# Linagliptin Receives Approval in Europe for the Treatment of Type 2 Diabetes

## Linagliptin is the only DPP-4 inhibitor to be approved at one dosage strength for adults with type 2 diabetes in Europe, without any need for dose adjustments

RIDGEFIELD, Conn., and INDIANAPOLIS, Aug. 25, 2011 /PRNewswire/ -- Boehringer Ingelheim and Eli Lilly and Company (NYSE: LLY) today received Marketing Authorization from the European Commission for linagliptin 5 mg film-coated tablets (to be marketed under the trade name Trajenta® in Europe) for the treatment of adults with type 2 diabetes. The European Commission has approved linagliptin in combination with metformin and metformin plus sulfonylurea.(1) Linagliptin is also approved for use as monotherapy in patients inadequately controlled by diet and exercise alone and for whom metformin is inappropriate due to intolerance, or contraindicated due to renal impairment.(1)

In the U.S., linagliptin 5 mg is marketed under the trade name Tradjenta™ (linagliptin) tablets 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. Linagliptin is also approved for use in other countries, including Japan (trade name Trazenta).

"The Phase III clinical trial program has demonstrated efficacy with linagliptin in the treatment of adults with type 2 diabetes," said Prof. Klaus Dugi, corporate senior vice president medicine, Boehringer Ingelheim. "We are delighted that linagliptin will soon be available to patients across Europe."

Studies show linagliptin has a demonstrated efficacy and safety profile, reducing hemoglobin A1C (HbA1C or A1C) levels by a mean of -0.6 to -0.7 percent(2,3) (compared to placebo). A1C is measured in people with diabetes to provide an index of blood glucose control for the previous two to three months and is used as a marker to determine the efficacy of glucose-lowering therapies.

"Linagliptin is primarily excreted unmetabolized via bile and gut, meaning no dose adjustment is needed in adult patients with kidney or liver impairment," said Prof. Anthony Barnett, professor of medicine and clinical director of the Department of Diabetes and Endocrinology, Heart of England NHS Foundation Trust, Birmingham, UK. "This means that linagliptin is available at only one dose."

The approval of linagliptin in Europe was based on a clinical trial program which involved approximately 6,000 adults with type 2 diabetes. Included in the program were placebo-controlled studies evaluating linagliptin as monotherapy(4) and in combination with the commonly prescribed oral antihyperglycemic medications metformin and/or sulfonylurea.(2,5-6) In two monotherapy studies, linagliptin showed a statistically significant mean difference in A1C from placebo of -0.6 to -0.7 percent.(3-4) In patients who were not adequately controlled on metformin or metformin plus sulfonylurea, the addition of linagliptin also resulted in a statistically significant mean difference in A1C from placebo of -0.6 percent.(2,5) The incidence of hypoglycemia was similar to placebo and weight did not change significantly from baseline.(2,5)

In the pooled analysis of the placebo-controlled trials, the overall incidence of adverse events in patients treated with placebo was similar to that seen with linagliptin (53.8 percent versus 55.0 percent).

The most frequently reported adverse reaction was hypoglycemia observed with the triple combination of linagliptin plus metformin plus sulfonylurea.

"The EU approval of linagliptin marks another major regulatory milestone for the Boehringer Ingelheim and Lilly alliance in diabetes," said Enrique Conterno, president of Lilly Diabetes. "Linagliptin can be an important treatment option for adults living with type 2 diabetes."

**What is TRADJENTA?**

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).

It is not known if TRADJENTA is safe and effective when used with insulin.

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

Tell your doctor if you take other medicines that can lower your blood sugar, such as a sulfonylurea or insulin. If you take TRADJENTA with another medicine that can cause low blood sugar (hypoglycemia), such as a sulfonylurea or insulin, your risk of getting low blood sugar is higher. The dose of your sulfonylurea medicine 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 heart beat, 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.

**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.

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.

**About Diabetes**

Approximately 25.8 million Americans(7) and an estimated 220 million people worldwide(8) 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.(7) Diabetes is a chronic disease that occurs when the body either does not properly produce, or use, the hormone insulin.(9)

**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 linagliptin tablets 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 linagliptin 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)Trajenta™ (linagliptin) tablets. EMA Summary of Product Characteristics. 2011.

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(3)Del Prato S, Barnett AH, Huisman H, et al: Effect of linagliptin monotherapy on glycaemic control and markers of B-cell function in patients with inadequately controlled type 2 diabetes: a randomised controlled trial. Diabetes Obes Metab 2011;13:193-287.

(4)Barnett AH, Harper R, Toorawa R, et al: Linagliptin monotherapy improves glycaemic control in type 2 diabetes patients for whom metformin therapy is inappropriate, 46th Annual Meeting of the European Association for the Study of Diabetes. Stockholm, Sweden, 2010, pp Poster 823.

(5)Owens DR, Swallow R, Woerle HJ, et al: Linagliptin improves glycemic control in type 2 diabetes patients inadequately controlled by metformin and sulfonylurea without weight gain and low risk of hypoglycemia, 70th American Diabetes Association Scientific Sessions. Orlando, Florida, U.S.A., 2010, pp Poster 548-P.

(6)Lewin AJ, Arvay L, Liu D, et al: Safety and efficacy of linagliptin as add-on therapy to a sulphonylurea in inadequately controlled type 2 diabetes, 46th Annual Meeting of the European Association for the Study of Diabetes. Stockholm, Sweden, 2010, pp Poster 821-P.

(7)Centers for Disease Control and Prevention. National Diabetes Fact Sheet 2011. Available at http://www.cdc.gov/diabetes/pubs/pdf/ndfs_2011.pdf. Accessed on: August 16, 2011.

(8)World Health Organization. Fact Sheet No. 312: What is Diabetes? Available at: http://www.who.int/mediacentre/factsheets/fs312/en/. Accessed on: August 16, 2011.

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

SOURCE Eli Lilly and Company