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Scientific Presentations of Exenatide Data Show Improvements in Glucose Control and Restored Insulin Response in People with Type 2 Diabetes

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Amylin Pharmaceuticals, Inc., (Nasdaq: AMLN) and Eli Lilly and Company (NYSE: LLY) plan to present detailed results from two clinical studies of exenatide during an oral abstract presentation at the American Diabetes Association's (ADA) 64th Scientific Sessions in Orlando, Florida on June 8, 2004. Exenatide is the first potential therapy in a new class of drugs under investigation for the treatment of type 2 diabetes known as *incretin mimetics*. The first presentation will highlight data from one of three Phase 3 pivotal studies for exenatide. Of patients who completed the 30-week study, 41 percent taking 10 micrograms of exenatide achieved A1C levels of seven percent or less. A1C is a measure that reflects a person's average glucose (blood sugar) levels over the prior three to four months. Exenatide treatment also resulted in reductions in body weight. In addition to 30-week data, results from an open-label extension study will be presented, showing that after 52 weeks, exenatide demonstrated sustained effect on both A1C and body weight.

Results from a separate study will be presented showing that exenatide restored the ability of beta cells to release insulin immediately following an influx of glucose into the bloodstream, an action known as first-phase insulin response. A first-phase insulin response is the normal pattern of insulin secretion found in healthy individuals, and it is lost early in the development of type 2 diabetes.

"These data suggest that exenatide may address a fundamental defect of type 2 diabetes by enhancing the body's ability to produce and release its own insulin in a manner that mimics that of people without diabetes," said John Buse, M.D., professor of medicine and director, Diabetes Care Center, University of North Carolina School of Medicine at Chapel Hill.

Pivotal Trial Design/Protocol

The pivotal trial was a 30-week, triple-blind, placebo-controlled study. This study involved 377 diabetes patients unable to achieve glycemic control using maximally effective doses of sulfonylureas, a commonly used oral agent. The study was divided into three arms of patients taking either 10 micrograms of exenatide, 5 micrograms of exenatide, or placebo via subcutaneous injection twice daily in addition to their maximally effective doses of sulfonylureas. At the conclusion of the initial 30-week study, participants in all treatment arms were offered the opportunity to continue in an open-label extension study in which they received 10 micrograms of exenatide, twice daily.

Key Pivotal Study Findings

At the outset of the study, the average A1C of patients was 8.6 percent. After 30 weeks, those taking 10 micrograms of exenatide experienced an average reduction in A1C of one percent (difference from placebo). These reductions in A1C were accompanied by average reductions in weight of approximately 2.2 pounds or 1 kilogram (difference from placebo).

The most common adverse event reported was mild to moderate nausea, which occurred most frequently early in the study. The dropout rate due to nausea was four percent for 10 micrograms and zero percent for placebo. As expected, some patients taking exenatide in combination with sulfonylurea experienced mild-to-moderate hypoglycemia. The incidence of mild-to-moderate hypoglycemia was 36 percent in the 10 microgram group and 3 percent in the placebo group.

Sustained reductions in A1C and body weight were observed at 52 weeks in patients who continued in the open-label extension study. In the 35 patients who completed 52 weeks on 10 micrograms of exenatide, the average reduction in A1C from baseline was 1.4 percent with average reductions in body weight of approximately 6.4 pounds (2.9 kilograms).

"These results demonstrate exenatide's potential to help patients reduce their A1Cs to a healthy range. In addition, patients also experienced reductions in body weight and showed evidence of improved beta cell function," said Buse. "That combination could be a very important and unique contribution to type 2 diabetes treatment."

Improvements in Beta Cell Function

In a separate crossover clinical study examining short-term beta-cell function, beta-cell response to an intravenous glucose infusion was measured in 25 subjects (12 healthy participants and 13 type 2 diabetes subjects) following treatment with exenatide or placebo. Researchers assessed beta-cell function by measuring blood concentrations of glucose, insulin and C-peptide (a marker for insulin production) at specific intervals following the glucose infusion. When receiving placebo, type 2 subjects demonstrated a blunted insulin response following the glucose infusion, a pattern typical with type 2 patients. Following treatment with exenatide, when given the same level of intravenous glucose, those same patients showed a beta-cell response that was equivalent to or greater than that of healthy subjects of comparable weight.

"Type 2 diabetes is caused by the progressive and inevitable failure of the insulin-producing cells of the pancreas known as the beta cells. Beta cell failure is progressive despite diet, exercise and currently available therapies," said Dr. Michael Nauck, head of the Diabetes Center, Bad Lauterberg, Germany. "This restoration of first-phase insulin release by the beta cells is a potentially important development in the treatment of type 2 diabetes."

About Exenatide

Exenatide is the first in a new class of drugs being investigated for the treatment of type 2 diabetes called *incretin mimetics*, and exhibits many of the same effects as the human incretin hormone GLP-1. GLP-1 has multiple effects on the gut, liver, pancreas and brain that work in concert to improve blood sugar¹.

About Diabetes

Diabetes affects an estimated 194 million adults worldwide² and more than 18 million in the United States.³ Approximately 90-95 percent of those affected have type 2 diabetes, in which the body does not produce enough insulin and the cells in the body do not respond normally to the insulin. According to the U.S. Center for Disease Control and Prevention's National Health and Nutrition Examination Survey, approximately 60 percent of diabetes patients do not achieve target A1C levels with their current treatment regimen. According to the ADA, patients with A1Cs above target are more likely to develop diabetes-related complications, such as kidney disease, blindness and heart disease.⁴

About Amylin and Lilly

Amylin Pharmaceuticals is committed to improving the lives of people with diabetes and other metabolic disorders through the discovery, development and commercialization of innovative, cost-effective medicines. Further information on Amylin Pharmaceuticals and its pipeline in metabolism is available at www.amylin.com.

Lilly, a leading innovation-driven corporation is developing a growing portfolio of first-in-class and best-in-class pharmaceutical products by applying the latest research from its own worldwide laboratories and from collaborations with eminent scientific organizations. Headquartered in Indianapolis, Indiana, 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.

This press release contains forward-looking statements, which involve risks and uncertainties. Actual results could differ materially from those discussed or implied in this press release due to a number of factors, including the risk that clinical study results may not be replicated or confirmed, risks that a new drug application for exenatide will not be filed on a timely basis, risks that exenatide may not receive regulatory approvals or such approvals may be delayed or limited, or risks that exenatide may not prove to be commercially successful. These and additional risks and uncertainties are described more fully in Lilly and Amylin's most recently filed SEC documents such as their Annual Reports on Form 10-K, and Amylin's recently filed Form S-3.

References

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