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VALENCIA, Calif.--(BUSINESS WIRE)--Aug. 14, 2013-- **MannKind Corporation (Nasdaq: MNKD)** today announced positive preliminary results from Study 171, a Phase 3 clinical study of AFREZZA® (insulin human [rDNA origin]) Inhalation Powder, an investigational, ultra rapid-acting mealtime insulin therapy, administered using MannKind's next-generation (Gen2) inhaler (also known as the Dreamboat™ inhaler), in patients with type 1 diabetes.

Highlights

AFREZZA-Gen2, compared to insulin aspart, showed:

- Non-inferior decreases in A1c levels;
- Significantly less hypoglycemia;
- Significant decreases in fasting blood glucose levels; and
- Significant weight advantage.

In addition, the changes in pulmonary function observed in the AFREZZA-Gen2 group were no different than those observed in an AFREZZA treatment group that utilized MannKind's first-generation (MedTone) inhaler. This finding will facilitate bridging the Gen2 inhaler to the pulmonary safety data that was collected in earlier clinical studies using the MedTone inhaler.

"We are pleased that Study 171 met its primary endpoint of non-inferiority, by demonstrating that AFREZZA produces A1c reductions comparable to insulin aspart," stated Alfred Mann, Chairman and Chief Executive Officer of MannKind Corporation. "Importantly, this study also established a bridge between the Gen2 inhaler and the large body of pulmonary safety data that was previously collected for AFREZZA using the MedTone inhaler. Consistent with previous studies of AFREZZA, including a two-year safety study involving 2,035 subjects, the use of AFREZZA was associated with a clinically insignificant decrease in lung function that appeared at the onset of therapy, did not progress during therapy and resolved fully upon cessation of therapy. Based on the results of this study, we believe that AFREZZA can be used to achieve glycemic control that is comparable to the current standard of care while at the same time offering potential advantages in terms of lower fasting blood glucose levels, weight neutrality and a lower overall risk of hypoglycemia."

Study 171

Study 171 was an open-label study involving 518 patients with type 1 diabetes on basal/bolus insulin therapy who were studied at sites in the United States, Russia, Ukraine and Brazil. After a four-week run-in period to optimize their basal insulin, patients entered a 24-week treatment period in which they were randomized in one of three ways:

- Continuing on subcutaneous insulin aspart in combination with a basal insulin (170 patients);
- Switching to AFREZZA administered using the Gen2 inhaler in combination with their basal insulin (174 patients); or
- Switching to AFREZZA administered using the MedTone inhaler in combination with their basal insulin (174 patients).

The treatment period consisted of 12 weeks of prandial insulin optimization with continued basal titration followed by a 12-week period during which subjects maintained stable doses of insulin (prandial and basal). There was also a follow-up visit four weeks after completion of the treatment period.

Over the 24-week treatment period of this study, A1c levels decreased comparably in the AFREZZA-Gen2 group (-0.21%) and the insulin aspart group (-0.40%). The 95% confidence interval (0.02% to 0.36%) of the between-group difference did not exceed the predetermined threshold of 0.40%, thereby establishing non-inferiority between AFREZZA-Gen2 and insulin aspart, which was the primary endpoint of the study.

Other Results

There was a significant difference in fasting blood glucose (FBG) levels in the AFREZZA-Gen2 group compared to the insulin aspart group. In the AFREZZA-Gen2 group, mean FBG levels decreased by 25.3 mg/dL by the end of the treatment period whereas the insulin aspart group experienced an increase of 10.2 mg/dL in FBG levels over the same period ($p=0.0027$). After the four-week follow-up period, during which all patients received insulin aspart and a basal insulin, there was no longer any difference in FBG levels between the treatment groups, demonstrating that this effect on FBG levels was attributable to AFREZZA therapy.

Significantly less total hypoglycemia was observed in the AFREZZA-Gen2 group (9.80 events per subject-month) compared to the insulin aspart group (13.97 events per subject-month; $p<0.0001$). The event rate of severe hypoglycemia was also lower in the AFREZZA-Gen2 group (8.05 events per

subject-month) than in the insulin aspart group (14.45 events per subject-month); however, this difference was not statistically significant (p=0.1022).

The proportion of subjects achieving A1c target levels ≤7.0% or ≤6.5% at the end of the 24-week treatment period was less in the AFREZZA-Gen2 group than in the insulin aspart group; however, among patients who achieved A1c levels ≤7.0% and ≤6.5% at the end of the 24-week treatment period, the event rates for overall hypoglycemia (mild, moderate and severe) were all significantly lower in the AFREZZA-Gen2 group than in the insulin aspart group.

There was also a significant difference in weight outcomes. Patients in the AFREZZA-Gen2 group lost an average of 0.39 kg over the treatment period compared to an average gain of 0.93 kg in the insulin aspart group (p=0.0102).

The main safety objective of this study was to compare changes in FEV_1 (forced expiratory volume in one second) from randomization to week 24 between the AFREZZA-Gen2 and AFREZZA-MedTone groups. Over this period, there was an insignificant difference of 0.01 L in mean change in FEV_1 between the two AFREZZA groups (p=0.5364). Over the same 24-week treatment period, the decrease in FEV_1 seen in the AFREZZA-Gen2 group was slightly greater than that seen in the aspart group (0.03 L). After cessation of the treatment period, FEV_1 values in both AFREZZA groups increased, so that by the follow-up visit at week 28 there were virtually no differences in FEV_1 among the three treatment groups.

In general, treatment with AFREZZA was well-tolerated over 24 weeks by subjects with type 1 diabetes. The incidence of serious adverse events related to study drug was similar in the AFREZZA-Gen2 (2.3%), AFREZZA-MedTone (2.9%) and insulin aspart (1.8%) groups. There were no serious cardiovascular events reported in this study. The most common drug-related adverse event was cough, reported by 30.5% of AFREZZA-Gen2 patients, 20.8% of AFREZZA-MedTone patients and 0% of insulin aspart patients. Cough was predominantly dry, intermittent, and usually occurred within 10 minutes of inhalation. The incidence of cough was highest during the first week of the treatment period and diminished quickly thereafter. The discontinuation rate due to cough was low (AFREZZA-Gen2: 5.7%; AFREZZA-MedTone: 2.9%; insulin aspart: 0%).

These preliminary results are subject to further analysis.

About AFREZZA®

AFREZZA® is a novel, ultra rapid-acting mealtime insulin therapy being developed by MannKind Corporation for the treatment of adult patients with type 1 or type 2 diabetes for the control of hyperglycemia. It is a drug-device combination product, consisting of AFREZZA Inhalation Powder, pre-metered into single-use cartridges, and a light, discreet and easy-to-use inhaler. Administered at the start of a meal, AFREZZA dissolves immediately upon inhalation and delivers insulin quickly to the bloodstream. Peak insulin levels are achieved within 12 to 14 minutes of administration, effectively mimicking the release of meal-time insulin observed in healthy individuals, but which is absent in patients with diabetes.

About MannKind Corporation

MannKind Corporation (Nasdaq: MNKD) focuses on the discovery, development and commercialization of therapeutic products for patients with diseases such as diabetes. Its lead product candidate, AFREZZA®, has completed Phase 3 clinical trials. 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, including statements related to the results of clinical studies, the bridging to an earlier clinical program, the potential use of AFREZZA to achieve glycemic control in type 1 diabetes patients that is comparable to the current standard of care, and the potential advantages of AFREZZA over current treatments, that involve risks and uncertainties. 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 Company'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, difficulties or delays in obtaining regulatory feedback or completing and analyzing the results of clinical studies, completion of further statistical analysis of the results of Study 171, whether the data from Study 171, as well as Study 175, the Phase 3 clinical study of AFREZZA in type 2 diabetes patients, will satisfy all requirements of the Food and Drug Administration and will be sufficient to support approval of an amended new drug application for AFREZZA, the timing of regulatory review and decisions, 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, 2012 and periodic reports on Form 10-Q and 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.

Source: MannKind Corporation

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