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# **Dear Stockholders,**

In 2007, we made substantial progress toward our goal of bringing Technosphere Insulin to the tens of millions of diabetes patients in the United States and around the world. Our main focus during the past year was the execution of a large and challenging Phase 3 clinical program for Technosphere® Insulin, involving more than 350 clinical trial sites in a dozen countries. This program is on schedule for completion in the third quarter of 2008. As well, we moved ahead with the expansion of our Danbury, Connecticut manufacturing facility for the production of Technosphere® Insulin. During the past year, we also accelerated the development of other products in our pipeline, initiating trials for a second diabetes compound and clearing an IND for a second cancer compound.

For other companies involved in the development and commercialization of inhaled insulin, the last few months have been quite difficult. Their struggles have not been surprising. Indeed, none of the inhaled insulin products of Pfizer, Novo Nordisk and Eli Lilly offered a clinical benefit over current (injectable) insulin therapy. We have always believed that they would suffer by comparison to our novel technology, because Technosphere® Insulin offers a fundamentally different approach to treating diabetes. In particular, our Technosphere® technology delivers insulin more rapidly and in an active form that can be readily and quickly used by the body. As a result, Technosphere® Insulin is a superior insulin that most closely mimics normal body physiology, resulting in tighter post-prandial glycemic control and decreased risk of hypoglycemia (see sidebar below).

# Clinical and Safety Benefits of Technosphere® Insulin

- A significant reduction in post-prandial glucose excursions, comparable to the levels seen in normal people. Glucose excursions are believed to be an important risk factor in the development of diabetes complications.
- The ability to achieve comparable levels of overall glucose control compared with present "state of the art" treatment, as measured by HbA1c the standard efficacy measure for diabetes treatments.
- A lower risk of hypoglycemia, which is considered to be a major problem for patients using presently available insulins and many oral treatments.

- No weight gain and even weight loss in patients treated with Technosphere® Insulin, in contrast to the weight gain that is usually considered a major downside of insulin therapy.
- No need for complex meal titration, as utilized in our studies to date, significantly simplifying treatment and reducing the training typically needed for insulin therapy.
- No adverse effect on the measures of pulmonary function that have been reported to occur with other inhaled insulins.



The Technosphere® platform is not merely another approach to inhaled insulin or another drug-delivery offering. It is a combination of medical device and formulation technology that permits us to deliver drugs directly to the enormous surface area of the deep lung, which is in direct contact with the circulatory system. With our approach, hormones such as insulin and GLP-1 get into the bloodstream within minutes of inhalation, enabling patients to restore the signaling function that is normally played by these compounds in people without diabetes. We are only beginning to explore the clinical potential of our unique pulmonary arterial delivery system.

Nonetheless, the withdrawal by Pfizer, Novo Nordisk and Eli Lilly from the inhaled insulin market has raised questions about whether Technosphere® Insulin can be a successful product. However attractive Technosphere® Insulin may be from a clinical perspective, our current challenge is to also demonstrate its commercial potential. To do so, we are conducting a variety of activities that will bring the commercial potential of Technosphere® Insulin into sharper focus. We have begun a Phase 3b trial that will provide further insight into the ways in which Technosphere® Insulin is differentiated from other insulin therapies. We are continuing our marketing research in order to refine our positioning, our understanding of the market segmentation and our messaging. We are also undertaking a number of technical refinements that are designed to add robustness and to lower the cost of our product.

These activities are being conducted in parallel with the ongoing clinical development of MKC253, our GLP-1 product, and the preclinical development of a third peptide hormone for the treatment of obesity. In a recent Phase 1 study, we observed that inhalation of MKC253 by healthy volunteers produced a sharp pulse of GLP-1 in the bloodstream within three minutes, followed within six minutes by a GLP-1-induced release of insulin from the pancreas. Surprisingly, there were no reports of the side effects normally associated with such levels of GLP-1, such as profuse sweating, nausea and vomiting. These results support the hypothesis that inhalation of MKC253 may be able to simulate the physiological role played by GLP-1 that is lost in patients with type 2 diabetes. We attribute these findings to the unique properties of our pulmonary arterial delivery system, providing further evidence of the value of our Technosphere® platform.

We know that external events are testing your patience right now. On behalf of our 600 employees, we would like to thank you for your commitment to MannKind. We look forward to keeping you informed of our progress in 2008, and particularly in reporting the clinical data from our Phase 3 program.

Yours sincerely,

Hakan Edstrom

Malan Seller

President and Chief Operating Officer

**Alfred Mann** 

Chairman and Chief Executive Officer