# Analyses Find Type 2 Diabetes Patients Treated with BYDUREON(TM) Experienced Reduction in Cardiovascular Risk Factors: Results Presented at EASD 2011

September 13, 2011

***Composite Endpoint Included Body Weight, Blood Pressure and Lipid Levels***

LISBON, Portugal, Sep 12, 2011 (BUSINESS WIRE) --

Amylin Pharmaceuticals, Inc. (Nasdaq: AMLN), Eli Lilly and Company (NYSE: LLY) and Alkermes, Inc. (Nasdaq: ALKS) today announced new analyses from the DURATION-3 and -4 trials demonstrating patients treated with the investigational medication BYDUREON(TM)(exenatide extended-release for injectable suspension) experienced significant improvements in select cardiovascular risk factors, in comparison to patients who received commonly prescribed diabetes treatments. The analyses showed that patients receiving BYDUREON for the treatment of type 2 diabetes experienced improvements in composite endpoints related to body weight, abnormal blood pressure and abnormal lipid levels. These findings will be presented at the 47th European Association for the Study of Diabetes Annual Meeting in Lisbon, Portugal.

"Patients with diabetes are at least twice as likely as people without the disease to have heart disease or a stroke. Having other chronic conditions including obesity, high blood pressure or high cholesterol further increases this risk," said James Malone, MD, global exenatide medical director, Lilly Diabetes. "These data underscore the need to consider not only glycemic control but also the important role played by other medical conditions that are common among patients with type 2 diabetes."

**Study Results:**

Patients participating in the DURATION-3 study received BYDUREON or Lantus(R) (insulin glargine) in addition to metformin or metformin plus a sulfonylurea. Interim results from the study's ongoing extension found that patients receiving BYDUREON and completing 84 weeks of therapy:

- Demonstrated statistically significant reduction in body weight (vs. Lantus; treatment difference: 9.8 pounds).

Also, statistically significantly more patients in the BYDUREON treatment arm:

- Met a composite endpoint of A1C <7 percent plus target systolic blood pressure (<130 mmHg) and LDL cholesterol (<100 mg/dL) (15.7 percent vs. 7.9 percent with Lantus); and
- Met a composite endpoint of A1C less-than or equal to 6.5 percent plus target systolic blood pressure (<130 mmHg) and LDL cholesterol (<100 mg/dL) (11.2 percent vs. 5.1 percent with Lantus).

Drug-naïve patients with type 2 diabetes participating in the DURATION-4 trial were randomized to one of four treatment arms: BYDUREON, metformin, Actos(R) (pioglitazone HCl) and Januvia(R) (sitagliptin). The post-hoc analyses showed patients treated with BYDUREON or metformin were more likely to achieve clinically relevant composite goals than patients treated with Actos or Januvia. Researchers evaluated how many patients in each treatment group:

- Achieved a composite endpoint of A1C <7 percent, no weight gain and no minor or major hypoglycemia (48 percent for BYDUREON vs. 22 percent for Actos, 35 percent for Januvia and 46 percent for metformin); and
- Reached a composite endpoint of A1C <7 percent plus target systolic blood pressure (<130 mmHg) and target LDL cholesterol (<100 mg/dL) (16 percent for BYDUREON vs. 10 percent for Actos, 7 percent for Januvia and 13 percent for metformin).

In the DURATION-3 study, gastrointestinal adverse events were among those most commonly reported; however, the number of new cases of all adverse events declined during the extension phase of the trial. In the DURATION-4 study, the most frequently reported adverse events among BYDUREON users were nausea and diarrhea. These data are consistent with the previously reported profiles of BYDUREON and BYETTA(R) (exenatide) injection.

BYDUREON is the proposed brand name for exenatide extended-release for injectable suspension. It is an investigational medication for type 2 diabetes designed to deliver continuous therapeutic levels of exenatide in a single weekly dose. BYDUREON is a once-weekly formulation of exenatide, the active ingredient in BYETTA, which has been available in the U.S. since June 2005 and is used in more than 70 countries worldwide to improve glycemic control in adults with type 2 diabetes. BYDUREON received marketing authorization in the European Union in June 2011 and is currently under review in the U.S., with a Prescription Drug User Fee Action (PDUFA) date of January 28, 2012. It is available in the UK and will launch in other major European countries as soon as possible.

**Study and Presentation Details:**

***DURATION-3***

***Presentation Number 778***
***Poster Session 062--Exenatide: twice daily to once weekly***
***Tuesday, Sept. 13, 2011, 1:30-2:30 p.m. Western European Summer Time***

The initial trial was an open-label study of 467 patients not achieving adequate glucose control using metformin therapy alone or in combination with a sulfonylurea. Subjects were randomized to receive treatment with BYDUREON or titrated doses of Lantus. The primary endpoint was reduction in A1C; secondary endpoints included change in body weight along with other parameters of glucose control, safety endpoints including hypoglycemia, cardiovascular risk biomarkers and patient-reported outcomes.

The comparator-controlled extension study evaluated sustained use of BYDUREON or Lantus and is ongoing. Interim results include data from patients (n=346) who entered the extension study and remained on their initial therapy for a total of 84 weeks. Post-hoc analyses examined changes in systolic blood pressure, diastolic blood pressure, LDL cholesterol, HDL cholesterol, triglycerides, total cholesterol and high-sensitivity C-reactive protein in patients with abnormal baseline values; correlations between these cardiovascular risk factors and body weight changes; and the percentage of patients achieving composite endpoint goals (A1C <7 or less-than or equal to 6.5 percent plus systolic blood pressure <130 mmHg and LDL cholesterol <100 mg/dL).

***DURATION-4***
***Presentation Number 779***
***Poster Session 062--Exenatide: twice daily to once weekly***
***Tuesday, Sept. 13, 2011, 1:30-2:30 p.m. Western European Summer Time***

The 26-week, double-blind, randomized, four-arm parallel study enrolled 820 drug-naïve patients with type 2 diabetes and compared BYDUREON with metformin, Januvia and Actos monotherapies. The primary endpoint was reduction in A1C levels, while secondary endpoints included change in body weight along with other parameters of glucose control, cardiovascular health and patient-reported outcomes.

The post-hoc analyses assessed change in cardiovascular risk factors; correlations between changes in risk factors and body weight for each treatment group; and the percentage of patients achieving composite goals (A1C <7 percent, no weight gain and no minor or major hypoglycemia; and A1C <7 percent, systolic blood pressure <130 mmHg and LDL cholesterol <100 mg/dL). At baseline, more than 50 percent of patients had abnormal blood pressure and lipids, except for total cholesterol.

**About Diabetes**

Diabetes affects nearly 26 million people in the U.S. and an estimated 347 million adults worldwide.[1,2] Approximately 90-95 percent of those affected have type 2 diabetes. In the U.S., diabetes costs more than $174 billion per year in direct and indirect medical expenses.[3]

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.[4] In addition, 85 percent of type 2 diabetes patients are overweight and 55 percent are considered obese.[5] Data indicate that weight loss (even a modest amount) supports patients in their efforts to achieve and sustain glycemic control.[6,7]

**About BYETTA(R) (exenatide) injection**

BYETTA was the first glucagon-like peptide-1 (GLP-1) receptor agonist to be approved by the FDA for the treatment of type 2 diabetes. BYETTA exhibits many of the same effects as the human incretin hormone 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 currently recommended to be taken with insulin. BYETTA is not for people with type 1 diabetes or people with diabetic ketoacidosis. BYETTA has not been studied in people who have pancreatitis.

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 the U.S. in April 2005 and in Europe in November 2006 and has been used by more than 1.8 million patients since its introduction. See important safety information below. Additional information about BYETTA is available at 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. Patients should be observed for signs and symptoms of pancreatitis after initiation or dose escalation of BYETTA. 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. Antibodies may develop with use of BYETTA. Patients who develop high titers to exenatide could have worsening or failure to achieve adequate glycemic control. Consider alternative therapy if this occurs. Severe allergic reactions can happen with BYETTA. There have been no clinical studies establishing conclusive evidence of macrovascular risk reduction with BYETTA or any other antidiabetic drug.

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) and Medication Guide (www.byetta.com/mg).**

**About Amylin, Lilly and Alkermes**

Amylin and Lilly partnered to develop and market BYDUREON, which is based on proprietary technology for long-acting medications developed by Alkermes, Inc. BYDUREON is approved in the EU and is under regulatory review in the U.S.

Amylin Pharmaceuticals is a biopharmaceutical company dedicated to improving lives of patients through the discovery, development and commercialization of innovative medicines. 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 and has a commercial manufacturing facility in Ohio.

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 the 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.

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, Lilly provides answers - through medicines and information - for some of the world's most urgent medical needs.

Alkermes, Inc. is a fully integrated biotechnology company committed to developing innovative medicines to improve patients' lives. Alkermes' robust pipeline includes extended-release injectable and oral products for the treatment of prevalent, chronic diseases, such as central nervous system disorders, addiction and diabetes. Headquartered in Waltham, Mass., Alkermes has a research facility in Massachusetts and a commercial manufacturing facility in Ohio.

*This press release contains forward-looking statements about Amylin, Lilly and Alkermes. 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 BYDUREON may not be approved by the FDA in a timely manner or at all; the information provided in the companies' response to the FDA's complete response letter may not satisfy the FDA; the FDA may request additional information prior to approval; BYETTA and/or the approval of BYDUREON and the revenues or royalties generated from these products may be affected by competition; unexpected new data; safety and technical issues; the analyses mentioned in this press release not being predictive of real-world use; 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 or NDA filings not receiving regulatory approval; the commercial launch of BYDUREON in the United States, if approved, or European countries being delayed; or manufacturing and supply issues. The potential for BYETTA and/or BYDUREON 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, Lilly and/or Alkermes. These and additional risks and uncertainties are described more fully in Amylin's, Lilly's and Alkermes' most recent SEC filings including their Quarterly Reports on Form 10-Q and Annual Reports on Form 10-K. Amylin, Lilly and Alkermes undertake no duty to update these forward-looking statements.*



[1] Diabetes Statistics. American Diabetes Association. Available at: http://www.diabetes.org/diabetes-basics/diabetes-statistics/. Accessed September 2, 2011.

[2] Danaei G, et al. National, regional, and global trends in fasting plasma glucose and diabetes prevalence since 1980: systematic analysis of health examination surveys and epidemiological studies with 370 country-years and 2.7 million participants. *Lancet*. 2011;DOI:10.1016/S0140-6736(11)60679-X.

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

[5] Bays HE, Chapman RH, 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.

[6] Nutrition Recommendations and Interventions for Diabetes: a position statement of the American Diabetes Association. *Diabetes Care.* 2008;31 Suppl 1;S61-78.

[7] Anderson JW, Kendall CW, 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.

SOURCE: Alkermes, Inc.

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