Exenatide tQT Study Showed No Prolongation of QT Interval

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Results to be Included in BYDUREON™ New Drug Application Resubmission in the Third Quarter of 2011

SAN DIEGO & INDIANAPOLIS & WALTHAM, Mass., Jul 07, 2011 (BUSINESS WIRE) -- Amylin Pharmaceuticals, Inc. (Nasdaq: AMLN), Eli Lilly and Company (NYSE: LLY) and Alkermes, Inc. (Nasdaq: ALKS) today announced results from a thorough QT (tQT) study that assessed the potential of exenatide to increase the QT interval across a wide range of plasma concentrations. The study was conducted to satisfy a requirement by the U.S. Food and Drug Administration (FDA) in support of the New Drug Application (NDA) for BYDUREON™ (exenatide extended-release for injectable suspension), an investigational medication for type 2 diabetes. Using multiple heart rate correction methodologies, the study met the pre-specified primary endpoint, demonstrating that exenatide at and above therapeutic levels did not prolong the corrected QT (QTc) interval in healthy individuals. Further, the study found no relationship between QTc interval and plasma exenatide concentrations.

The QT interval represents the amount of time the heart's electrical system takes to repolarize, or recharge, after each beat.[1] As prolongation of the QT interval may increase the risk for cardiac arrhythmias, the FDA requires a tQT study for most new drugs in development. A tQT study is a specialized clinical trial designed to assess whether an investigational medication has the potential to prolong the QT interval.

"The findings of this tQT study are clear. Exenatide did not lead to QT prolongation, even at very high concentrations in the blood," said Christian Weyer, M.D., senior vice president, research and development, Amylin Pharmaceuticals. "This study was designed in accordance with existing guidelines and in consultation with the FDA. We are confident in these results and will continue to work toward making BYDUREON available to patients in the U.S. as soon as possible."

In its October 2010 complete response letter, the FDA requested a tQT study with exposures of exenatide at higher than typical therapeutic levels of BYDUREON, such as those that might be achieved in patients with impaired renal function. The companies plan to submit results of the tQT study to the FDA in the third quarter of 2011 as part of their reply to the complete response letter for the BYDUREON NDA.

Study Details

This randomized double-blind study, designed in accordance with the FDA's published guidance on clinical evaluation of QT/QTc interval (ICH E14), compared the effects of exenatide at or above therapeutic concentrations to placebo on the QT interval in approximately 75 healthy volunteers. The primary endpoint was to determine whether exenatide administered at therapeutic and supratherapeutic concentrations differed from placebo in the mean change in the QTc interval (defined as the upper bound of the 95% confidence interval for placebo-corrected, baseline subtracted QTc being <10 milliseconds). All heart rate correction methodologies that satisfied the pre-specified selection criteria, including QTcP, QTcF and QTcI, met the primary endpoint. Moxifloxacin, an antibiotic known to prolong the QT interval, was used as a positive control. The companies plan to present the full data set at a major medical meeting and submit the data for publication.

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® (exenatide) injection, 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.

About Diabetes

Diabetes affects nearly 36 million people in the U.S. and an estimated 347 million adults worldwide.[2] Approximately 90-95 percent of those affected have type 2 diabetes. 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® (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 http://www.BYETTA.com.

Important Safety Information for BYETTA® (exenatide) injection

Based on postmarketing 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 the tQT study results mentioned in this press release may not be predictive; BYDUREON may not be approved by the FDA as soon as anticipated or at all; the companies' response to the FDA's complete response letter may not be submitted in the third quarter of 2011 and/or the information provided in such response may not satisfy the FDA; the FDA may request additional information prior to approval; BYETTA and/or the approval of BYDUREON and the revenues generated from these products may be affected by competition; unexpected new data; safety and technical issues; 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 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] Long QT Syndrome. Heart Rhythm Society. Available at: http://www.hrsonline.org/PatientInfo/HeartRhythmDisorders/IDisorders/index.cfm. Accessed July 7, 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.

[3] 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 July 7, 2011.

[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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