitis [6.9, 2.5, 4.2, 4.0], headache [7.5, 9.9, 6.3, 5.2], diaphoresis [6.9, 9.6, 3.0, 7.3] and hypertension [4.7, 5.3, 4.5, 3.4].

The reported hypoglycemic events were: 3.4 percent for saxagliptin 5 mg + metformin, 5.0 percent for saxagliptin 10 mg + metformin, 1.5 percent for saxagliptin 10 mg + placebo and 4.0 percent for metformin + placebo. The occurrence of confirmed hypoglycemia (symptoms of hypoglycemia with a fingerstick glucose less than or equal to 50 mg/dL) was: two cases (0.6 percent) in the saxagliptin 10 mg + metformin group and one case (0.3 percent) in the metformin + placebo monotherapy group, with no cases of confirmed hypoglycemia in the saxagliptin 5 mg + metformin or the saxagliptin 10 mg + placebo groups.

Similar reductions in weight were seen across all treatment groups. Mean change from baseline in body weight at Week 24 was: -1.8 kg for saxagliptin 5 mg + metformin, -1.4 kg for saxagliptin 10 mg + metformin, -1.1 kg for saxagliptin 10 mg + placebo and -1.6 kg for metformin + placebo.

**About ONGLYZA**

ONGLYZA, the proposed tradename for saxagliptin, is an investigational DPP-4 inhibitor, under joint development by Bristol-Myers Squibb and AstraZeneca for the treatment of type 2 diabetes. Saxagliptin is being studied in clinical trials as a once-daily therapy to determine its efficacy and safety. Saxagliptin was specifically designed to be a selective inhibitor with extended binding to the DPP-4 enzyme, with dual routes of clearance. The name ONGLYZA, if approved by the FDA and the EMEA, will serve as the trade name for saxagliptin.

Saxagliptin Phase III data have previously been presented as a monotherapy, as well as in combination with metformin, sulfonylureas and thiazolidinediones, commonly prescribed oral anti-diabetic medications. The overall clinical development program included over 5,000 individuals -- more than 4,000 of whom were given saxagliptin.

**About DPP-4 Inhibitors**

DPP-4 inhibitors are a class of compounds that work by affecting the action of natural hormones in the body called incretins. Incretins decrease elevated blood sugar levels (glucose) by increasing the body’s utilization of sugar, mainly through increasing insulin production in the pancreas, and by reducing the liver’s production of glucose.

**About Type 2 Diabetes**

Diabetes (diabetes mellitus) is a chronic disease in which the body does not produce or properly use insulin. Insulin is a hormone that is needed to convert sugar, starches (carbohydrates) and other nutrients into energy needed for daily life. The cause of diabetes continues to be investigated, and both genetic and environmental factors such as obesity and lack of exercise appear to play a role. Diabetes is associated with long-term complications that affect almost every part of the body. The disease may lead to blindness, heart and blood vessel disease, stroke, kidney failure, amputations and nerve damage.

There are two primary underlying causes associated with type 2 diabetes: the body does not produce enough insulin (insulin deficiency), or the cells ignore the insulin (insulin resistance). Symptoms of type 2 diabetes develop gradually, and their onset is not as sudden as in type 1 diabetes. Symptoms may include fatigue, frequent urination, increased thirst and hunger, weight loss, blurred vision, and slow healing of wounds or sores. Some people, however, have no symptoms.

Type 2 diabetes is most often associated with older age, obesity, family history of diabetes, previous history of gestational diabetes, physical inactivity and certain ethnicities. People with type 2 diabetes often are characterized with: insulin resistance, abdominal obesity, a sedentary lifestyle, having low HDL-C (“good”) cholesterol levels and high triglyceride levels and hypertension.

Type 2 diabetes accounts for approximately 90 to 95 percent of all diabetes. This equates to roughly 221 million people with type 2 diabetes globally, and 21.2 million people in the U.S. alone.

The American Diabetes Association recommends a hemoglobin A1C measurement of less than 7 percent for most people with type 2 diabetes. Hemoglobin A1C is a measurement of a person’s average blood glucose level over a two-to-three month period and is considered an important marker of long-term glucose control. Other important markers for type 2 diabetes include fasting plasma glucose, a measure of a person’s blood glucose after at least eight hours of fasting, and postprandial glucose, a measure of a person’s blood glucose after a meal.

**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 two investigational drugs for type 2 diabetes – saxagliptin and dapagliflozin. 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 extend and enhance human life. For more information, visit [www.bms.com](http://www.bms.com).
Bristol-Myers Squibb Forward-Looking Statement

This press release contains “forward-looking statements” as that term is defined in the Private Securities Litigation Reform Act of 1995, regarding the research, development and commercialization of products. 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 the product described in this release will receive regulatory approval. There can be no assurance that if approved, the product will be commercially successful. Forward-looking statements in the 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, 2007, its Quarterly Reports on Form 10-Q, and 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 major international healthcare business engaged in the research, development, manufacturing and marketing of meaningful prescription medicines and supplier for healthcare services. AstraZeneca is one of the world’s leading pharmaceutical companies with healthcare sales of $29.55 billion and is a leader in gastrointestinal, cardiovascular, neuroscience, respiratory, oncology and infectious disease medicines. In the United States, AstraZeneca is a $13.35 billion dollar healthcare business with 12,200 employees committed to improving people’s lives. AstraZeneca is listed in the Dow Jones Sustainability Index (Global) as well as the FTSE4Good Index.

For more information about AstraZeneca, please visit www.astrazeneca-us.com.

AstraZeneca Forward-Looking Statement

The statements contain herein include forward-looking statements. Although we believe our expectations are based on reasonable assumptions, any forward-looking statements, by their very nature, involve risks and uncertainties and may be influenced by factors that could cause actual outcomes and results to be materially different from those predicted. The forward-looking statements reflect knowledge and information available at the date of the preparation of this press release and the Company undertakes no obligation to update these forward-looking statements. Important factors that could cause actual results to differ materially from those contained in forward-looking statements, certain of which are beyond our control, include, among other things, those risk factors identified in the Company's Annual Report/Form 20-F for 2007. Nothing contained herein should be construed as a profit forecast.

ONGLYZA is a trademark of the Bristol-Myers Squibb Company

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