



## Improvement in Beta-Cell Function Observed After Three Years of BYETTA(R) Therapy: Data Presented at ADA 2010

### Study Showed Improvements Compared to Lantus(R)

ORLANDO, Fla., June 26, 2010 /PRNewswire via COMTEX News Network/ -- Amylin Pharmaceuticals, Inc. (Nasdaq: AMLN) and Eli Lilly and Company (NYSE: LLY) today announced results from a study comparing the effect of long-term treatment with either BYETTA(R) (exenatide) injection or Lantus(R) (insulin glargine) on overall beta-cell function. (Beta cells are cells in the pancreas that produce insulin.) Three years of BYETTA therapy improved indices of beta-cell function assessed four weeks after discontinuing therapy. These findings were presented at the 70th Annual Scientific Sessions of the American Diabetes Association (ADA) in Orlando, Fla.

After three years of treatment, both therapies reduced A1C similarly (by 0.7 percentage points to 6.6 percent for BYETTA and by 0.5 percentage points to 6.9 percent for Lantus). A1C is a measure of average blood sugar over three months. In addition, BYETTA significantly reduced body weight compared to Lantus (17-pound difference between groups). After completion of three years of therapy, a four-week off-drug period followed to allow assessment of parameters of metabolic state including beta-cell function. Beta-cell function was assessed using a calculated disposition index (insulin secretion adjusted for insulin sensitivity). BYETTA increased insulin sensitivity by 39 percent and increased the disposition index, indicating an improvement in background beta-cell function. Lantus had no effect on insulin sensitivity or disposition index.

"Type 2 diabetes is a progressive disease in which insulin production typically decreases over time," said Michaela Diamant, M.D., professor of diabetology, director, Diabetes Center VUMC, Amsterdam, the Netherlands, and principal investigator of the study. "These findings suggest that with extended use, BYETTA treatment may help improve insulin production and help people with type 2 diabetes better control their blood sugar levels."

### Study Design and Findings

In the controlled portion of the study, metformin-treated patients with type 2 diabetes were randomized to receive BYETTA (n=36) or Lantus (n=33) and measures of beta-cell function, blood sugar control and weight change were compared. Baseline characteristics were age 59+/-8 years; A1C 7.5+/-0.8 percent; BMI 31+/-4 kg/m<sup>2</sup>; weight 202+/-29 pounds. One-year study results, previously published in *Diabetes Care*, found that patients receiving BYETTA, compared to those treated with Lantus, showed significant improvements in beta-cell function. However, the improvements were not sustained following an initial four-week off-drug period.

In this study, a total of 46 patients entered the two-year open-label extension period, and 36 completed the study (BYETTA n=16; Lantus n=20). Insulin sensitivity and beta-cell function were assessed at baseline and after a second four-week off-drug period, following a total of three years of treatment. To assess beta-cell function, an estimate of insulin secretion (first-phase glucose stimulated C-peptide secretion) was measured. This measurement was adjusted for insulin sensitivity in the calculated disposition index. Both therapies reduced A1C similarly (to 6.6+/-0.2 percent and 6.9+/-0.2 percent for BYETTA and Lantus, respectively) after three years of treatment. After the four-week off-drug period, the disposition index was increased in the BYETTA-treated group compared to baseline (+1.43+/-0.78). The disposition index was reduced with Lantus (-0.99+/-0.65). In addition, BYETTA increased insulin sensitivity by 39 percent, while Lantus treatment showed no effect. Thus, both insulin sensitivity and beta-cell function were improved after BYETTA therapy for three years.

### About Diabetes

Diabetes affects more than 24 million people in the U.S. and an estimated 285 million adults worldwide. (i,ii) Approximately 90-95 percent of those affected have type 2 diabetes. Diabetes is the fifth leading cause of death by disease in the U.S. and costs approximately \$174 billion per year in direct and indirect medical expenses. (iii)

According to the Centers for Disease Control and Prevention's National Health and Nutrition Examination Survey, approximately 60 percent of people with diabetes do not achieve their target blood sugar levels with their current treatment regimen. (iv) In addition, 85 percent of type 2 diabetes patients are overweight and 55 percent are considered obese. (v) Data indicate that weight loss (even a modest amount) supports patients in their efforts to achieve and sustain glycemic control. (vi, vii)

### About BYETTA(R) (exenatide) injection

BYETTA is the first FDA-approved GLP-1 receptor agonist for the treatment of type 2 diabetes. BYETTA is not indicated to improve beta-cell function. BYETTA exhibits many of the same effects as the human incretin hormone glucagon-like peptide-1 (GLP-1). GLP-1 improves blood sugar after food intake through multiple effects that work in concert on the stomach, liver, pancreas and brain.

BYETTA is an injectable prescription medicine that may improve blood sugar (glucose) control in adults with type 2 diabetes mellitus, when used with a diet and exercise program. BYETTA is not insulin and should not be taken instead of insulin. BYETTA is not recommended to be taken with insulin. BYETTA is not for people with type 1 diabetes or people with diabetic ketoacidosis.

BYETTA provides sustained A1C control and low incidence of hypoglycemia when used alone or in combination with metformin or a thiazolidinedione, with potential weight loss. BYETTA is not a weight-loss product. BYETTA was approved in April 2005 and has been used by more than one million patients since its introduction. See important safety information below. Additional information about BYETTA is available at [www.BYETTA.com](http://www.BYETTA.com).

### **Important Safety Information for BYETTA(R) (exenatide) injection**

Based on post-marketing data, BYETTA has been associated with acute pancreatitis, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis. The risk for getting low blood sugar is higher if BYETTA is taken with another medicine that can cause low blood sugar, such as a sulfonylurea. BYETTA should not be used in people who have severe kidney problems, and should be used with caution in people who have had a kidney transplant. Patients should talk with their healthcare provider if they have severe problems with their stomach, such as delayed emptying of the stomach (gastroparesis) or problems with digesting food. Severe allergic reactions can happen with BYETTA.

The most common side effects with BYETTA include nausea, vomiting, diarrhea, dizziness, headache, feeling jittery, and acid stomach. Nausea most commonly happens when first starting BYETTA, but may become less over time.

These are not all the side effects from use of BYETTA. A healthcare provider should be consulted about any side effect that is bothersome or does not go away.

**For additional important safety information about BYETTA, please see the full Prescribing Information ([www.byetta.com/pi](http://www.byetta.com/pi)) and Medication Guide ([www.byetta.com/mg](http://www.byetta.com/mg)).**

### **About Amylin and Lilly**

Amylin Pharmaceuticals is a biopharmaceutical company dedicated to improving lives of patients through the discovery, development and commercialization of innovative medicines. Amylin has developed and gained approval for two first-in-class medicines for diabetes, SYMLIN(R) (pramlintide acetate) injection and BYETTA(R) (exenatide) injection. Amylin's research and development activities leverage the Company's expertise in metabolism to develop potential therapies to treat diabetes and obesity. Amylin is headquartered in San Diego, California. Further information on Amylin Pharmaceuticals is available at [www.amylin.com](http://www.amylin.com).

Through a long-standing commitment to diabetes care, Lilly seeks to provide 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 healthcare professionals improve the lives of people with diabetes, and research continues on innovative medicines to address the unmet needs of patients. For more information about Lilly's current diabetes products, visit [www.lillydiabetes.com](http://www.lillydiabetes.com).

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, Ind., 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](http://www.lilly.com).

*This press release contains forward-looking statements about Amylin and Lilly. Actual results could differ materially from those discussed or implied in this press release due to a number of risks and uncertainties, including the risk that BYETTA, and/or the revenues generated from BYETTA, may be affected by competition; unexpected new data; safety and technical issues; the study results mentioned in this press release not being predictive of real-world results; clinical trials not being completed in a timely manner, not confirming previous results, not being predictive of real-world use, or not achieving the intended clinical endpoints; label expansion requests not receiving regulatory approval; or manufacturing and supply issues. The potential for BYETTA may also be affected by government and commercial reimbursement and pricing decisions; the pace of market acceptance; or scientific, regulatory and other issues and risks inherent in the development and commercialization of pharmaceutical products, including those inherent in the collaboration with and dependence upon Amylin and/or Lilly. These and additional risks and uncertainties are described more fully in Amylin's and Lilly's most recent SEC filings, including their Quarterly Reports on Form 10-Q and Annual Reports on Form 10-K. Amylin and Lilly undertake no duty to update these*

*forward-looking statements.*

BYETTA<sup>(R)</sup> is a registered trademark of Amylin Pharmaceuticals, Inc. All other marks are the marks of their respective owners.

**P-LLY**

(i) The International Diabetes Federation Diabetes Atlas. Available at: <http://www.diabetesatlas.org/content/some-285-million-people-worldwide-will-live-diabetes-2010>. Accessed June 19, 2010.

(ii) Diabetes Statistics. American Diabetes Association. Available at: <http://www.diabetes.org/diabetes-basics/diabetes-statistics/>. Accessed June 19, 2010.

(iii) Direct and Indirect Costs of Diabetes in the United States. American Diabetes Association. Available at: <http://www.diabetes.org/how-to-help/action/resources/cost-of-diabetes.html>. Accessed June 19, 2010.

(iv) Saydah SH, Fradkin J and Cowie CC. Poor control of risk factors for vascular disease among adults with previously diagnosed diabetes. *JAMA*. 2004;291:335-42.

(v) Bays HE, Chapman RH and Grandy S. The relationship of body mass index to diabetes mellitus, hypertension and dyslipidaemia: comparison of data from two national surveys. *Int J Clin Pract*. 2007;61:737-47.

(vi) Nutrition Recommendations and Interventions for Diabetes: a position statement of the American Diabetes Association. *Diabetes Care*. 2007;30 Suppl 1:S48-65.

(vii) Anderson JW, Kendall CW and Jenkins DJ. Importance of weight management in type 2 diabetes: review with meta-analysis of clinical studies. *J Am Coll Nutr*. 2003;22:331-9.

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