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Data on AIR(R) Inhaled Insulin System Presented at American Diabetes Association Meeting

Results Include First-Ever Data on Inhaled Insulin in Patients with COPD and Studies on Patient Training and Dosing Flexibility

WASHINGTON, D.C., June 10, 2006 /PRNewswire-FirstCall via COMTEX News Network/ -- Eli Lilly and Company (NYSE: LLY) and Alkermes, Inc. (Nasdaq: ALKS) today reported new study results of the companies' investigational AIR(R) Inhaled Insulin System(1) (AIR insulin system), including the first published analysis of the effect of chronic obstructive pulmonary disease (COPD) on inhaled insulin absorption and action; the importance to patients of simple, patient-directed training of an inhaled insulin system; and dosing flexibility with the AIR insulin system. These study findings were presented at the American Diabetes Association's (ADA) 66th Annual Scientific Sessions. The AIR insulin system is currently in Phase 3 clinical development by Lilly and Alkermes, and is being studied as an innovative treatment for type 1 and type 2 diabetes.

Oral presentation (Abstract 111-OR): "Pharmacokinetics (PK) and Glucodynamics (GD) of Human Insulin Inhalation Powder (HIIP) in Subjects with Chronic Obstructive Pulmonary Disease (COPD)," Klaus Rave, MD, Profil Institute for Metabolic Research, Neuss, Germany.

This Phase 1 study is the first published analysis of the effect of COPD on inhaled insulin absorption and action and was designed to evaluate the impact compromised lung function has on inhaled insulin dose delivery. As expected in a patient population with compromised lung function, the absorption and action of AIR(R) Inhaled Insulin (AIR insulin) was reduced by a consistent amount in the presence of COPD. The results also demonstrate that AIR insulin was able to deliver similar results on different days in patients with or without COPD and was generally well-tolerated.

According to the National Heart, Lung, and Blood Institute, more than 12 million people in the United States have been diagnosed with COPD -- a progressive condition made up of emphysema and chronic bronchitis, both inflammatory diseases of the lungs. It is speculated that COPD may also be a risk factor, particularly among women, for developing type 2 diabetes.(2)

"Having a non-invasive insulin option that is safe and effective in multiple patient populations is potentially an important advance in the treatment of diabetes and could help patients move earlier and more easily to insulin use," said Klaus Rave, MD, Profil Institute for Metabolic Research, Neuss, Germany. "Because of COPD's prevalence and its potential correlation with type 2 diabetes, particularly in women, it's important to study the safety, efficacy and predictability of AIR insulin in many patient populations, including in people with compromised lung function."

Study Design

In this open-label, randomized, three-period crossover trial, pharmacokinetic and glucodynamic responses to AIR insulin were compared with subcutaneous insulin lispro in 15 nonsmoking healthy subjects (mean age 38y) and 30 nonsmoking subjects with moderate COPD -- 15 each with chronic bronchitis (mean age 53y) and emphysema (mean age 58y) -- using standard glucose clamp methodology, a process for measuring the absorption of and an individual's response to insulin. Subjects received two single doses of AIR insulin (5.2 mg) and one dose of subcutaneous insulin lispro (12 units). Pharmacokinetic and glucodynamic measures were assessed using blood tests, and safety was assessed using pulmonary function tests (PFTs) before and after each clamp and by spirometry -- bedside breathing tests -- performed four times during clamps. Key results included:

* Total insulin exposure and metabolic effect after subcutaneous insulin lispro were comparable in all three groups. Compared with healthy subjects, AIR insulin absorption was reduced by 22 percent ($p=0.13$) in subjects with emphysema and by 44 percent ($p < .001$) in those with chronic bronchitis. The metabolic effect of the AIR insulin dose was reduced in emphysema subjects (33%, $p < .01$) and chronic bronchitis subjects (40%, $p < .01$).

* AIR insulin was well-tolerated by patients with COPD. PFTs and spirometry safety measures showed no difference between AIR insulin and subcutaneous insulin lispro treatments, with modest decreases in FEV1 (forced expiratory volume) and FVC (forced vital capacity) in both COPD groups. No statistically significant differences between the pre- and post-clamp PFTs were observed.

* The reproducibility of action and absorption responses to repeat administration of the same dose of AIR insulin was similar in

healthy subjects and in patients with COPD.

Training Study Data

Poster presentation (Abstract 424-P): "A Comparison of Standard vs Intensive Training on Usage of the Human Insulin Inhalation Powder (HIIP) Delivery System in Type 2 Diabetes (T2D) Patients," Julio Rosenstock, MD, Dallas Diabetes and Endocrine Center at Medical City.

Study Design

This Phase 2 trial in people with type 2 diabetes was designed to compare two levels of training intensity, either standard/patient-directed training, or intensive/provider-coached training for the AIR insulin system on overall blood glucose levels. In this Phase 2, four-week, multi-center, single-blind noninferiority trial, 102 patients with type 2 diabetes were randomized to receive preprandial AIR insulin plus metformin and one of two different levels of training intensity, either standard/patient-directed training or intensive/provider-coached training. Standard training consisted of written directions and a call-in number for assistance. Intensive training included standard training in addition to observation and coaching feedback from a clinician as well as inhalation spirometry training.

The impact of the level of training on blood sugar control was evaluated based on measures of 2-hour postprandial blood glucose (PPBG) and HbA1c (A1C) and the impact the level of training has on safety and blood sugar control. Safety assessments included PFTs, chest x-rays, insulin antibody binding, hypoglycemia, adverse events and body weight. System suitability, compliance with directions, inhalation flow rate and pharmacokinetics were also investigated. Key results included:

* Results demonstrated that the AIR insulin system is easy to use and can be supported by simple, patient-driven training while helping patients manage blood sugar levels.

* Both PPBG and A1C improved similarly and significantly ($p < 0.001$) from baseline in the standard and intensive patient groups.

* Both training methods had similar rates of compliance with training directions (> 90%), and similar safety profiles. As noted in previous studies, cough was the most commonly reported adverse event and was reported by eight percent of all subjects in the study.

* AIR insulin exposure was also similar between groups.

* No discontinuations occurred due to difficulty of use or dislike of the system.

This poster presentation will take place on Monday, June 12, from 12 - 2 p.m. EDT.

"An insulin delivery system should be simple and easy for patients to use, especially in type 2 diabetes, to facilitate insulin initiation and optimization," said Julio Rosenstock, MD, lead investigator from the Dallas Diabetes and Endocrine Center at Medical City. "An inhaled insulin delivery system that can be easily incorporated into daily life while helping patients manage their blood sugar could help patients move earlier and more easily to insulin use and become a highly desirable diabetes management tool for physicians and patients."

Additional Data Presented at ADA

Data from studies focusing on additional attributes of the investigational AIR insulin system also will be presented at ADA. The following poster presentations will take place Monday, June 12, from 12 - 2 p.m. EDT:

* Poster presentation (Abstract 421-P): "Interchangeability Between Three 2U and One 6U Human Insulin Inhalation Powder (HIIP) Capsules," Masako Nakano, Clinical Research Physician, Eli Lilly and Company.

* A Phase 1, single-center, open-label, randomized study with 16 healthy, nondiabetic Japanese males was conducted to compare the differences in action and absorption between three 2 unit-equivalent (U) (0.9 mg/capsule) and one 6 U (2.6 mg/capsule) dose of AIR insulin.

* Subjects were randomly assigned to one of four possible dosing sequences and received four single doses of AIR insulin: one 6U capsule; two 6U capsules; three 6U capsules; three 2U capsules and one dose of subcutaneous insulin lispro (12U, 0.4mg).

* Results showed that either three 2U or one 6U dose could be used in the clinical setting with the same expected effect on insulin absorption and action. Results from other dosing sequences will be available in future publications.

* Poster presentation (Abstract 413-P): "The Importance and Correlates of Insulin Delivery System Attributes in Patients with Type 1 Diabetes," Risa Hayes, Senior Health Outcomes Research Scientist, Eli Lilly and Company.

* A Phase 2, randomized, 24-week cross-over study of 137 type 1 patients (47% male, mean age = 39, mean baseline A1C = 8.1) was conducted to validate the importance of 12 attributes of the insulin delivery system (IDS).

* Participants were asked to rate the importance of 12 IDS attributes on a scale of one (not at all) to five (very) at baseline. Patients were also asked to rank the importance of the attributes (from one to 12) and were administered the Diabetes Treatment Satisfaction Questionnaire (DTSQ). IDS data were correlated with DTSQ scores, A1C, and demographics.

* Ranked attributes included: easy to control my blood sugar; easy to get insulin dose needed; easy to see dose of insulin to be used; easy to select a dose; easy to incorporate into daily life; convenient; easy to carry; after using easy to get ready for next dose; does not interfere with short trips; reduces my reluctance to use insulin; not noticeable to others; reduced my embarrassment when used away from home.

* Results showed that efficacy was the most important attribute to patients in the study, with ease of delivery ranked second. Positive assessments related to ease of delivery, ease of dose selection and system portability (overall ranked two, four and seven) were significantly associated with lower A1C levels. System conspicuousness and feelings of embarrassment and self-consciousness (overall ranked 11 and 12) were significantly associated with less treatment satisfaction with current insulin delivery systems.

"Taken together, these studies suggest that the AIR insulin system could be incorporated into real-life situations if approved in the future," said Bernard Silverman, Vice President, Clinical Development at Alkermes. "We know that patients and physicians want products that are simple, flexible and easy to understand, while helping to manage blood sugar. The AIR insulin system is being studied as an innovative treatment option to help address these challenges."

Lilly/Alkermes AIR(R) Insulin Program

Lilly and Alkermes are conducting Phase 3 clinical trials for an inhaled insulin system (known as the AIR insulin system) that delivers insulin via inhalation based on Alkermes' AIR(R) pulmonary drug delivery technology. The Lilly/Alkermes program is focused on developing an innovative treatment option that can help address the challenges associated with managing type 1 and type 2 diabetes. The AIR insulin system uses a small, simple inhaler that fits in the palm of a hand. For more information about the Phase 3 trials, visit: www.lillytrials.com.

About Diabetes

Diabetes affects an estimated 194 million adults worldwide and an estimated 20.8 million in the United States. 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.(3) Nearly two- thirds of patients on therapies are not achieving treatment goals for controlling blood sugar. (4) Diabetes is associated with an increased risk for a number of serious complications, including heart disease, stroke, amputation, blindness and kidney failure.

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 products include: the first and only long- acting atypical antipsychotic medication approved for use in schizophrenia, marketed worldwide by Janssen-Cilag (Janssen), a wholly owned subsidiary of Johnson & Johnson; and VIVITROL(TM) (naltrexone for extended-release injectable suspension), the first and only once-monthly injectable medication approved 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. For more information about Lilly's current diabetes products visit www.lillydiabetes.com.

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, IN, 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.

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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(1) AIR(R) is a registered trademark of Alkermes, Inc.

(2) J. Rana, M. Mittleman, J. Sheikh, F. Hu, J. Manson, G. Colditz, F. Speizer, R.G. Barr. Chronic Pulmonary Obstructive Disease, Asthma, and Risk of Type 2 Diabetes in Women. Diabetes Care. 27:2478-2484, 2004.

(3) Centers for Disease Control and Prevention. National Diabetes Fact Sheet: General Information and National Estimate on Diabetes in the United States, 2005. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, 2005.

(4) Saydah SH, Fradkin J, Cowie CC. Poor control of risk factors for vascular disease among adults with previously diagnosed diabetes. JAMA. 2004;291:335-342.

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