June 11, 2012

Lilly and Boehringer Ingelheim Present Data at the 72nd American Diabetes Association Scientific Sessions® from Phase II Studies Comparing Investigational Novel Basal Insulin to Insulin Glargine

Results showed LY2605541 lowered blood sugar with weight loss in type 1 and type 2 diabetes patients

PHILADELPHIA, June 11, 2012 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) and Boehringer Ingelheim today announced results from two Phase II studies of their investigational novel basal insulin analog, LY2605541. Results of the type 1 diabetes study showed that LY2605541 was associated with greater improvements of glycemic control (lowering blood sugar levels) than insulin glargine. In the type 2 diabetes study, the primary measure showed that LY2605541 and insulin glargine had similar improvements in glycemic control. These data and additional measures from the studies will be presented at the 72nd American Diabetes Association (ADA) Scientific Sessions® in Philadelphia, June 8-12, 2012.

"As a clinical investigator, these Phase II results are intriguing, as they showed that LY2605541 improved glycemic control in patients with type 1 and type 2 diabetes and produced additional effects, such as weight loss and less variability of blood glucose readings, both within the same day and between days," said Richard Bergenstal, MD, executive director, International Diabetes Center at Park Nicollet and clinical professor, Department of Medicine, University of Minnesota.

"Lilly and Boehringer Ingelheim are excited to have the opportunity to share both the pre-clinical and clinical study data completed to date for LY2605541, and are pleased that these Phase II study results support the continued clinical development of this basal insulin," said David Kendall, MD, distinguished medical fellow, Lilly Diabetes. "Based on the pre-clinical studies completed, compared to injected human insulin, LY2605541 appeared to work preferentially in the liver, which is more like the body's own insulin. We look forward to results from our ongoing Phase III clinical trials."

Glycemic Control
In adults with type 1 diabetes, patients treated with LY2605541 showed better glycemic control after eight weeks than those who received glargine. LY2605541-treated patients' average daily blood glucose readings (from self-testing) were significantly reduced (mean difference vs. glargine equaled -10 mg/dL), and their reduction in hemoglobin A1C (average blood glucose levels) was significantly greater (-0.6 percent from baseline vs. -0.4 percent from baseline for glargine). In addition, patients in the LY2605541 group had a 17 percent reduction in their mealtime insulin dose while glargine-treated patients had a 7 percent increase (the difference between treatments is statistically significant).

In patients with type 2 diabetes, LY2605541 and glargine had similar effects on lowering average daily self-monitored fasting (before breakfast) glucose levels, and A1C over 12 weeks.

Weight
In both studies, treatment with LY2605541 was associated with weight loss, and statistically significant differences in weight compared to insulin glargine.

- LY2605541-treated patients with type 1 diabetes lost weight, while glargine-treated patients gained weight (mean change -2.65 lbs. [-1.2 kg] vs. +1.52 lbs. [+0.7 kg] for glargine), a -4.17-lb. [-1.9 kg] difference in mean weight change. The mean baseline weight was 183 pounds (83 kg).
- A 5 percent or greater loss in body weight was statistically significantly more frequent in the LY2605541 group with type 1 diabetes (12 percent vs. 1 percent for glargine).
- Type 2 patients treated with LY2605541 achieved significant mean weight loss (-1.28 lbs [-0.58 kg]) compared with insulin glargine (+0.68 lbs. [+0.31 kg]) at 12 weeks, a -1.85-lb. [-0.84 kg] difference in mean weight change compared to glargine-treated patients. The mean baseline weight for patients treated with LY2605541 was 200 pounds (91 kg) and for those treated with glargine the mean baseline weight was 198 pounds (90 kg).
- A 5 percent or more loss in body weight was more frequent in the LY2605541 group with type 2 diabetes (5 percent vs. 0 percent on glargine).

Hypoglycemia
LY2605541 was associated with a statistically significant higher overall hypoglycemia rate (blood glucose less than or equal to 70 mg/dL) in patients with type 1 diabetes (8.7 events/30 days vs. 7.4 events/30 days with glargine), but a statistically significant lower rate of nocturnal hypoglycemia (0.9 events/30 days vs. 1.1 events/30 days with glargine). In the type 1

diabetes study, the unanticipated need for lower prandial (mealtime) insulin doses at study initiation contributed to the slightly higher rate of overall hypoglycemia with LY2605541 than with insulin glargine. Despite the reduction later of mealtime insulin doses throughout the trial, glycemic control continued to improve throughout the study.

The treatments had similar overall rates of hypoglycemia in the type 2 study, but patients treated with LY2605541 had a 48 percent reduced rate of nocturnal hypoglycemia compared to glargine (0.25 vs. 0.39 events/30 days/patient, after adjusting for baseline hypoglycemia events).

In a subset of patients with type 2 diabetes, hypoglycemia was assessed by continuous glucose monitoring (CGM), which measures a person's glucose level every five minutes for up to three days. Glargine treatment increased the time patients spent in hypoglycemia as measured by CGM. In contrast, in LY2605541-treated patients, the time spent in hypoglycemia was not different from baseline and was significantly less compared to glargine. Fewer LY2605541-treated patients experienced hypoglycemia episodes compared to glargine-treated patients (50.0 percent vs. 78.3 percent), and fewer LY2605541-treated patients also experienced nocturnal hypoglycemia events (20.5 percent vs. 47.8 percent).

Glucose Variability
In the type 1 study, LY2605541-treated patients showed less within-day glucose variability at eight weeks (i.e., their self-monitored blood glucose levels stayed within a narrower range) (standard deviation of 52 vs. 58 mg/dL).

In the type 2 study, there was a significant reduction in within-day blood glucose variability with LY2605541 compared to glargine (standard deviation of 34 vs. 39 mg/dL). In the subset of patients with type 2 diabetes assessed by CGM, LY2605541-treated patients had statistically significant less within-day glucose variability compared with insulin glargine in both the nighttime period (standard deviation of 18 vs. 24 mg/dL) and the daytime period (standard deviation of 37 vs. 45 mg/dL).

Additional Safety Results
In both studies, following treatment with LY2605541, blood tests on liver function (as measured by mean ALT and AST levels) statistically significantly increased from baseline and were higher than with insulin glargine. The mean levels of both liver enzymes remained within the normal range during the study for glargine and LY2605541-treated patients.

In the type 1 study, patients treated with LY2605541 had a modest increase in triglycerides (91 mg/dL to 113 mg/dL) and LDL-C (96 mg/dL to 102 mg/dL), and HDL-C decreased modestly (60 mg/dL to 54 mg/dL) at the study's endpoint. These changes were statistically significant from baseline and compared to insulin glargine. In the type 2 study, triglyceride levels in patients treated with LY2605541 were not significantly different from baseline (163 mg/dL to 172 mg/dL), but statistically higher compared to insulin glargine (160 mg/dL vs. 147 mg/dL). There was no significant difference in LDL-C or HDL-C in patients treated with LY2605541 from baseline or compared with insulin glargine.

Adverse events in type 1 patients, including severe hypoglycemia, were similar in both treatment groups. Patients in the LY2605541 group had a statistically significant increase in gastrointestinal events (dyspepsia, nausea, abdominal distension) (15 percent vs. 4 percent). This observation was not noted in the type 2 patients, with 14 percent of glargine-treated patients reporting gastrointestinal events compared to 10 percent of LY2605541-treated patients. This was not statistically significant. Other adverse events were similar across treatments in type 2 patients.

About the Phase II Studies

Study in Type 1 Diabetes
The Phase II, randomized, open-label, 2x2 crossover study evaluated whether LY2605541 was non-inferior (similar) to standard treatment (in this case, insulin glargine) in reducing daily mean blood glucose in adults with type 1 diabetes (margin of 10.8 mg/dL). One hundred and thirty-seven patients received LY2605541 or glargine once daily, plus mealtime insulin, for eight weeks; they then switched treatments for an additional eight weeks. Daily mean blood glucose values were obtained from self-monitoring of blood glucose (SMBG) profiles (blood glucose readings before and two hours after a meal, at bedtime and at 3:00 a.m.) the week prior to each visit.

Study in Type 2 Diabetes
The Phase II, randomized, open-label, parallel study evaluated LY2605541 in lowering self-monitored fasting blood glucose levels compared to insulin glargine in adults with type 2 diabetes. Patients were converted to morning insulin administration during a four-week lead-in period and were randomized 2:1 to morning administration of LY2605541 (195 patients) or glargine (93 patients) for a total of 12 weeks.

In addition to self-monitoring, a subset of these patients (LY2605541, 51 patients; glargine, 25 patients) also used continuous glucose monitoring (CGM) on three consecutive days to determine hypoglycemia events and glucose variability. Patients were considered hypoglycemic when interstitial glucose levels (glucose levels measured from fluid taken from just under the skin) reached 70 mg/dL and stayed below that level for 15 minutes (or for three time points).

About Diabetes
Approximately 25.8 million Americans(1) and an estimated 366 million people(2) 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. Diabetes is a chronic disease that occurs when the body either does not properly produce, or use, the hormone insulin(3).

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.
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 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 www.boehringer-ingelheim.com.

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 our continued commitment to providing real solutions — from medicines to support programs and more — to make lives better. For more information, visit www.lillydiabetes.com.

P-LLY

This press release contains forward-looking statements that are based on Lilly's current expectations, but actual results may differ materially due to various factors. There are significant risks and uncertainties in pharmaceutical research and development. There can be no guarantee that novel basal insulin will receive the necessary clinical and manufacturing regulatory approvals or that it will prove to be commercially successful. In addition, there can be no guarantee that the companies will realize the financial and commercial results anticipated from this collaboration. Other risk factors that may affect Lilly's results can be found in the company's latest Forms 10-K and 10-Q filed with the U.S. Securities and Exchange Commission. The companies undertake no duty to update forward-looking statements.

REFERENCES

1. Centers for Disease Control. National Diabetes Fact Sheet-2011. Available at: http://www.cdc.gov/diabetes/pubs/pdf/ndfs_2011.pdf. Accessed on: February 22, 2012.

2. International Diabetes Federation. Diabetes Atlas, 5th Edition: Fact Sheet. 2011.

3. International Diabetes Federation. Diabetes Atlas, 5th Edition: What is Diabetes? http://www.idf.org/diabetesatlas/5e/what-is-diabetes. Accessed on: February 22, 2012.

(Logo: http://photos.prnewswire.com/prnh/20031219/LLYLOGO)

(Logo: http://photos.prnewswire.com/prnh/20110825/DE57898LOGO)

SOURCE Eli Lilly and Company; Boehringer Ingelheim Pharmaceuticals, Inc.