mannkind

MannKind Announces Late-Breaking Data Demonstrating Faster Onset and Shorter Duration of Action Compared to Mealtime Insulins

June 12, 2016 7:00 PM EDT

Data presented at ADA show Afrezza has a 25-to 35-minute faster onset of action than Lispro, with a duration that is up to two hours shorter

MannKind Corporation reaffirms commitment to Afrezza, the only inhaled insulin available in the U.S., in advance of product relaunch in July

NEW ORLEANS, June 12, 2016 (GLOBE NEWSWIRE) -- MannKind Corporation (Nasdaq:MNKD) (TASE:MNKD) today announced results of two late-breaking posters and four additional analyses of Afrezza® (insulin human) Inhalation Powder, including three posters demonstrating a faster onset of action and a shorter duration than rapid-acting insulin analogs in patients with diabetes mellitus. These data were presented at the American Diabetes Association's 76th Scientific Sessions (ADA). Afrezza, approved by the FDA in 2014 to improve glycemic control in adult patients with type 1 and type 2 diabetes mellitus, is the only inhaled insulin product available in the U.S.

A randomized, controlled, six-treatment, crossover dose-response study (Poster #100-LB) comparing Afrezza to the rapid-acting insulin analog, Lispro, in 30 patients with type 1 diabetes was presented as a late-breaking poster. Results for doses matched to provide the same GIR-AUC (activity parameter) demonstrated:

- Onset of action within 16 to 21 minutes for Afrezza compared to 45 to 52 minutes for subcutaneous insulin across studies
- Afrezza's duration of action at clinically relevant doses was consistently shorter by 2 to 3 hours
- Afrezza's labeled dose overestimates its effect reinforcing the need for appropriate dose titration

Similar results were presented in Poster# 975-P and in a separate meta-analysis of three open-label clamp trials (Poster #931-P) comparing the onset of action of Afrezza with that of subcutaneous Lispro or regular human insulin, which showed onset of action (time to 10% GIR-AUC $_{0\text{-}240}$) with Afrezza was faster at 25 to 34 minutes compared to 53 to 60 minutes with Lispro.

These data highlight the faster onset of action of Afrezza compared with subcutaneous insulins is relevant for optimal dosing, and supports Afrezza's use for rapidly controlling elevated glucose levels.

Many people with type 1 diabetes and progressed type 2 diabetes inject rapid-acting insulin analogs to address rising blood sugar levels caused by food.[i] Hypoglycemia, a dangerous condition that occurs when blood sugar levels drop too low, can be a concern when the effects of rapid-acting insulin analogs extend past mealtime and food absorption. Insulin-related hypoglycemia resulted in nearly 100,000 hospital visits per year in the U.S. between 2007 and 2011, with a cost of $600 million during that five-year period.[ii]

"When administering an inhaled rapid-acting insulin or an injectable rapid-acting insulin analog, it is critical to strike the balance of providing prandial glucose control while minimizing the risk for post-prandial hypoglycemic events," said Raymond W. Urbanski, MD, PhD, Chief Medical Officer of MannKind. "These data show Afrezza begins to work in the body more rapidly and leaves the bloodstream more quickly than an injectable rapid-acting insulin analog, which could translate into more flexibility in the timing of administration and a lower potential for hypoglycemic episodes following meals."

Additional data presented in Poster #100-LB shed light on the dosing of Afrezza relative to subcutaneous rapid-acting insulin. Though no single conversion factor could fully describe the effect, it was noted that the faster response and shorter duration were maintained across matched dosing. As a result, investigators on the late-breaking study reinforced the importance of dose titration for each patient. Based on pharmacokinetic and pharmacodynamic data, it was observed that a 4 unit Afrezza cartridge provides approximately the same insulin exposure as 3.1 IU Lispro.

"There can be significant variability in the way individuals respond to any insulin treatment, often resulting in difficulty with dose selection or a perceived lack of response," said Tim Heise, MD, of the Profil Institute for Clinical Research in Germany and a study investigator. "The findings presented at ADA are important in helping physicians understanding how to dose and titrate Afrezza in order to maintain optimal insulin response and glucose control."

Two additional analyses looking at pulmonary function tests from 4,271 patients (Posters #937-P and #973-P) showed that baseline FEV_1, a common measure of lung function, was not correlated with the proportion of patients experiencing hypoglycemia, reporting cough or reaching A1C targets with Afrezza. The analyses also showed:

- A pooled analysis of seven studies demonstrated slightly greater declines in pulmonary function (FEV_1) in those treated with Afrezza compared with comparator treatments (oral antidiabetic medications or insulin therapy) during the first three months (approximately 30 to 40 mL difference)
- After three months, the change in pulmonary function was similar to comparators up to 24 months
- FEV_1 reductions were small in both Afrezza and comparator groups; they represented a small

fraction of pulmonary capacity, and the observed treatment group difference disappeared within one month of cessation of Afrezza therapy

"Afrezza fills an important role in the management of blood sugar for people with diabetes, and MannKind is devoted to ensuring patients who can benefit from it are aware that it is available and that their doctors are appropriately trained on how to use it," said Matthew Pfeffer, Chief Executive Officer of MannKind. "When we relaunch next month, we will be pulling from nearly two years of learnings related to patient selection, access and titration, in order to simplify the process of getting this important treatment option into the hands of individuals with diabetes."

MannKind recently reacquired the rights to Afrezza and will be launching its own fully integrated commercialization infrastructure along with MannKind-branded supply of the treatment in July. Patients and healthcare providers should be aware that MannKind is committed to ensuring Afrezza remains available to diabetes patients in the United States with no disruptions in access. In addition, MannKind earlier this week announced a new collaboration with JDRF to advance therapies for all patients with type 1 diabetes.

AFREZZA STUDIES PRESENTED AT ADA

- Abstract #100B - *Technosphere® Insulin Inhalation Powder (TI) Displays Earlier Onset and Shorter Duration than Insulin Lispro (Lispro)*
- Abstract #102LB -*Within-Subject Variability of Insulin Exposure and Metabolic Activity Following Replicate Doses of Technosphere® Insulin Inhalation Powder (TI) in Patients with T1DM*
- Abstract #931P - *Technosphere Inhaled (TI) Human Insulin has a More Rapid Onset of Action Than Subcutaneous Insulins - Meta Analysis of Clamp Data From Three Clinical Studies*
- Abstract #975P - *A Population PK/PD Model of Technosphere Insulin Administered to Healthy Subjects*
- Abstract #937P - *Effects of Inhaled Technosphere Insulin (TI) on the Pulmonary Function of Patients with T1D and T2D*
- Abstract #973P -*The Impact of Baseline Lung Function on Outcomes With Inhaled Technosphere Insulin*

ABOUT DIABETES MELLITUS

Currently, diabetes mellitus affects 29.1 million people in the United States, according to the Centers for Disease Control and Prevention. Diabetes mellitus is characterized by the body's inability to regulate levels of blood glucose properly. Insulin, a hormone produced by the pancreas, normally regulates the body's glucose levels, but in people with diabetes mellitus insufficient levels of insulin are produced or the body fails to respond adequately to the insulin it produces. In patients with diabetes, current injected insulins are absorbed into the bloodstream slower than the body's own insulin would be released if the pancreas was healthy.[iii]

INDICATION

Prescription Afrezza® (insulin human) Inhalation Powder is a rapid-acting inhaled insulin used to treat adults with diabetes for the control of high blood sugar.

LIMITATIONS OF USE

Do not use Afrezza as a substitute for long-acting insulin; Afrezza must be used in combination with long-acting insulin in patients with type 1 diabetes.

Do not use Afrezza to treat diabetic ketoacidosis.

Afrezza is not recommended in patients who smoke or who have recently stopped smoking.

IMPORTANT SAFETY INFORMATION FOR AFREZZA

WARNING: RISK OF ACUTE BRONCHOSPASM IN PATIENTS WITH CHRONIC LUNG DISEASE

- Acute bronchospasm has been observed in patients with asthma and COPD using Afrezza.
- Afrezza is contraindicated in patients with chronic lung disease such as asthma or COPD.
- Before initiating Afrezza, perform a detailed medical history, physical examination, and spirometry (FEV1) to identify potential lung disease in all patients.

Do not use Afrezza if you have problems with your lungs, such as asthma or COPD. Do not use Afrezza during a low blood sugar reaction (hypoglycemia). If you are allergic to any of the ingredients in Afrezza, do not use Afrezza as this may cause a significant and severe allergic reaction.

Before using Afrezza, your doctor will take a medical history and do a physical exam and a breathing test (called spirometry) to determine if you have lung problems. Patients with lung problems should not use Afrezza. If your doctor finds you have lung problems, use of Afrezza may cause a severe asthma-like breathing problem. Afrezza can reduce lung function, so your doctor will also want to test your breathing 6 months after starting Afrezza, and then each year after that, with more frequent testing done if you have symptoms such as wheezing or coughing. Tell your doctor if you currently have lung cancer or have had it in the past, or if you have an increased risk of developing lung cancer.

You must test your blood sugar levels while using insulin such as Afrezza. Do not make any changes to your dose or type of insulin without talking to your healthcare provider. Any change of insulin should be made carefully and only under your doctor's care.

The most common side effect of insulin, including Afrezza® (insulin human) Inhalation Powder, is low blood sugar (hypoglycemia), which can be serious and life-threatening. Some people may experience symptoms such as shaking, sweating, fast heartbeat, and blurred vision. It may cause harm to your heart or brain. It is important for you to understand how to manage the use of Afrezza, and to understand how to lessen the risk of hypoglycemia events.

Tell your doctor about other medicines you take, especially ones commonly called TZDs (thiazolidinediones) and supplements, because they can change the way insulin works. If you have heart failure or other heart problems, it may get worse while you take TZDs with Afrezza. Before starting Afrezza, it is important to tell your doctor about all your medical conditions including if you have a history of lung problems, if you are pregnant or plan to become pregnant, or if you are breastfeeding or planning to breastfeed.

In addition to low blood sugar (hypoglycemia), other possible side effects associated with Afrezza include cough, throat pain or irritation, headache, diarrhea, tiredness, and nausea.
Please see full Prescribing Information for Afrezza, including Boxed WARNING and www.afrezza.com.

ABOUT AFREZZA®
Afrezza is available in 4-unit, 8-unit and 12-unit single-dose cartridges of insulin powder that can be used, as prescribed by a health care professional, in combination with other diabetes medications to achieve target blood sugar levels. For Afrezza doses exceeding 12 units, patients may use a combination of 4-unit, 8-unit and 12-unit cartridges. The disposable inhaler can be used for up to 15 days, should be kept in a clean, dry place with the mouthpiece cover on and may be wiped with a clean, dry cloth if needed.

ABOUT MANNKIND CORPORATION
MannKind Corporation (Nasdaq:MNKD) (TASE:MNKD) focuses on the discovery and development of therapeutic products for patients with diseases such as diabetes. MannKind maintains a website at www.mannkindcorp.com to which MannKind regularly posts copies of its press releases as well as additional information about MannKind. Interested persons can subscribe on the MannKind website to e-mail alerts that are sent automatically when MannKind issues press releases, files its reports with the Securities and Exchange Commission or posts certain other information to the website.

FORWARD-LOOKING STATEMENTS
This press release contains forward-looking statements that involve risks and uncertainties, including statements regarding MannKind's ability to directly commercialize Afrezza and the commercial potential of
Afrezza. Words such as "believes", "anticipates", "plans", "expects", "intend", "will", "goal", "potential" and similar expressions are intended to identify forward-looking statements. These forward-looking statements are based upon the MannKind's current expectations. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of these risks and uncertainties, which include, without limitation, completing and analyzing the results of clinical studies, difficulties or delays in obtaining regulatory feedback or concurrence with regulatory authorities on the interpretation of study results, the ability to generate significant product sales for MannKind, MannKind's ability to manage its existing cash resources or raise additional cash resources, stock price volatility and other risks detailed in MannKind's filings with the Securities and Exchange Commission, including the Annual Report on Form 10-K for the year ended December 31, 2015 and subsequent periodic reports on Form 10-Q and current reports on Form 8-K. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date of this press release. All forward-looking statements are qualified in their entirety by this cautionary statement, and MannKind undertakes no obligation to revise or update any forward-looking statements to reflect events or circumstances after the date of this press release.

---

[i] http://www.diabetes.org/living-with-diabetes/treatment-and-care/medication/insulin/insulin-basics.html

[ii] https://archinte.jamanetwork.com/article.aspx?articleid=1835360

[iii] http://www.niddk.nih.gov/health-information/health-topics/Diabetes/your-guide-diabetes/Pages/index.aspx

Company Contact:
Rose Alinaya
SVP, Finance
661-775-5300
ralinaya@mannkindcorp.com