Two-Year Data Comparing Cardiovascular Events with Linagliptin and the Sulfonylurea, Glimepiride, Presented as Late-Breaking Poster at ADA

Linagliptin plus metformin combination was as effective at lowering hemoglobin A1c as glimepiride plus metformin, and with weight loss and less hypoglycemia

SAN DIEGO, June 24, 2011 /PRNewswire/ -- Boehringer Ingelheim and Eli Lilly and Company (NYSE: LLY) today announce results presented at a late-breaking poster session demonstrating linagliptin was as effective at lowering blood sugar as glimepiride, and with weight loss instead of weight gain (-1.5 kg with linagliptin versus +1.3 kg with glimepiride), a lower incidence of investigator-defined hypoglycemia (7.5 percent versus 36.1 percent; p<0.0001) and fewer cardiovascular (CV) events in adult patients with type 2 diabetes (T2D). In the study, twice as many patients taking glimepiride (26 patients) experienced CV events compared to those taking linagliptin (12 patients), demonstrating a 50 percent reduction in relative risk for the combined CV endpoint (CV death, non-fatal myocardial infarction or stroke, and unstable angina with hospitalization).(1) The Phase III results will be presented at the 71st American Diabetes Association (ADA) Scientific Sessions in San Diego on June 24-28. Linagliptin, 5 mg, is marketed under the trade name Tradjenta™ (linagliptin) tablets in the U.S. and was approved by the U.S. Food and Drug Administration (FDA) in May 2011 to be used along with diet and exercise to lower blood sugar in adults with type 2 diabetes. Linagliptin should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis (increased ketones in the blood or urine). It has not been studied in combination with insulin.

To view the multimedia assets associated with this release, please click: http://multivu.prnewswire.com/mnr/tradjenta/50871/

The two-year efficacy and safety profile of adding linagliptin or glimepiride to metformin to treat patients with T2D who have not achieved glycemic control, as measured by hemoglobin A1c (HbA1c or A1C), was evaluated in this randomized, double-blind, non-inferiority study (n=1551). Efficacy analyses were based on A1C change from baseline in the full analysis set (FAS) and per-protocol (PP) populations.(1) Similar results were observed in both populations with adjusted mean A1C changes from baseline of -0.4 percent for linagliptin and -0.5 percent for glimepiride.(1)

"The combination of linagliptin plus metformin lowered A1C and was associated with fewer CV events and less hypoglycemia than the combination of sulfonylurea plus metformin," said Prof. Baptist Gallwitz, MD, Department of Medicine IV and the Outpatient Clinics for Endocrinology, Diabetes, and Metabolism, Eberhard-Karls-University of Tubingen, Germany. "A long-term outcomes study will provide more information on the cardiovascular data seen with linagliptin to date."

In a second late-breaking study — a prospective meta-analysis evaluating all CV events from eight Phase III, randomized trials (n = 5239) — adjudicated primary CV events occurred half as much in patients receiving linagliptin (11 patients; 0.3 percent) as three comparators, placebo, glimepiride or voglibose (23 patients; 1.2 percent). The hazard ratio for the primary endpoint (composite of CV death, non-fatal stroke, non-fatal myocardial infarction and hospitalization for unstable angina pectoris) was significantly lower for linagliptin versus the comparators. Hazard ratios were similar or significantly lower with linagliptin for all other CV endpoints.(2)

"These CV data for linagliptin are encouraging for the millions of adults with type 2 diabetes who may be at risk for CV disease," said John J. Smith, MD, PhD, senior vice president for clinical development and medical affairs, Boehringer Ingelheim Pharmaceuticals, Inc. "Boehringer Ingelheim and Lilly are committed to further evaluating the safety and efficacy of linagliptin and look forward to results from the long-term CV outcomes study that is currently underway."

Additional Information about the Linagliptin Late-breaking Studies

Two-year Data Comparing CV Events with Linagliptin and the Sulfonylurea Glimepiride

(39-LB)(1)

- The study assessed linagliptin (n=764) or glimepiride 1 to 4 mg/d (n=755), as add-on to 1500 mg/d or more of ongoing (at least 10 weeks) metformin for two years.
- Baseline characteristics were well balanced in the FAS and PP groups (A1C 7.7 percent for both).
- The efficacy endpoint was the change in A1C from baseline in the two groups.
- The safety endpoint evaluated pre-specified, prospective and adjudicated capture of CV events (CV death, non-fatal myocardial infarction or stroke, and unstable angina with hospitalization).

CV Risk in Patients with T2D: A Pre-specified, Prospective, and Adjudicated Meta-Analysis (30-LB)(2)

- Of the 5239 patients in the studies, 3319 received linagliptin once daily (5 mg: n=3159, 10 mg: n=160) and 1920 received comparators (placebo: n=977, glimepiride: n=781, voglibose: n=162).
- Cumulative exposure (person-years) was 2060 for linagliptin and 1372 for comparators (placebo: n=422, glimepiride: n=872, voglibose: n=78).
- The primary endpoint was a composite of CV death, non-fatal stroke, non-fatal myocardial infarction (MI), and hospitalization for unstable angina pectoris (UAP).
- Other secondary and tertiary CV endpoints were also assessed, including FDA-custom major adverse CV events (MACE).

To learn more about TRADJENTA and for full prescribing information visit: www.TRADJENTA.com or call Boehringer Ingelheim Pharmaceuticals, Inc. at 1-800-542-6257.

Please report any unexpected effects or product problems to the Boehringer Ingelheim Drug Information Unit by calling 1-800-542-6257.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

About Diabetes

Approximately 25.8 million Americans(3) and an estimated 220 million people(4) worldwide have type 1 and type 2 diabetes. Type 2 diabetes is the most common type, accounting for an estimated 90 to 95 percent of all diabetes cases.(3) Diabetes is a chronic disease that occurs when the body either does not properly produce, or use, the hormone insulin.(5)

Indication and Important Limitations of Use

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

TRADJENTA should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis.

TRADJENTA has not been studied in combination with insulin.

Important Safety Information

CONTRAINDICATIONS

TRADJENTA is contraindicated in patients with a history of hypersensitivity reaction to linagliptin, such as urticaria, angioedema or bronchial hyperreactivity.

WARNINGS AND PRECAUTIONS

Use with Medications Known to Cause Hypoglycemia

Insulin secretagogues (e.g., sulfonylurea) are known to cause hypoglycemia. Therefore, a lower dose of the insulin secretagogue may be required to reduce the risk of hypoglycemia when used in combination with TRADJENTA.

Macrovascular Outcomes

There have been no clinical studies establishing conclusive evidence of macrovascular risk reduction with TRADJENTA or any other antidiabetic drug.

ADVERSE REACTIONS

Adverse reactions reported in greater than or equal to 5% of patients treated with TRADJENTA and more commonly than in patients treated with placebo included nasopharyngitis.

Hypoglycemia was more commonly reported in patients treated with the combination of TRADJENTA and sulfonylurea

compared with those treated with the combination of placebo and sulfonylurea. Pancreatitis was reported more often in patients randomized to linagliptin (1 per 538 person-years versus zero in 433 person-years for comparator).

DRUG INTERACTIONS

The efficacy of TRADJENTA may be reduced when administered in combination with a strong P-glycoprotein or CYP3A4 inducer (e.g., rifampin). Therefore, use of alternative treatments is strongly recommended.

USE IN SPECIFIC POPULATIONS

There are no adequate and well-controlled studies in pregnant women. Therefore, TRADJENTA should be used during pregnancy only if clearly needed. It is not known whether linagliptin is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when TRADJENTA is administered to a nursing woman. Safety and effectiveness of TRADJENTA in patients below the age of 18 have not been established.

Boehringer Ingelheim and Eli Lilly and Company

In January 2011, Boehringer Ingelheim and Eli Lilly and Company announced an alliance in the field of diabetes that centers on four pipeline compounds representing several of the largest treatment classes. This alliance leverages the companies' strengths as two of the world's leading pharmaceutical companies, combining Boehringer Ingelheim's solid track record of research-driven innovation and Lilly's innovative research, experience, and pioneering history in diabetes. By joining forces, the companies demonstrate commitment in the care of patients with diabetes and stand together to focus on patient needs. Find out more about the alliance at www.boehringer-ingelheim.com or www.lilly.com.

About Boehringer Ingelheim Pharmaceuticals, Inc.

Boehringer Ingelheim Pharmaceuticals, Inc., based in Ridgefield, CT, is the largest U.S. subsidiary of Boehringer Ingelheim Corporation (Ridgefield, CT) and a member of the Boehringer Ingelheim group of companies.

The Boehringer Ingelheim group is one of the world's 20 leading pharmaceutical companies. Headquartered in Ingelheim, Germany, it operates globally with 145 affiliates and more than 42,000 employees. Since it was founded in 1885, the family-owned company has been committed to researching, developing, manufacturing and marketing novel products of high therapeutic value for human and veterinary medicine.

As a central element of its culture, Boehringer Ingelheim pledges to act socially responsible. Involvement in social projects, caring for employees and their families, and providing equal opportunities for all employees form the foundation of the global operations. Mutual cooperation and respect, as well as environmental protection and sustainability are intrinsic factors in all of Boehringer Ingelheim's endeavors.

In 2010, Boehringer Ingelheim posted net sales of approximately $16.7 billion (about 12.6 billion euro) while spending almost 24 percent of net sales in its largest business segment, Prescription Medicines, on research and development.

For more information, please visit http://us.boehringer-ingelheim.com and follow us on Twitter at http://twitter.com/boehringerus.

About Eli Lilly and Company

Lilly, a leading innovation-driven corporation, is developing a growing portfolio of pharmaceutical products by applying the latest research from its own worldwide laboratories and from collaborations with eminent scientific organizations. Headquartered in Indianapolis, IN, Lilly provides answers — through medicines and information — for some of the world's most urgent medical needs. Additional information about Lilly is available at www.lilly.com.

About Lilly Diabetes

For more than 85 years, Lilly has been a worldwide leader in pioneering industry-leading solutions to support people living with and treating diabetes. Lilly introduced the world's first commercial insulin in 1923, and remains at the forefront of medical and delivery device innovation to manage diabetes. Lilly is also committed to providing solutions beyond therapy — practical tools, education, and support programs to help overcome barriers to success along the diabetes journey. At Lilly, the journeys of each person living with or treating diabetes inspire ours. For more information, visit www.lillydiabetes.com.

This press release contains forward-looking statements about TRADJENTA for the treatment of type 2 diabetes. It reflects Lilly's current beliefs; however, as with any such undertaking, there are substantial risks and uncertainties in the process of drug development and commercialization. There is no guarantee that future study results and patient experience will be

consistent with study findings to date or that TRADJENTA will be commercially successful. For further discussion of these and other risks and uncertainties, please see Lilly's latest Forms 10-Q and 10-K filed with the U.S. Securities and Exchange Commission. Lilly undertakes no duty to update forward-looking statements.

P-LLY

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1. Gallwitz B, et al: Linagliptin has similar efficacy to glimepiride but improved cardiovascular safety over 2 years in patients with type 2 diabetes inadequately controlled on metformin. (39-LB)

2. Johansen O-D, et al: Cardiovascular risk with linagliptin in patients with type 2 diabetes: a pre-specified, prospective, and adjudicated meta-analysis from a large phase III program. (30-LB)

3. International Diabetes Federation. Diabetes Atlas. 3rd edn. Brussels: International Diabetes Federation, 2006.

4. Centers for Disease Control. National Diabetes Fact Sheet-2007. Available at: http://www.cdc.gov/diabetes/pubs/pdf/ndfs_2007.pdf. Accessed on: June 3, 2011.

5. World Health Organization. Fact Sheet No. 312: What is Diabetes? Available at: http://www.who.int/mediacentre/factsheets/fs312/en/. Accessed on: June 7, 2011.

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