Phase 2 Study Shows Lilly/Alkermes Inhaled Insulin System Achieved Blood Sugar Levels Similar to Injected Insulin; 80 Percent of Diabetes Patients in Study Preferred Inhaled Insulin System to Mealtime Injections

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ATHENS, Greece--(BUSINESS WIRE)--Sept. 12, 2005--Eli Lilly and Company (NYSE: LLY) and Alkermes, Inc. (Nasdaq: ALKS) today presented detailed results from a Phase 2 clinical study of inhaled insulin in people with type 1 diabetes, showing that patients using the Lilly/Alkermes inhaled insulin system achieved blood sugar levels similar to patients treated with injected insulin. In addition, 80 percent of patients in this study expressed a preference for the Lilly/Alkermes inhaled insulin system at mealtime over injected insulin.

Using the standard measure of blood sugar, A1C, patients achieved an average level of 7.9 using the Lilly/Alkermes inhaled insulin system, compared to 8.0 in the injected insulin group. A1C is an average measure of blood sugar (glucose) over a three-month period. The study was designed to evaluate whether inhaled insulin delivered through the Lilly/Alkermes system and injected insulin showed similar safety and effectiveness at controlling blood sugar based on dosing regimens commonly used in the every day management of diabetes. These findings are the first disclosure of these results in Europe and were presented today at the 41st annual meeting of the European Association for the Study of Diabetes in Athens, Greece.

Researchers also presented results from a Phase 1 dose response and equivalence study, which showed that the Lilly/Alkermes inhaled insulin system and injected insulin lispro were generally well-tolerated and the overall effect on blood sugar was similar, illustrating that doses could be reliably correlated. This is the first comparative study of dose equivalence between inhaled insulin and insulin lispro, a rapid-acting insulin analog and a commonly-used mealtime insulin.

"Our goal is to provide patients with an innovative product that offers a more acceptable treatment option for patients and may enable them to achieve better blood sugar control, a key aspect in managing diabetes," said Dr. Douglas B. Muchmore, Medical Fellow, Eli Lilly and Company. "These studies, taken together, show that inhaled insulin delivered by the Lilly/Alkermes system is equivalent in various clinical measures to injected insulin. The Lilly/Alkermes Alliance is committed to conducting additional studies needed to confirm the safety and efficacy of inhaled insulin."

Lilly and Alkermes established an alliance in 2001 to develop an inhaled insulin system that delivers human insulin inhalation powder (known as HIIP), based on Alkermes' AIR(R) pulmonary drug delivery technology. The Lilly/Alkermes program is focused on developing an innovative treatment option that can address the challenges associated with managing type 1 and type 2 diabetes. The HIIP delivery system uses a small, simple inhaler that fits in the palm of a hand.

"Despite the health benefits of tight blood glucose control, some physicians and patients are reluctant to initiate insulin therapy. Delaying insulin treatment can contribute to higher blood sugar levels, which can lead to complications such as nerve damage, vision loss and kidney disease," Dr. Satish Garg, Chief of Young Adult Clinics at the Barbara Davis Center for Childhood Diabetes and Professor of Pediatrics and Medicine at the University of Colorado School of Medicine Health Sciences Center, USA. "These studies suggest that inhaled insulin, such as the Lilly/Alkermes system, may encourage patients to move more quickly to a therapy that best improves glucose control."

Phase 3 trials initiated

Lilly and Alkermes initiated a comprehensive Phase 3 clinical program, including pivotal efficacy studies and additional long-term safety studies in both type 1 and type 2 patients, in July 2005 with the start of Phase 3 safety trials required for registration. Those safety studies will be conducted with approximately 1,000 patients at multiple sites in 15 countries, including four countries in Europe: Belgium, Bulgaria, Croatia and Hungary.

Other sites will enroll patients in North America (United States, Canada and Mexico), South America (Argentina, Chile and Columbia) and Asia-Pacific (India, the Philippines, Singapore, Taiwan and Thailand). The studies will be up to 24 months duration and will include patients with type 1 and type 2 diabetes who also have chronic obstructive pulmonary disease or asthma, as well as patients with type 1 diabetes without lung disease.

Study results at EASD

Phase 2 Study Results in Type 1 Patients: Safety and Efficacy of Inhaled Insulin Compared to Injected Insulin

The Phase 2 randomized, open-label, noninferiority crossover study compared the safety and efficacy of the Lilly/Alkermes system using human insulin inhalation powder (HIIP) and subcutaneous injected insulin in patients with type 1 diabetes.

Patients with type 1 diabetes and normal lung function were randomized to pre-meal HIIP (N = 133) or insulin injections (N = 126), both with long-acting insulin glargine once-daily, for 12 weeks. The primary endpoint was based on noninferiority of A1C values (margin of 0.3%) between inhaled insulin and injected insulin. A1C is an average measure of blood glucose over a three-month period. Safety measures included hypoglycemia (low blood sugar) rates, fasting blood glucose (FBG) and carbon monoxide lung diffusing capacity (DL(CO)), a measure of gas exchange capacity of the lung. Key results included:

- Based on A1C, the HIIP and injected insulin treatments were equivalent in controlling blood glucose. The A1C levels were an average of 7.9 in the HIIP group, compared to an average of 8.0 in the injected insulin group.
- HIIP and injected insulin were generally well tolerated. There were no clinically meaningful differences with respect to FBG, DL(CO) and severe hypoglycemia.

- 80 percent of patients preferred the Lilly/Alkermes inhaled insulin system over mealtime injections.

Phase 1 Study of Dose Response and Equivalency of Inhaled Insulin Compared to Injected Insulin Lispro

The Phase 1 open-label, randomized, seven-period crossover trial compared the absorption and action of insulin following a dose of HIIP using the Lilly/Alkermes inhaled insulin system to a similar dose of subcutaneous injected, rapid-acting insulin lispro. Twenty healthy, nonsmoking male (N = 10) and female subjects received up to four single doses of HIIP and three doses of insulin lispro. The primary endpoint was based on pharmacokinetic and glucodynamic assessments. Pulmonary lung function was also evaluated. Key findings included:

- Based on t(max) (time to maximum serum insulin concentration) the Lilly/Alkermes HIIP showed an initial rapid absorption similar to insulin lispro.
- Pharmacokinetic and glucodynamic measures showed that doses of HIIP could be reliably correlated with doses of insulin lispro.
- Intra-patient dosing variability, assessed by administering replicate doses of HIIP and insulin lispro, demonstrated that HIIP had a comparable degree of dosing variability as compared to insulin lispro (coefficient of variability 31 and 29 percent, respectively).
- HIIP and insulin lispro were equally well tolerated. There were no statistically significant differences between patients' pre-dose and post-dose pulmonary function and there were no serious adverse events.

About Diabetes

Diabetes affects an estimated 194 million adults worldwide(1) and around 48.4 million in Europe.(1) Of those affected approximately 85 to 95 percent have type 2 diabetes, a condition where the body does not produce enough insulin and/or the cells in the body do not respond normally to insulin.(2) Type 2 diabetes usually occurs in adults over the age of 40, but is increasingly common in younger people.(2) In virtually every developed society, diabetes is ranked among the leading causes of blindness, renal failure and lower limb amputation, as well as death through its effects on cardiovascular disease (70-80 percent of people with diabetes die of cardiovascular disease)(3). The calculated estimates of the costs of diabetes care in Europe amount to 42.8 million International Dollars per year.(4)

About Alkermes, Inc.

Alkermes, Inc. is a pharmaceutical company that develops products based on sophisticated drug delivery technologies to enhance therapeutic outcomes in major diseases. The Company's lead commercial product is the first and only long-acting atypical antipsychotic medication approved for use in schizophrenia, and is marketed worldwide by Janssen-Cilag ("Janssen"), a wholly owned subsidiary of Johnson & Johnson. The Company's lead proprietary product candidate, Vivitrex(R) (naltrexone long-acting injection), is being developed as a once-monthly injection for the treatment of alcohol dependence. The Company has a pipeline of extended-release injectable products and pulmonary drug products based on its proprietary technology and expertise. Alkermes' product development strategy is twofold: the Company partners its proprietary technology systems and drug delivery expertise with several of the world's finest pharmaceutical companies and it also develops novel, proprietary drug candidates for its own account. The Company's headquarters are in Cambridge, Massachusetts, and it operates research and manufacturing facilities in Massachusetts and Ohio.

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 the 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.

About Lilly

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

This press release contains forward-looking statements about the investigational compound inhaled insulin, and its efficacy and rate of adoption by patients, and reflects Lilly's and Alkermes' current beliefs. However, as with any pharmaceutical product under development, there are substantial risks and uncertainties in the process of development and regulatory review. There is no guarantee that the product will receive regulatory approvals, or that the regulatory approval will be for the indication(s) anticipated by the company. There is also no guarantee that the product will enhance current levels of glucose control or prove to be commercially successful. For further discussion of these and other risks and uncertainties, see Lilly's and Alkermes' filings with the United States Securities and Exchange Commission. Lilly and Alkermes undertake no duty to update forward-looking statements.

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(4) The International Diabetes Federation, Diabetes Atlas, Second edition. The Economic Impact of Diabetes. 2003: 186.

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