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

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Eli Lilly and Company and Amylin Pharmaceuticals, Inc., today presented comprehensive results from the three pivotal Phase 3 studies of exenatide as well as data from a separate crossover study at the 40th Annual Meeting of the European Association for the Study of Diabetes (EASD) in Munich, Germany. Exenatide is the first potential therapy in a new class of drugs -- known as *incretin mimetics* -- under investigation for the treatment of people with type 2 diabetes who are not taking insulin but are unsuccessful at controlling their blood sugar levels using oral medications. Exenatide is not approved for use in Germany or Europe.

Results from the three pivotal studies showed that exenatide significantly lowered average glucose (blood sugar) levels, measured by A1C, in patients who have failed to achieve adequate glucose control on common oral regimens. In addition, exenatide treatment resulted in reductions in body weight.

52-week data from open-label extension studies of these pivotal trials were also presented, demonstrating exenatide consistently generated a sustained effect on A1C and body weight, resulting in A1C reductions from baseline between 1 and 1.4 percent and reductions in weight from baseline between 2.9 and 4.5 kilograms. A1C reductions tended to be larger for patients with a higher starting baseline. In the 52-week studies, subjects received a fixed dose of exenatide (10 micrograms) twice a day and required no further dose adjustment.

In addition to the pivotal studies, results from a separate crossover study showed 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 results demonstrate exenatide's potential to help patients reduce and maintain their A1Cs at a healthy range. In addition, patients also experienced reductions in body weight and showed evidence of improved beta cell function," said Dr. Anthony Barnett, professor of medicine and honorary consultant physician at the University of Birmingham, United Kingdom. "This combination could be a very important and unique contribution to type 2 diabetes treatment."

Phase 3 Study Design/Protocol
Approximately 1,400 patients unable to achieve adequate control with commonly prescribed oral therapies were involved in the three 30-week, triple-blind, placebo-controlled pivotal phase 3 studies of exenatide. The studies evaluated exenatide in three settings: in conjunction with metformin, in conjunction with sulfonylureas, or in combination with both metformin and sulfonylurea. In these studies, patients continued their pre-study oral therapies and were randomized to one of three arms in which they received either 10 micrograms of exenatide, 5 micrograms of exenatide, or placebo via subcutaneous injection at breakfast and dinner. At the conclusion of the 30-week studies, participants in all three treatment arms were offered the option to continue in open-label extension studies in which all subjects received 10 micrograms of exenatide twice a day.

Phase 3 Key Study Findings (Studies 112, 113 and 115)

AMIGO 1 - Exenatide with Metformin (Study 112)
The first 30-week study examined the effects of exenatide or placebo in 336 patients (average disease duration six years) who were unable to achieve glycemic control with metformin alone. Of patients completing the study, 46 percent in the 10 microgram arm achieved an A1C of seven percent or less. A1C is a measure that reflects a person's average glucose levels over the prior three to four months. At the study's outset, the average A1C of all subjects was 8.2 percent. At the end of the study, the average A1C for the 10 microgram group was reduced by 0.9 percent (difference from placebo). These reductions in A1C were accompanied by average reductions in weight of 2.5 kilograms (difference from placebo).

Exenatide was generally well-tolerated and the most common adverse event reported was mild to moderate nausea, which occurred most frequently early in the study. In this study, 45 percent of patients taking 10 micrograms reported nausea,

compared to 23 percent for placebo. The dropout rate due to nausea was three percent for 10 micrograms and zero percent for placebo. Hypoglycemia rates were consistent with exenatide's glucose-dependent action, with no difference between the placebo and drug arms (five percent for each group).

AMIGO 2 - Exenatide with Sulfonylurea (Study 113)
The second 30-week study involved 377 diabetes patients unable to achieve glycemic control using maximally effective doses of a sulfonylurea, a commonly used oral agent. At the outset of the study, the average A1C of patients was 8.6 percent. Of patients completing the study, 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 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.

AMIGO 3 - Exenatide with Combination of Metformin and Sulfonylurea (Study 115)
In the third 30-week study, researchers evaluated 733 patients (average disease duration nine years) who were unable to achieve glycemic control using a combination of metformin and sulfonylureas. At the study's outset, the average A1C of all subjects was 8.5 percent. Of patients completing the study, 34 percent taking 10 micrograms of exenatide achieved an A1C of seven percent or less. The average reduction in A1C in the 10 microgram arm was one percent (difference from placebo). The average reduction in weight for the 10 microgram group was 0.7 kilograms (difference from placebo).

The most common adverse event reported was mild to moderate nausea, which occurred most frequently early in the study. In this study, 49 percent of patients taking 10 micrograms reported nausea compared to 21 percent for placebo. The dropout rate due to nausea was four percent for 10 micrograms and less than one percent for placebo. As expected, some patients taking exenatide in combination with metformin and maximally effective doses of sulfonylurea experienced mild-to-moderate hypoglycemia, with those taking metformin and minimally effective doses of sulfonylureas reporting a lower incidence than those taking maximally effective doses. The overall incidence of mild-to-moderate hypoglycemia was 28 percent in the 10 microgram group and 13 percent in the placebo group. One episode of severe hypoglycemia was reported in the 5 microgram arm of this study. No participants withdrew from the study because of hypoglycemia.

Across all three studies, the overall dropout rate due to nausea was less than four percent.

One-Year Open-Label Data Shows Sustained Effect
To evaluate the durability of exenatide's effect at the highest dose tested, a group of patients from the open-label extensions of the AMIGO studies who had received 10 micrograms of exenatide for 52 weeks were examined. Results demonstrated that across all three studies, exenatide consistently generated a sustained effect on A1C and body weight, resulting in A1C reductions from baseline between 1 and 1.4 percent and reductions in weight from baseline between 2.9 and 4.5 kilograms. A1C reductions tended to be larger for patients with a higher starting baseline.

Specifically,

- In the 51 patients who completed 52 weeks on 10 micrograms of exenatide in combination with metformin, the average reduction in A1C from baseline was 1.1 percent with average reductions in body weight of 4.5 kilograms.
- In the 35 patients who completed 52 weeks on 10 micrograms of exenatide in combination with sulfonylurea, the average reduction in A1C from baseline was 1.4 percent with average reductions in body weight of approximately 2.9 kilograms.
- In the 77 patients who had completed 52 weeks on 10 micrograms of exenatide and a metformin-sulfonylurea combination, the average reduction in A1C from baseline was 1.0 percent with average reductions in body weight of 3.3 kilograms.

Separate Study Results at EASD - 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 intravenous 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 of 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 dysfunction 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 sugar[1]. Exenatide has been submitted to the U.S. Food and Drug Administration for use by people with type 2 diabetes who are not taking insulin but are unsuccessful at controlling their blood sugar levels using oral medications.

About Diabetes
Diabetes affects an estimated 194 million adults worldwide[2] and more than 32 million adults in the IDF European Region.[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. Centers 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. The UKPDS (United Kingdom Prospective Diabetes Study) showed that with every 1 percent decrease in target A1C levels, a person's risk for diabetes-related complications is reduced by 12 percent, while the risk for microvascular complications (eye, kidney and nerve disease) decreases by 25 percent and the risk for heart attacks decreased by 16 percent.

Lilly's Leadership in Diabetes
Through a long-standing commitment to diabetes care, Lilly provides patients with breakthrough treatments that enable them to live longer, healthier and fuller lives. Since 1923, Lilly has been an industry leader in pioneering therapies to help health care professionals improve the lives of people with diabetes, and research continues on innovative medicines to address the unmet needs of patients.

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.

About Amylin
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.

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 the NDA for exenatide will not be accepted for filing by the FDA, risks that the FDA may request additional information or data regarding exenatide, risks that exenatide may not receive FDA approval or such approval 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 and quarterly reports on Forms 10-K and 10-Q, and Amylin's recently filed Form S-3.

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