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# AFREZZA(R) Suppresses Endogenous Glucose Production More Rapidly Than Currently Available Insulin Therapy

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ORLANDO, Fla., Jun 26, 2010 (BUSINESS WIRE) --

AFREZZA® (insulin human [rDNA origin]) Inhalation Powder, a well-tolerated, investigational ultra rapid acting mealtime insulin, provides more rapid suppression of endogenous glucose production (EGP) after a meal than the subcutaneously-injected insulin lispro in patients with Type 2 diabetes, according to data presented today at the American Diabetes Association's 70th Scientific Sessions. "The proper control of endogenous blood sugar after meals is crucial to the successful management of patients with Type 2 diabetes, and our findings show that AFREZZA achieves this goal more rapidly than standard therapy with insulin lispro," said Dr. Peter Richardson, MRCP, Corporate Vice President and Chief Scientific Officer, MannKind Corporation. "Additionally, the finding that the effect of AFREZZA on free fatty acids and glucagon was dose-dependent may be very important in understanding the consistent effect that we see with AFREZZA on fasting glucose levels. Free fatty acids play a major role in the pathophysiology of insulin resistance, and we anticipate conducting further research in this area." Diabetes, which affects 23.6 million people in the U.S., is characterized by the body's inability to properly regulate levels of blood glucose, or blood sugar. Insulin, a hormone produced by the pancreas, normally regulates the body's glucose levels, but in people with diabetes insufficient levels of insulin are produced or the body fails to respond adequately to the insulin it produces. Historically, mealtime insulin therapy regimens have had a number of limitations, including the risk of severe hypoglycemia, the likelihood of weight gain, inadequate post-meal glucose control, the need for complex titration of insulin doses in connection with meals and the need for injections. Additionally, these therapies have not mimicked the natural time-action profile of insulin normally seen in healthy individuals and presented challenges in maintaining compliance. AFREZZA™ is a novel, ultra rapid acting mealtime insulin therapy being developed by MannKind Corporation for the treatment of adult patients with Type 1 and 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 dose cartridges and the light, discreet and easy-to-use AFREZZA Inhaler. Administered at the start of a meal, AFREZZA dissolves immediately upon inhalation and delivers insulin quickly to the blood stream. Peak insulin levels are achieved within 12 to 14 minutes of administration, mimicking the release of meal-time insulin observed in healthy individuals. To date, the AFREZZA clinical program has involved more than 50 different studies and over 5,000 adult patients. *Study Design and Key Findings* Single doses of 60U and 90U AFREZZA were compared with 10 IU subcutaneous lispro insulin in an open-label, two-way crossover study incorporating a meal challenge (BoostPlus® 12 fl oz enriched with [U-13C]glucose) in insulin-treated subjects with Type 2 diabetes and normal pulmonary function. The dose of 60U of AFREZZA, using MannKind's first-generation inhalation device, provided approximately the same insulin exposure as the 10 IU dose of injected lispro. Before the meal, subjects' blood glucose was kept at 110±10 mg/dl using a continuous low-dose intravenous insulin infusion fixed 90 minutes before dosing. If needed, glucose was infused postdose to maintain a blood glucose level of at least 75 mg/dl. Maximal EGP suppression occurred markedly earlier with AFREZZA (45 and 60 minutes for 60 and 90U) than with lispro (105 minutes) based on mean profiles, and the greatest decrease from baseline EGP was observed after 90U AFREZZA (10.3 mol/kg/minutes) versus 60U AFREZZA and lispro (6.9 and 7.1 mol/kg/minutes). Total EGP areas over curve (AOC) were comparable across groups. A significantly greater proportion of EGP AOC was observed with AFREZZA up to 140 minutes postdose ($p<0.03$) versus with lispro. The effect of AFREZZA on free fatty acids (FFA) and glucagon was dose dependent, with an earlier (AFREZZA 90 and 60U) and greater (AFREZZA 90U) decrease from baseline. The highest FFA AOC was observed after AFREZZA 90U, while lispro and 60U AFREZZA were comparable. Peak glucagon concentrations and area under curve were substantially lower after 90U AFREZZA dose than after either lispro or 60U AFREZZA. **About MannKind Corporation** MannKind Corporation (Nasdaq: MNKD) focuses on the discovery, development and commercialization of therapeutic products for patients with diseases such as diabetes and cancer. Its diabetes pipeline includes AFREZZA® and MKC253. MKC253 is currently in phase 1 clinical trials. In March 2009, MannKind submitted a New Drug Application (NDA) to the U.S. Food and Drug Administration (FDA) requesting approval of AFREZZA for the treatment of adults with Type 1 or Type 2 diabetes for the control of hyperglycemia. In March 2010, MannKind received a Complete Response to this NDA from the FDA requesting additional information. An End-of-Review meeting was held in June 2010 and MannKind is currently preparing its resubmission of the AFREZZA NDA. Other products in MannKind's pipeline include the cancer immunotherapy products MKC1106-PP and MKC1106-MT, which are currently in phase 1 clinical trials. MannKind maintains a website at http://cts.businesswire.com/ct/CT?id=smartlink&url=http%3A%2F%2Fwww.mannkindcorp.com&esheet=6338730&lan=en-US&anchor=http%3A%2F%2Fwww.mannkindcorp.com&index=1&md5=93b4e9aaa5f55759fe48a3ef5b3c4b64 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.

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*Study Design and Key Findings*

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