Exenatide Clinical Data Analysis Shows No Increased Risk of Cardiovascular Events

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Large Cardiovascular Outcomes Study To Be Initiated

Manufacturing Comparability Analysis Complete: Exenatide Once Weekly NDA Submission Remains On Track

SAN DIEGO, INDIANAPOLIS, and CAMBRIDGE, Mass., March 26 /PRNewswire-FirstCall/ -- Amylin Pharmaceuticals, Inc., (Nasdaq: AMLN), Eli Lilly and Company (NYSE: LLY) and Alkermes, Inc. (Nasdaq: ALKS) today announced that a meta-analysis of primary cardiovascular events across controlled clinical studies of three months or greater, from the BYETTA(R) (exenatide) injection database, showed no increased risk of cardiovascular events associated with exenatide use. This analysis was done in a manner consistent with U.S. Food and Drug Administration's (FDA's) updated guidance for evaluating cardiovascular risk in type 2 diabetes agents. Results of this analysis indicate that the relative risk of cardiovascular events in exenatide-treated patients, compared to controls, was 0.70 with a 95 percent confidence interval of 0.38 - 1.31. In this analysis, cardiovascular events included cardiovascular mortality, myocardial infarction, stroke, hospitalization for acute coronary syndrome and revascularization procedures. This finding suggests there is no increased risk of exenatide on cardiovascular outcomes and will be used to support the cardiovascular safety of exenatide once weekly, a phase 3 investigational formulation of exenatide, the active ingredient in BYETTA.

To determine if there are favorable cardiovascular effects of exenatide treatment, Lilly and Amylin intend to initiate a large cardiovascular outcomes trial with a superiority design that will evaluate the effects of exenatide once weekly on major cardiovascular events, compared to standard of care with traditional antidiabetes medications. The global study will be sponsored by Amylin and Lilly, and active discussions are ongoing to have the study led by two academic research centers, The Diabetes Trial Unit at the Oxford Centre for Diabetes (Oxford, England) and Duke Clinical Research Institute at Duke University (Durham, N.C.). The steering committee for this study is chaired by Professor Rury Holman, FRCP, director, Diabetes Trial Unit, Oxford University, and Robert M. Califf, M.D., vice chancellor for clinical research and professor of medicine in the Division of Cardiology at Duke.

"There is a major unmet need for proven therapies that can help reduce the excess cardiovascular morbidity and mortality associated with type 2 diabetes," commented Professor Holman. "This trial is designed to determine the extent to which exenatide may reduce cardiovascular risk, in addition to lowering glucose."

Exenatide Once Weekly NDA Submission On Track By End Of Second Quarter 2009

The analyses to demonstrate comparability necessary for the regulatory submission of exenatide once weekly have been successfully completed and will be part of the New Drug Application (NDA) submitted to FDA. These analyses include data from the ongoing extension of the DURATION-1 study, and will be used to support comparability between intermediate-scale clinical trial material made in Alkermes' manufacturing facility and commercial-scale drug product made at Amylin's manufacturing facility.

"Both the manufacturing comparability data and the meta-analysis of the exenatide clinical trial database are key components of our submission. We believe that the material made at commercial scale is comparable to the clinical-scale material, and we are confident that we will have a strong submission package for exenatide once weekly," said Orville G. Kolterman, M.D., senior vice president of research and development at Amylin. "If approved, this therapy has the potential to become the first weekly therapy to treat type 2 diabetes with glucose control and weight loss. This could offer a unique value proposition for patients, payers and physicians."

Initiation Of New DURATION-5 Clinical Study

The companies have initiated DURATION-5, a new phase 3b study in which patients with type 2 diabetes will use exenatide once weekly commercial-scale drug product in its final commercial configuration. This randomized, 26-week, open-label study in approximately 240 patients has broad utility and is designed to show superiority of exenatide once weekly compared to BYETTA, support regulatory submissions outside the United States and provide additional controlled clinical data on the commercially manufactured product.

"In the near-term, we are working to bring this important therapy to market as quickly as possible," said David Vondle, Lilly's global brand development leader for exenatide. "In the long-term, we are executing on a clinical trial program aimed to show superiority of exenatide once weekly over other diabetes medications."

About Diabetes

Diabetes affects more than 23 million people in the United States and an estimated 246 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 United States and costs approximately $132 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 support 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 and only FDA-approved incretin mimetic for the treatment of type 2 diabetes. 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 approved by the FDA for use by people with type 2 diabetes who are unsuccessful at controlling

their blood sugar levels. BYETTA is an add-on therapy for people currently using metformin, a sulfonylurea, or a thiazolidinedione. BYETTA provides sustained A1C control and low incidence of hypoglycemia when used 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. For full prescribing information, visit www.BYETTA.com.

Important Safety Information for BYETTA

BYETTA improves glucose (blood sugar) control in adults with type 2 diabetes. It is used with metformin, a sulfonylurea, or a thiazolidinedione. BYETTA is not a substitute for insulin in patients whose diabetes requires insulin treatment. BYETTA is not recommended for use in patients with severe problems digesting food or those who have severe disease of the stomach or kidney.

When BYETTA is used with a medicine that contains a sulfonylurea, hypoglycemia (low blood sugar) is a possible side effect. To reduce this possibility, the dose of sulfonylurea medicine may need to be reduced while using BYETTA. Other common side effects with BYETTA include nausea, vomiting, diarrhea, dizziness, headache, feeling jittery, and acid stomach. Nausea is the most common side effect when first starting BYETTA, but decreases over time in most patients.

If patients experience the following severe and persistent symptoms (alone or in combination): abdominal pain, nausea, vomiting, or diarrhea, they should talk to their healthcare provider because these symptoms could be signs of serious medical conditions. BYETTA may reduce appetite, the amount of food eaten, and body weight. No changes in dose are needed for these side effects. These are not all of 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 full prescribing information, visit www.BYETTA.com.

About Amylin, Lilly and Alkermes

Amylin, Lilly, and Alkermes are working together to develop exenatide once weekly, a subcutaneous injection of exenatide for the treatment of type 2 diabetes based on Alkermes' proprietary technology for long-acting medications. Exenatide once weekly is not currently approved by any regulatory agencies.

Amylin Pharmaceuticals is a biopharmaceutical company committed to improving lives 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, California.

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 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.

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

This press release contains forward-looking statements about Amylin, Lilly and Alkermes and the investigational drug, exenatide once weekly. 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 exenatide once weekly and the revenues generated from BYETTA may be affected by competition; unexpected new data; safety and technical issues; clinical trials, including the clinical trials mentioned in this press release, not being completed in a timely manner, not confirming previous results, or not achieving the intended clinical endpoints; the DURATION-1 study extension results potentially not being accepted to support comparability; pre-clinical trials not predicting future results; label expansion requests or NDA filings, including the NDA filing mentioned in this press release, not being submitted in a timely manner; regulatory approval being delayed or not received; or manufacturing and supply issues. The potential for BYETTA and/or exenatide once weekly 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.

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SOURCE Amylin Pharmaceuticals, Inc.

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