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Studies assess linagliptin treatment in adults with type 2 diabetes (T2D), as well as add-on to basal insulin therapy

Boehringer Ingelheim and Lilly Diabetes Alliance present new findings at the 48th European Association for the Study of Diabetes (EASD) Annual Meeting

RIDGEFIELD, Conn. and INDIANAPOLIS, Oct. 2, 2012 /PRNewswire/ -- Boehringer Ingelheim Pharmaceuticals, Inc. and Eli Lilly and Company (NYSE: LLY) today announce data from three pooled analyses for linagliptin at the 48th European Association for the Study of Diabetes (EASD) Annual Meeting in Berlin. The new analyses show linagliptin, alone or in combination with other diabetes therapies, lowered hemoglobin A1c (HbA1c or A1C) in elderly patients with type 2 diabetes, as well as in adults with type 2 diabetes with diabetic nephropathy (renal disease).[1,2,3] Data from a fourth study found adding linagliptin to a stable dose of basal insulin improved blood glucose control over 52 weeks without an additional risk of hypoglycemia or weight gain compared to placebo.[4]

Linagliptin, marketed in the U.S. as Tradjenta®, is a once-daily tablet used along with diet and exercise to improve glycemic control in adults with type 2 diabetes. TRADJENTA should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis (increased ketones in the blood or urine).[5]

"We are committed to developing and providing therapeutic solutions, such as linagliptin, for adult patients with type 2 diabetes," said Christophe Arbet-Engels, MD, PhD, MBA, vice president, metabolic-clinical development and medical affairs, Boehringer Ingelheim. "We look forward to continuing our ongoing clinical trial program to assess how linagliptin may address the various needs of these patients."

An analysis of data pooled from seven phase III trials among 1,331 patients (poster #850) showed linagliptin, used alone or as add-on to various glucose-lowering therapies, had a placebo-adjusted reduction in A1C of 0.62 percent from a baseline A1C of 8.0 percent at 24 weeks in elderly patients ($\geq$65 years) with type 2 diabetes. A1C is measured in people with diabetes to provide an index of blood glucose control for the previous two to three months. These patients also experienced a placebo-adjusted reduction in fasting plasma glucose (FPG) of 14.8 mg/dL.

Adverse events (AEs) were experienced by 71.3% and 73.3% of patients who received linagliptin and placebo, respectively, and drug-related AEs were reported in 18.1% of patients treated with linagliptin compared with 19.8% of patients treated with placebo. The incidence of hypoglycemia was 21.4% in patients who received linagliptin compared with 25.7% in patients who received placebo. Severe hypoglycemic events requiring assistance were reported in both groups (1.0% and 1.8%, respectively). Overall AE reporting for GI disorders was comparable between both groups (14.1% and 15.5%, respectively).[1]

A second post-hoc analysis of seven randomized trials with treatment durations of 24 to 52 weeks (Presentation #36) assessed the clinical effect of linagliptin on albuminuria in adult and elderly ($\geq$65 years) patients with type 2 diabetes who had diabetic nephropathy (n=2,472). The primary endpoint of the analysis was changes to the urinary albumin-to-creatinine ratio (UACR) — a measure of glomerular integrity in patients with type 2 diabetes and diabetic nephropathy — after week 24. Overall, patients treated with linagliptin showed a significant reduction in UACR. This included a 29 percent placebo-adjusted reduction in UACR among patients with type 2 diabetes receiving linagliptin with or without oral glucose-lowering therapies and stable treatment with one of two types of blood pressure medicines that are the standard treatment for diabetic renal disease (angiotensin-converting enzyme inhibitors [ACEs] and angiotensin receptor blockers [ARBs]), and also a 30 percent reduction in UACR among elderly patients with diabetic nephropathy.[2]

"Many patients are found to have diabetic nephropathy after diagnosis with type 2 diabetes," said Lance A. Sloan, MD, FACE, President and Chief Medical Officer, Texas Institute for Kidney and Endocrine Disorders. "Unfortunately, as kidney function declines, treatment choices for patients become more complex and limited. At this point, patients require additional monitoring to maintain optimal dosing and efficacy."

In a third abstract (presentation #6), patients with type 2 diabetes treated with linagliptin in combination with a stable dose of basal insulin showed a placebo-adjusted reduction in A1C of 0.53 percent from baseline after 52 weeks (n=1,261). This was accompanied by a mean change in basal insulin dose of +2.6 +/- 0.8 IU/day for linagliptin plus basal insulin vs. +4.2 +/- 0.8

IU/day for placebo plus basal insulin. The incidence of hypoglycemia was similar between the groups (linagliptin, 31.4%; placebo, 32.9%), as was the number of severe hypoglycemic events over one year (linagliptin, 1.7%; placebo, 1.1%). In addition, the average changes in body weight were comparable between the treatment groups (linagliptin, -0.30 +/- 3.7kg; placebo, -0.04 +/- 3.1kg).[4]

In a fourth abstract (poster #848), linagliptin as add-on to basal insulin therapy vs. placebo also was studied in elderly patients (≥70 years) in a separate pre-specified pooled analysis of two Phase III studies over 24 weeks (poster #848). Linagliptin achieved improvements in glycemic control of -0.77% (placebo-adjusted change in A1C from baseline [P < 0.0001]), with a rate of hypoglycemia of 28.6% in linagliptin-treated patients and 37.2% in placebo-treated patients. In this population, the overall incidence of AEs for linagliptin in combination with basal insulin was not higher than placebo (75.4% and 81.0%, respectively).[3]

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.

Poster #850 Study Design
This post-hoc analysis included seven randomized, double-blind, placebo-controlled phase III trials of linagliptin 5 mg once daily as monotherapy or add-on to various glucose-lowering therapies of at least 24 weeks' duration. The trial included 1,331 patients aged 65 years, including 841 patients on linagliptin and 490 patients on placebo. Overall, 21 percent of patients had renal function decline, more than 80 percent had diabetes for at least five years, and more than 60 percent were receiving two or more glucose-lowering drugs.[1]

Presentation #36 Study Design
Data from seven randomized, double-blind, 24- to 52-week, placebo-controlled trials of linagliptin monotherapy or as add-on to various glucose-lowering medicines were pooled for the analysis. This included patients from four clinical trials (n=2,472) who had early diabetic nephropathy and were on stable ACE/ARB therapy and elderly patients from all seven trials (n=377) who had diabetic nephropathy and met the UACR inclusion criteria (30 to 3,000 mg/g creatinine). The endpoint in both data sets was the percentage change in geometric mean UACR after 24 weeks of treatment. In all trials, blood pressure and renal function were not affected to a clinically-meaningful extent by either treatment.[2]

Presentation #6 Study Design
In the 52-week insulin study, a total of 1,261 patients inadequately controlled on basal insulin (glargine, insulin detemir, or NPH insulin) were randomized to receive linagliptin 5 mg once daily or placebo. Background basal insulin had to be kept stable for the first 24 weeks but could then be adjusted as needed, to mirror real-world use with basal insulin.[4]

Poster #848 Study Design
Data from two phase III studies evaluating linagliptin vs. placebo as add-on therapy to basal insulin and as T2D management in elderly patients (age ≥70 years) were pooled for a pre-specified analysis exploring its safety and efficacy. A total of 247 patients inadequately controlled on insulin glargine, insulin detemir, or NPH insulin received either linagliptin 5 mg once daily (n=126) or placebo (n=121). Mean insulin doses were 35.0 IU and 36.6 IU, respectively. The primary efficacy endpoint was change from baseline to week 24 in A1C. Safety and tolerability based on AEs also were assessed.[3]

What are TRADJENTA (linagliptin) tablets?
TRADJENTA is a prescription medicine that is used along with diet and exercise to lower blood sugar in adults with type 2 diabetes.

TRADJENTA is not for people with type 1 diabetes or for people with diabetic ketoacidosis (increased ketones in the blood or urine).

Important Safety Information

Who should not take TRADJENTA?
Do not take TRADJENTA if you are allergic to linagliptin or any of the ingredients in TRADJENTA.

Symptoms of a serious allergic reaction to TRADJENTA are rash, raised red patches on your skin (hives), swelling of your face, lips, and throat that may cause difficulty breathing or swallowing. If you have any symptoms of a serious allergic reaction, stop taking TRADJENTA and call your doctor right away.

What should I tell my doctor before taking TRADJENTA?
Tell your doctor if you take other medicines that can lower your blood sugar, such as a sulfonylurea or insulin.

TRADJENTA may cause serious side effects, including low blood sugar (hypoglycemia). If you take TRADJENTA with another

medicine that can cause low blood sugar, such as sulfonylurea or insulin, your risk of getting low blood sugar is higher. The dose of your sulfonylurea or insulin may need to be lowered while you take TRADJENTA.

Signs and symptoms of low blood sugar may include headache, drowsiness, weakness, dizziness, confusion, irritability, hunger, fast heartbeat, sweating, or feeling jittery.

Also tell your doctor if you take rifampin (Rifadin®, Rimactane®, Rifater®, Rifamate®), an antibiotic that is used to treat tuberculosis.

TRADJENTA may affect the way other medicines work, and other medicines may affect how TRADJENTA works.

Tell your doctor if you are pregnant or planning to become pregnant or are breastfeeding or plan to breastfeed.

Tell your doctor about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements.

What are the possible side effects of TRADJENTA?
The most common side effects of TRADJENTA include stuffy or runny nose and sore throat.

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.

For more safety information, please see Patient Information and full Prescribing Information.

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To learn more about TRADJENTA visit: www.TRADJENTA.com. For full prescribing information visit: http://bidocs.boehringer-ingelheim.com/BIWebAccess/ViewServlet.ser?docBase=renetnt&folderPath=/Prescribing+Information/PIs/Tradjenta/Tradjenta.pdf 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.

About Diabetes
Approximately 25.8 million Americans[6] and an estimated 366 million people worldwide[7] have type 1 or type 2 diabetes. Type 2 diabetes is the most common type, accounting for an estimated 90 to 95 percent of all diabetes cases.[6] Diabetes is a chronic disease that occurs when the body either does not properly produce, or use, the hormone insulin.[8]

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
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 44,000 employees. Since it was founded in 1885, the family-owned company has been committed to researching, developing, manufacturing and marketing novel medications 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 2011, Boehringer Ingelheim achieved net sales of about $17.1 billion (13.2 billion euro). R&D expenditure in the business area Prescription Medicines corresponds to 23.5% of its net sales.

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
Lilly has been a global leader in diabetes care since 1923, when we introduced the world's first commercial insulin. Today we work to meet the diverse needs of people with diabetes through research and collaboration, a broad and growing product portfolio and a continued commitment to providing real solutions—from medicines to support programs and more—to make lives better.

For more information, visit www.lillydiabetes.com.

This press release contains forward-looking statements about TRADJENTA (linagliptin) tablets. 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.

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1. Patel S, Schernthaner G, Barnett AH, et al. Safety and Efficacy of Linagliptin in Elderly Patients with Type 2 Diabetes: Evidence from 1331 Individuals Aged ≥65 years. Presented at the 48th European Association for the Study of Diabetes (EASD) Annual Meeting. October 1-5, Berlin, Germany.
2. Groop P-H, Cooper M, Perkovic V, et al. Effects of the DPP-4 Inhibitor Linagliptin on Albuminuria in Patients with Type 2 Diabetes and Diabetic Nephropathy. Presented at the 48th EASD Annual Meeting. October 1-5, Berlin, Germany.
3. Woerle H-J, Neubacher D, Patel S, von Eynatten M. Safety and Efficacy of Linagliptin Plus Basal Insulin Combination Therapy in a Vulnerable Population of Elderly Patients (age ≥ 70 years) with Type 2 Diabetes. Presented at the 48th EASD Annual Meeting. October 1-5, Berlin, Germany.
4. Yki-Järvinen H, Rosenstock J, Durán-Garcia S, et al. Long-term Safety and Efficacy of Linagliptin as Add-on Therapy to Basal Insulin in Patients with Type 2 Diabetes: A 52-week Randomised, Placebo-controlled Trial. Presented at the 48th EASD Annual Meeting. October 1-5, Berlin, Germany.
5. Tradjenta® (linagliptin) tablets. Highlights of Prescribing Information. Initial US Approval: 2011.
6. Centers for Disease Control and Prevention. National diabetes fact sheet: national estimates and general information on diabetes and prediabetes in the United States, 2011. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, 2011.
7. International Diabetes Federation. IDF Diabetes Atlas, 5th Edition: The Global Burden. 2011. http://www.idf.org/diabetesatlas/5e/the-global-burden. Accessed on: May 18, 2012.
8. International Diabetes Federation. IDF Diabetes Atlas, 5th Edition: What is Diabetes? http://www.idf.org/diabetesatlas/5e/what-is-diabetes. Accessed on: May 18, 2012.

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