

MANNKIND CORP  
Form 10-K  
March 14, 2008

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**UNITED STATES SECURITIES AND EXCHANGE COMMISSION  
Washington, D.C. 20549**

**Form 10-K**

- ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**  
For the fiscal year ended **December 31, 2007**
- or**
- TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**  
For the transition period from        to        .

**Commission file number: 000-50865**  
**MannKind Corporation**  
*(Exact name of registrant as specified in its charter)*

**Delaware**  
*(State or other jurisdiction of incorporation or organization)*

**13-3607736**  
*(I.R.S. Employer Identification No.)*

**28903 North Avenue Paine  
Valencia, California**  
*(Address of principal executive offices)*

**91355**  
*(Zip Code)*

**Registrant's telephone number, including area code**  
**(661) 775-5300**

**Securities registered pursuant to Section 12(b) of the Act:**

Title of Class	Name of Each Exchange on Which Registered
Common Stock, par value \$0.01 per share	The Nasdaq Stock Market

**Securities registered pursuant to Section 12(g) of the Act:**

**None**  
*(Title of class)*

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes  No

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes  No

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Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes  No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of large accelerated filer, accelerated filer and smaller reporting company in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer  Accelerated filer  Non-accelerated filer  Smaller reporting company   
(Do not check if a smaller reporting company)

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes  No

As of June 30, 2007, the aggregate market value of the voting stock held by non-affiliates of the registrant, computed by reference to the last sale price of such stock as of such date on the Nasdaq Global Market, was approximately \$301,878,953.

As of March 10, 2008, there were 101,418,675 shares of the registrant's Common Stock outstanding.

**DOCUMENTS INCORPORATED BY REFERENCE:**

Portions of the registrant's definitive Proxy Statement, or the Proxy Statement, for the 2008 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission pursuant to Regulation 14A not later than 120 days after the end of the fiscal year covered by this Form 10-K, are incorporated by reference in Part III, Items 10-14 of this Annual Report on Form 10-K.

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**MANNKIND CORPORATION**

**Annual Report on Form 10-K  
For the Fiscal Year Ended December 31, 2007**

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### **Forward-Looking Statements**

Statements in this report that are not strictly historical in nature are forward-looking statements. These statements include, but are not limited to, statements about: the progress or success of our research, development and clinical programs, the timing of completion of enrollment in our clinical trials, the timing of the interim analyses and the timing or success of the commercialization of our Technosphere Insulin System, or any other products or therapies that we may develop; our ability to market, commercialize and achieve market acceptance for our Technosphere Insulin System, or any other products or therapies that we may develop; our ability to protect our intellectual property and operate our business without infringing upon the intellectual property rights of others; our estimates for future performance; our estimates regarding anticipated operating losses, future revenues, capital requirements and our needs for additional financing; and scientific studies and the conclusions we draw from them. In some cases, you can identify forward-looking statements by terms such as anticipates, believes, could, estimates, expects, goal, i may, plans, potential, predicts, projects, should, will, would, and similar expressions intended to identify forward-looking statements. These statements are only predictions or conclusions based on current information and expectations and involve a number of risks and uncertainties. The underlying information and expectations are likely to change over time. Actual events or results may differ materially from those projected in the forward-looking statements due to various factors, including, but not limited to, those set forth under the caption Risks and Uncertainties That May Affect Results and elsewhere in this report. Except as required by law, we undertake no obligation to publicly update or revise any forward-looking statements, whether as a result of new information, future events or otherwise.

Technosphere® and MedTone® are our registered trademarks in the United States. We have also applied for or registered company trademarks in other jurisdictions, including Europe and Japan. This document also contains trademarks and service marks of other companies that are the property of their respective owners.

## **PART I**

### **Item 1. Business**

Unless the context requires otherwise, the words MannKind, we, company, us and our refer to MannKind Corporation and its subsidiary.

### **OVERVIEW**

MannKind Corporation is a biopharmaceutical company focused on the discovery, development and commercialization of therapeutic products for diseases such as diabetes and cancer. Our lead investigational product candidate, the Technosphere Insulin System, is currently in Phase 3 clinical trials in the United States, Europe and Latin America to study its safety and efficacy in the treatment of diabetes. This dry powder therapy consists of our proprietary Technosphere particles onto which insulin molecules are loaded. These loaded particles are then aerosolized and inhaled into the deep lung using our proprietary MedTone inhaler. We believe that the performance characteristics, unique kinetics, convenience and ease of use of our Technosphere Insulin System may have the potential to change the way diabetes is treated.

We believe that a distinguishing characteristic of the Technosphere Insulin System is that it produces a profile of insulin levels in the bloodstream that approximates the insulin profile normally seen in healthy individuals immediately following the beginning of a meal, but which is absent in patients with diabetes. Specifically, Technosphere Insulin is rapidly absorbed into the bloodstream following inhalation, reaching peak levels within 12 to 14 minutes. As a result of this rapid absorption, most of the glucose-lowering activity of Technosphere Insulin occurs within the first three hours of administration which is generally when glucose becomes available from a meal instead

of the much longer duration of action observed when insulin is injected subcutaneously. We believe that the relatively short duration of action of Technosphere Insulin reduces the need for patients to snack between meals in order to manage ongoing blood glucose excursions. In our clinical trials, we have observed that patients using the Technosphere Insulin System have achieved significant reductions in post-meal glucose excursions and significant improvements in overall glucose control, as measured by decreases in glycosylated hemoglobin, or A1C, levels, without the weight gain typically associated with insulin therapy.

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Our current development plans call for the completion of our pivotal Phase 3 trials of the Technosphere Insulin System in the third quarter of 2008. These trials include efficacy studies in patients with type 1 and type 2 diabetes and a two-year, Phase 3 safety trial that compares the pulmonary function of diabetes patients randomized to either Technosphere Insulin or standard diabetes care. Once we have analyzed the data from our Phase 3 program and have achieved operational readiness in our commercial manufacturing facility in Danbury, Connecticut, we intend to file a new drug application, or NDA, for the Technosphere Insulin System with the United States Food and Drug Administration, or FDA. We will only be able to market the Technosphere Insulin System once, and if, the FDA approves our application.

Our Technosphere Insulin System utilizes our proprietary Technosphere formulation technology, which is based on a class of organic molecules that are designed to self-assemble into small particles onto which drug molecules can be loaded. Currently, we are conducting clinical trials to evaluate the safety and efficacy of another Technosphere-based product for the treatment of diabetes and are developing additional formulations of active compounds loaded onto Technosphere particles, including even for treatment of obesity.

In addition to our Technosphere platform, we are developing therapies for the treatment of different types of cancer. We are currently conducting clinical trials of our therapeutic cancer vaccines. We are also engaged in the discovery and development of drugs that selectively interfere with the cellular processes associated with cancer cells.

We were incorporated in the State of Delaware in 1991. Our principal executive offices are located at 28903 North Avenue Paine, Valencia, California 91355, and our telephone number at that address is (661) 775-5300. Our website address is <http://www.mannkindcorp.com>. Our filings with the Securities and Exchange Commission, or SEC, including our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and any amendments to those reports are available free of charge through our website as soon as reasonably practicable after being electronically filed with or furnished to the SEC.

## **DIABETES**

Diabetes is a major disease characterized by the body's inability to properly regulate levels of blood glucose, or blood sugar. The cells of the body use glucose as fuel over the 24 hours of each day. Between meals, when glucose is not being supplied from food, the liver releases glucose into the blood to sustain adequate levels. Insulin is a hormone produced by the pancreas that regulates the body's blood glucose levels. Patients with diabetes develop abnormally high levels of glucose, a state known as hyperglycemia, either because they produce insufficient levels of insulin or because they fail to respond adequately to insulin produced by the body. Over time, poorly controlled levels of blood glucose can lead to major complications, including high blood pressure, blindness, amputation, kidney failure, heart attack, stroke and death.

According to the United States Centers for Disease Control, or CDC, approximately 20.8 million people in the United States, or 7% of the population, suffered from diabetes as of 2005. The CDC estimated that 14.6 million cases of diabetes were diagnosed and under treatment and that 1.5 million new cases would be diagnosed in 2005. More troubling is the fact that the incidence of diabetes is increasing. A study published by *Diabetes Care* in 2006 projected that in 2050 there would be 48.3 million people with diagnosed diabetes in the United States. Diabetes extracts a heavy toll from those who suffer from it. The CDC reported that diabetes was the sixth leading cause of death listed on death certificates in 2002, but that diabetes was likely to be underreported as a cause of death. Overall, the CDC found that the risk of death among people with diabetes is about twice that of people without diabetes of similar age. The economic costs of diabetes are high as well. The American Diabetes Association estimated that, in 2007, the total cost of diabetes in the United States was \$174 billion, an increase of 32% since 2002. This amount includes \$28 billion of direct costs for drug treatment for glucose control, of which approximately \$6 billion were for insulin and delivery supplies and approximately \$9 billion were for non-insulin oral medications.



There are two major forms of diabetes, type 1 and type 2. Type 1 diabetes is an autoimmune disease characterized by a rapid and complete loss of insulin secretion by the pancreas, so insulin must be supplied from outside the body in order to sustain life. In type 2 diabetes, the pancreas continues to produce insulin; however, insulin-dependent cells become resistant toward the insulin effect. Over time, the pancreas becomes increasingly

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unable to secrete adequate amounts of insulin to support metabolism. According to the CDC, type 2 diabetes is the more prevalent form of the disease, affecting approximately 90% to 95% of people diagnosed with diabetes.

### **Challenges of treating diabetes**

Since patients with type 1 diabetes produce no insulin of their own, the primary treatment for type 1 diabetes is daily intensive insulin therapy. Such patients usually require a daily injection of long-acting, or basal, insulin along with an injection of rapid- or fast-acting insulin at mealtimes.

When patients with type 2 diabetes are first diagnosed, the initial therapy is typically lifestyle intervention (diet and exercise) in order to try to normalize their blood glucose levels. The disease usually progresses rather quickly and today, treatment moves to various non-insulin oral medications. Often, the first drug introduced is metformin, which acts to reduce the glucose output of the liver. When this drug fails to reduce blood glucose levels, other drugs are added. Some of these additional medications act to increase the amount of insulin produced by the pancreas; others increase the sensitivity of muscle, fat and liver cells to the effects of insulin. Generally, these oral medications are limited in their ability to manage the disease effectively and tend to have significant side effects, such as weight gain and hypertension. Ultimately, many patients with type 2 diabetes will require insulin therapy in order to maintain appropriate levels of blood glucose.

Recently, the American Diabetes Association and the European Association for the Study of Diabetes published consensus treatment guidelines that advocated the initiation of insulin therapy after the failure of metformin. These groups emphasized that the early addition and intensification of insulin therapy was an important part of the treatment plan for patients with type 2 diabetes.

Although insulin therapy is accepted as an effective means to control glucose levels, the available insulin products have limitations, including:

- the risk of severe hypoglycemia, which is abnormally low levels of blood glucose that result from excessive insulin administration. Hypoglycemia can result in loss of mental acuity, confusion, increased heart rate, hunger, sweating and faintness and, at very low glucose levels, loss of consciousness, seizures, coma and death;

- 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.

Because of these limitations, patients tend not to comply with the prescribed treatment regimens and are often under-treated. More importantly, even when properly administered, subcutaneous injections of insulin do not replicate the natural time-action profile of insulin. In a person without diabetes, blood insulin levels rise within several minutes of the entry into the bloodstream of glucose from a meal. By contrast, injected insulin enters the bloodstream slowly, resulting in peak insulin levels in about 120 to 180 minutes for regular human insulin or 30-90 minutes for so-called rapid-acting insulin analogs. The consequence of these slower acting insulins is that patients do not have adequate levels of insulin present at the initiation of a meal and tend to be over-insulinized between meals. This lag in insulin delivery results in hyperglycemia early after meal onset, followed by a tendency for hypoglycemia to develop during the period between meals. Physicians who treat patients with diabetes are concerned about the risks of hypoglycemia

and, as a result, tend to undertreat the chronic hyperglycemia that is associated with the disease. However, the resultant extensive hyperglycemia significantly contributes to many of the long-term cardiovascular and other serious complications of diabetes.

**The Mannkind Solution Mimic Natural Insulin Release**

In our clinical trials to date, we have consistently observed that our Technosphere Insulin System produces a profile of insulin levels in the bloodstream that closely approximates the early insulin secretion normally seen in healthy individuals immediately following the beginning of a meal. The figure below, from a study published in

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*Diabetes* in May 2004, illustrates the normal insulin response measured in 17 healthy subjects in response to a standardized meal. Note that the insulin levels rise quickly in response to the glucose stimulus from the meal.

Post-meal insulin levels in healthy subjects

For comparison purposes, the figure below shows the average insulin response observed in 16 patients with type 2 diabetes who inhaled a dose of Technosphere Insulin prior to eating a standardized meal (our study 003B). This comparison illustrates the degree to which our Technosphere Insulin System approximates the insulin profile of healthy individuals following meal onset.

Post-meal insulin levels with Technosphere  
Insulin in patients with type 2 diabetes

This pharmacokinetic profile distinguishes our Technosphere Insulin System from other insulin therapies. A 2004 review article in the *British Journal of Diabetes and Vascular Diseases* reviewed different studies of pulmonary insulin products in development and compared their glucose-lowering activity to that of injectable rapid-acting insulin analogs. The graph below from this article shows that most pulmonary insulin formulations have comparable time-action profiles to injectable rapid-acting insulin. The one exception was the Technosphere Insulin System, which was observed to have a much more rapid onset of action than the other insulin therapies reviewed.

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Time-action profiles of inhaled insulin systems  
compared to a rapid-acting insulin analog

We believe the rapid action of Technosphere Insulin may be related to the unique aspects of both the carrier molecule as well as the way insulin is stabilized in our formulation. Our Technosphere formulation technology is centered on a class of pH-sensitive organic molecules that self-assemble into small particles under mildly acidic conditions. Certain drugs, such as insulin, can be loaded onto these particles by combining a mildly acidic solution of the drug with a suspension of Technosphere material, which is then dried to a powder. This powder is then filled into plastic cartridges and packaged. To administer Technosphere Insulin, a patient loads a cartridge into our palm-sized inhaler. By inhaling through this device, air is pulled through the cartridge, which aerosolizes the powder and pulls the particles into the air current and out through the mouthpiece. The individual particles within this aerosol are small and have aerodynamic properties that enable them to fly deep into the lungs. When the particles contact the moist lung surface with its neutral pH, the Technosphere particles dissolve immediately, releasing the insulin molecules to diffuse across a thin layer of cells into the bloodstream. We believe that the insulin absorption step is a passive process that occurs without any active assistance or enhancement and without disruption of either cell membranes or the tight junctions between cells.

Significantly, when the Technosphere particles dissociate, we believe that the insulin that is released is in a form that can be more readily used by the body. In most pharmaceutical dosage forms, regular human insulin exists as a hexamer, a complex of six associated insulin molecules. In order to exert a pharmacological effect, the hexamer must first dissociate into three dimers—complexes of two insulin molecules—which then further dissociate into individual insulin molecules, or monomers. Only insulin monomers can attach to the insulin receptor and exert a physiological effect. Rapid-acting insulin analogs are designed to be fragile hexamers that dissociate more quickly, thereby reducing the time required to achieve an effect, but this is still far slower than insulin that is released from a healthy pancreas. However, the insulin released from Technosphere particles is already largely in monomeric form. During the manufacture of Technosphere Insulin, we cause hexameric insulin to dissociate into monomeric insulin before being loaded onto Technosphere particles. When Technosphere Insulin particles dissolve in the deep lung, the insulin that is released diffuses across a thin layer of cells to reach the bloodstream. Little change is required before the insulin can rapidly exert its glucose-lowering effect in the body.

**More natural insulin profile translates into better glucose control**

***Post-meal glucose excursions***

In our efficacy trials involving patients with diabetes, we observed that our Technosphere Insulin System produces a significant decrease in glucose excursions after a meal. In one trial (study 003B), we compared the effect of mealtime doses of Technosphere Insulin on blood glucose levels to the effect of mealtime doses of subcutaneous

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insulin. This study employed a cross-over design, so that patients were treated with either Technosphere Insulin or subcutaneous injections of insulin at mealtimes for approximately one week and then, after a washout period, were transferred to the other treatment for a further week. At the end of each treatment period, patients were administered a standardized meal and their blood insulin and glucose levels were monitored for a four-hour period.

The graphs below show mean blood levels of insulin and glucose following administration of the meal to patients at the end of each treatment period. The panel on the left shows the characteristically rapid absorption of insulin when Technosphere Insulin is inhaled as compared to the much slower absorption following the subcutaneous injection of insulin. The panel on the right shows the corresponding post-meal excursions, or changes from baseline, of glucose absorbed from the meal following administration of either Technosphere Insulin or subcutaneous insulin. These data show that Technosphere Insulin was able to limit the excursion of blood glucose during the post-meal period in patients in this trial to a greater extent than insulin administered subcutaneously.

Post-meal insulin levels

Post-meal glucose excursions

***A1C levels***

In other efficacy trials, we studied the longer-term effects of meal-time Technosphere Insulin on average blood glucose levels in patients with type 2 diabetes. Average blood glucose levels are determined by measuring the levels of glycosylated hemoglobin, or A1C, in the blood. In studies 008 and 005, we found that the use of Technosphere Insulin produced a statistically significant, dose-dependent reduction in A1C levels over an 8- to 12-week period compared to meal-time placebo. Patients in these trials received basal insulin or oral medications as background treatment. In other trials, we compared the effect of Technosphere Insulin on A1C levels to that of a rapid-acting insulin analog. In study 101, a three-month, Phase 2 trial of 110 patients with type 1 diabetes, we observed significant reductions of A1C levels that were similar to the reductions achieved using insulin aspart, a rapid-acting insulin analog. Similarly, in study 014, a six-month Phase 3 study of 308 patients with type 2 diabetes, both patient groups achieved similar and statistically significant improvements in A1C levels.

We are continuing to study the effect of Technosphere Insulin on A1C levels in comparison to rapid-acting insulin analogs in our pivotal, Phase 3 trials of Technosphere Insulin. Study 009 compares the efficacy of mealtime use of Technosphere Insulin to mealtime use of rapid-acting subcutaneous insulin for a 12-month period in a population of approximately 509 patients with type 1 diabetes who are also treated with a long-acting insulin analog. Efficacy will be evaluated on the basis of changes in A1C levels as well as changes in blood glucose levels after a standardized meal. Study 102 compares the efficacy of mealtime use of Technosphere Insulin to the twice-daily use of premixed insulin (a mixture of intermediate-acting insulin and a rapid-acting insulin analog) in a population of approximately 670 patients with type 2 diabetes for a 12-month period. Efficacy will be evaluated on the basis of changes in A1C levels as well as changes in blood glucose levels after a standardized mixed meal. We expect to complete both of these pivotal studies during 2008.

We have also completed the active treatment stage of a Phase 3 trial (study 103) that evaluated the efficacy of Technosphere Insulin alone and in combination with metformin in 525 patients with type 2 diabetes who were not achieving desired glucose control with a combination of metformin and sulphonylurea, another oral diabetes medication. Efficacy was evaluated on the basis of changes in A1C levels after 26 weeks of treatment as well as

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changes in blood glucose levels after a standardized mixed meal. This was not a pivotal trial; rather it is intended to support label expansion. A subset of patients from this trial, as well as the pivotal trials, were given the option to enroll in a follow-on study that will examine pulmonary function during the period immediately following the withdrawal of Technosphere Insulin.

We are also planning several Phase 3b clinical trials that will examine the safety and efficacy of Technosphere Insulin in more detail in order to provide the support for additional claims that will permit us to better differentiate our product from other diabetes therapies. The first of these trials is study 117, in which Technosphere Insulin in combination with insulin glargine, a long-acting insulin, will be compared to a rapid-acting insulin analog (Humalog®) in combination with insulin glargine over a 16-week treatment period in patients with type 1 diabetes who are sub-optimally controlled with their current insulin regimen. This clinical trial will employ a variety of methods, including continuous glucose monitoring and self blood glucose monitoring, to give the investigators many more glycemic data points than have been available previously. This will allow for more aggressive use of insulin dosage than in previous trials of our Technosphere Insulin. The primary efficacy endpoint of this trial is change in A1C levels over the 16-week treatment period. Secondary endpoints include the percent of patients who reach A1C goals of <6.5% and <7.0%. We expect to enroll approximately 230 patients in this trial, commencing in the second quarter of 2008.

### **Favorable safety profile in clinical trials to date**

To date, our clinical trials indicate that our Technosphere Insulin has a favorable safety profile. In some patients, we have observed coughing, usually mild, of short duration and becoming less common over time. The occurrence of mild cough is well recognized with inhaled medications. Other adverse events reported in our clinical trials have not differed significantly from that seen with control treatments. In our first reported Phase 3 clinical trial, study 014, we found that significantly fewer patients in the Technosphere Insulin group (56 of 150 patients) experienced mild or moderate hypoglycemia compared to the rapid-acting insulin analog group (83 of 158 patients) and there were no severe hypoglycemic episodes.

The safety profile of Technosphere Insulin has also been examined in a number of non-clinical studies. In studies of the effect of Technosphere Insulin and Technosphere particles on lung tissue, we have seen no effect. We have also conducted a two-year carcinogenicity study in rats, in which we observed that Technosphere Insulin and Technosphere particles alone were well tolerated after daily inhalations for 104 consecutive weeks. There were no indications that our product or the carrier material alone had carcinogenic potential or caused cellular proliferation in the lungs. The survival rates over the course of the study were acceptable and comparable across all groups. We also recently completed a six-month carcinogenicity study in transgenic mice. We found no macroscopic indications of carcinogenicity in animals given daily subcutaneous injections of Technosphere Insulin or Technosphere particles for 26 consecutive weeks. The analysis of the histology data from this latter study will be completed later this year.

### ***Weight change***

In studies 014 and 101, we assessed subjects' weight over the treatment period. In both studies, we observed a statistically significant difference in the weight change over the treatment period between the groups that received the rapid-acting insulin analog (who gained weight during the study) and the groups that received Technosphere Insulin (who lost weight during the study). At the end of the treatment period (12 weeks for study 101; 24 weeks for study 014), the mean weight difference between groups was 2.2 pounds in study 014 and 3.7 pounds in study 101.

We believe that the observations of no weight gain, and even weight loss, in patients using our Technosphere Insulin System are a consequence of controlling blood glucose levels after a meal more tightly than is possible with regular or rapid-acting insulin. Meal digestion is somewhat variable, but lasts on average approximately three hours. In our

trials, we have observed that over 70% of the glucose-lowering activity of regular subcutaneous insulin is exerted *much later than three hours* after a meal. At this point, patients run the risk of becoming hypoglycemic. We believe that to avoid hypoglycemia this situation encourages patients to eat snacks between meals, contributing to the weight gain often associated with insulin therapy. By contrast, approximately 75% of the action of Technosphere Insulin is exerted *within the first three hours* after a meal. After this point, there is little insulin present to cause



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hypoglycemia, thereby alleviating the need to snack. We believe that this phenomenon may explain why we have seen no therapy-related weight gain in our clinical trials to date.

### ***Lung function***

Beginning with studies 008 and 005, we have assessed the pulmonary function of patients that received Technosphere Insulin. In these studies, we found that there was no clinically or statistically significant difference between the baseline values and the final test results for Technosphere Insulin patients. In studies 101 and 014, we compared pulmonary function in patients that received Technosphere Insulin to that of patients that received injections of rapid-acting insulin analog. At the end of the treatment period in each study, there was no difference between measures of pulmonary function for the two groups of patients, as measured by forced expiratory volume, or FEV<sub>1</sub>, (the volume of air that can be forced out in one second) and forced vital capacity, or FVC, (a measure of pulmonary capacity). In study 101, we also included measurements of DLCO (the diffusion capacity for carbon monoxide) and, again, we observed no difference between the two groups of patients at the end of the treatment period. In study 014, patients were followed for an additional six months after the treatment period ended. When FEV<sub>1</sub> and FVC measures were obtained after the withdrawal period, we again saw no difference between the two groups.

We are nearing completion of study 030 – a two-year, pivotal, Phase 3 safety trial that incorporates two design strategies. The first component is a randomized, open-label trial comparing pulmonary function in two groups of patients with diabetes. One group of patients is being treated with Technosphere Insulin and the other group of patients is being treated with existing oral and/or injectable therapies. The second component is a comparison of pulmonary function in the patients with diabetes who are not treated with Technosphere Insulin to a group of 125 subjects without diabetes. A total of 2,050 subjects were enrolled in this study. The last patient/last visit for study 030 will take place in September 2008.

We have an ongoing program of safety surveillance and adverse event reporting for the purpose of evaluating the ongoing safety data related to the use of our Technosphere Insulin System. All of our clinical trials are monitored by an independent data safety monitoring board that meets at regular intervals to review safety data. To date, the data safety monitoring board has fully endorsed continuation of the trials as planned. Our safety data are necessarily preliminary until we have completed longer-term safety trials.

### **Convenient and easy to use**

To facilitate the delivery of Technosphere-formulated drugs to the deep lung, we developed an inhaler that utilizes single-use, disposable, plastic cartridges containing drug-loaded powder. Our MedTone inhaler is light and easy to use, and fits in the palm of the patient's hand, which we believe facilitates patient compliance. To administer a dose, the patient opens the device, inserts a cartridge of Technosphere Insulin powder into the inhaler, inserts the mouthpiece into the mouth and takes a deep breath, thereby drawing the aerosolized particles deep into the lungs. The inhaler incorporates an airflow regulator that is designed to ensure a sufficient airflow from use to use, even in patients with restricted airflow capacity. In addition, the inhaler is breath actuated, which means that the patient does not need to coordinate a breath with any manipulation of the device, such as priming or pumping. In our clinical trials of our Technosphere Insulin System, patients have reported a high level of satisfaction with the MedTone inhaler.

We believe the ease of use of the MedTone inhaler complements the time-action profile of the Technosphere Insulin powder to produce a highly convenient system. Because insulin is transferred to the bloodstream rapidly with our therapy, we believe that the optimal and most convenient time for patients to take a dose of Technosphere Insulin is right at the start of a meal. In contrast, with subcutaneous regular insulin it is recommended that the user try to time an injection 15 to 45 minutes before the expected mealtime, raising issues such as miscalculation of time or unanticipated change in meal availability, which could result in adverse events.



**Table of Contents****Another Potential MannKind Solution Mimic Natural GLP-1 Secretion**

In a healthy person, the consumption of a meal triggers the release of insulin by the pancreas. However, the insulin response is much less robust if the same amount of glucose is administered by intravenous injection, effectively by-passing the intestinal tract. When glucose is administered intravenously, the intestinal tract is not stimulated to release incretins, which are hormones that stimulate the release of insulin by the pancreas. One such incretin is glucagon-like peptide-1, or GLP-1. In addition to its effect on the pancreas, GLP-1 slows stomach emptying and reduces food intake. The incretin effect—the robust release of insulin in response to meal consumption—is much less pronounced in patients with type 2 diabetes. This observation has suggested that augmenting the GLP-1 signal may be a useful strategy to help treat type 2 diabetes.

Under normal circumstances, GLP-1 is short-lived in the bloodstream; half the amount that is released by the intestinal tract is inactivated in about two minutes. Much of the circulating GLP-1 is degraded by an enzyme known as dipeptidyl peptidase-4, or DPP-4. The rapid degradation of GLP-1 by DPP-4 represents a challenge for the use of exogenous GLP-1 in the treatment of type 2 diabetes. Some drug manufacturers have responded to this challenge developing forms of GLP-1 that are resistant to DPP-4 degradation. Exenatide was the first so-called incretin mimetic to be marketed. Exenatide is a peptide derived from lizard venom that is sufficiently similar to human GLP-1 to have comparable effects, but it is much more resistant to DPP-4 degradation than human GLP-1. The marketed formulation of exenatide is indicated for twice-daily injection; however, a once-weekly injection is under development. Other drug manufacturers have developed drugs that inhibit DPP-4 activity. Sitagliptin was the first drug of this class to be approved. This drug is available as a once-daily pill.

With both incretin mimetic and DPP-4 inhibitor therapy, the objective is to augment the GLP-1 signal to the pancreas and other target organs. However, this approach does not truly reestablish the incretin effect—the robust release of insulin following meal consumption—that is lost in type 2 diabetes. These types of drugs act to increase the duration of elevated GLP-1 levels in the bloodstream, but they do not restore or simulate the short burst of GLP-1 that is released by the gut in response to meal ingestion.

Unlike incretin mimetics and DPP-4 inhibitors, our GLP-1 therapy—MKC253, a proprietary formulation of human GLP-1 loaded onto Technosphere particles—is intended to mimic gut physiology more closely. In a Phase 1 clinical trial involving 26 healthy subjects, inhalation of MKC253 produced a sharp pulse of GLP-1 in the bloodstream that peaked in less than three minutes after inhalation. Administering human GLP-1 in this manner was found to produce the desired response. We observed a GLP-1-induced release of insulin from the pancreas that peaked within six minutes of inhalation. The insulin response increased in proportion to the dose of MKC253 that was inhaled. In subjects that received the highest dose of MKC253 (1.5 mg of GLP-1), blood glucose levels were observed to decrease for a period of approximately 20 minutes after administration. All of the subjects that participated in this trial were fasted prior to administration of MKC253; thus, these results support the hypothesis that inhalation of MKC253 may be able to simulate the incretin effect that is lost in patients with type 2 diabetes.

The primary objective of this Phase 1a trial was to evaluate the tolerability of ascending doses of MKC253 as determined by the incidence and severity of reported adverse events. At all dose levels, MKC253 was well tolerated. Even in subjects that achieved plasma GLP-1 concentrations in excess of 100 pmol/L, the nausea and vomiting characteristically associated with such levels was not observed. This lack of side effects may be another benefit of administering MKC253 in a pulsatile manner rather than administering a longer acting formulation of a GLP-1 analogue that lingers in the bloodstream for hours or days.

Currently, we are conducting a second Phase 1 trial that will assess the safety of MKC253 as well as its effect on post-meal glucose excursions in patients with type 2 diabetes. Until we have conducted a full program of clinical trials, we will not be able to reach definitive conclusions about the safety and efficacy of MKC253.

**CANCER**

Cancer is the unregulated proliferation of cells that have the capacity to spread to other sites in the body. A neoplasm is an uncontrolled growth of abnormal cells. A neoplasm is considered benign if it does not spread; if it invades other tissues, however, it is considered malignant. The term cancer refers to a malignant neoplasm.

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The first goal of cancer treatment is to eradicate the cancer. Typically, this goal is pursued using treatment methods surgery, radiation and chemotherapy that can be highly toxic and may offer little clinical benefit. In the past decade or so, newer treatment methods have begun to emerge, such as:

cytokines biological response modifiers that exert a variety of effects on cellular processes, some of which are anti-tumor in nature;

monoclonal antibodies or passive immunotherapy large molecules that cause the destruction of specific types of cancer cells or the blood vessels that supply growing tumors;

active immunotherapy using approaches that attempt to induce the immune system to kill tumor cells instead of tolerating them; and

other targeted drug therapies small molecules that selectively interfere with a cellular process associated with cancer cells.

Our cancer program is focused on the latter two therapy areas immunotherapy and small molecule targeted drug therapy.

### **Cancer immunotherapy**

Our cancer immunotherapy program utilizes the body's immune system to help eradicate tumor cells. The immune system is a network of cells and organs that defends the body against infection and abnormal cells, such as tumor cells. A key element of the immune system is its ability to distinguish between healthy cells and foreign or diseased cells that do not belong in the body. The immune system accomplishes this task by recognizing distinctive molecules called epitopes on the surface of each cell as either normal or abnormal, and responding to them appropriately. Any substance capable of being recognized by the immune system is known as an antigen. An antigen can be all or part of a pathogenic organism or it can be a by-product of diseased cells. Certain specialized cells of the immune system (antigen-presenting cells or APC) sample antigens found in the body and present the epitopes associated with foreign antigens to other cells of the immune system, known as T-cells, whose function is to destroy any cell that expresses the same epitope; this process is known as cell-mediated immunity. In this way, the immune system can launch a very specific response to infection or disease.

Our approach uses DNA- and peptide-based compounds that correspond to tumor-associated antigens that are expressed in a range of tumors. We select as target antigens molecules that either play a role in disease progression or that are very selectively expressed by tumor cells. A patient's immune system is first primed by DNA-based compounds, or plasmids, that are injected directly into the patient's lymph nodes. This is designed to sensitize the immune system to the tumor-associated antigens encoded by the plasmids. After a period of time, the patient's lymph nodes are then injected with synthetic peptides that are designed to boost or greatly amplify the immune response to the target antigens. The immune response is maintained by repeated immunization cycles. This prime-boost regimen is designed to provoke a potent cell-mediated immune response that destroys cancer cells along with the underlying blood supply to tumors.

Our lead product candidate in this program, MKC1106-PP, is intended for the treatment of several solid-tumor cancers, including ovarian, colorectal, pancreatic, renal, breast, non-small cell lung and prostate carcinomas, glioblastoma and melanoma. In 2007, we commenced an open label Phase 1 clinical trial that is designed to evaluate the safety, tolerability and pharmacological response of MKC1106-PP in cancer patients with a variety of tumor types. At present, this study is continuing to enroll patients.

MKC1106-PP consists of three components: a plasmid that encodes pharmacological active elements from two tumor-associated antigens, known as PRAME and PSMA, and two synthetic peptides, one an analog of a PRAME epitope and one an analog of a PSMA epitope. In addition to melanoma, PRAME is expressed in carcinomas such as lung, breast, ovarian, renal, pancreatic and colorectal. PSMA was originally isolated from prostate carcinoma cells and later shown also to be expressed in the blood vessels that supply several types of carcinoma, including breast, lung, ovarian, pancreatic, renal and colorectal carcinoma and melanoma.

In January 2008, we received clearance from the FDA to initiate an open-label Phase1/2 clinical trial of our second immunotherapy product candidate, MKC1106-MT. This trial will evaluate the tolerability and clinical

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responses to the therapy in patients with advanced melanoma. MKC1106-MT consists of a plasmid that encodes portions of two antigens known as Melan-A and tyrosinase, and two synthetic peptides, one an analog of a Melan-A epitope and one an analog of a tyrosinase epitope. Melan-A and tyrosinase are antigens commonly expressed by melanoma tumor cells.

We believe that our cancer immunotherapy approach addresses several deficiencies inherent in earlier approaches to cancer immunotherapy, including:

*Specificity.* Instead of targeting the dominant epitopes expressed by cancerous cells to which the immune system is tolerant, we preferentially target cancer epitopes to which the immune system appears not to have developed a tolerance. Our approach is to identify appropriate target epitopes on the cancer cell surface and design plasmid and peptide analogs to activate an immune response against such epitopes.

*Administration.* In contrast to the conventional subcutaneous or intramuscular route of administration, our compounds are delivered directly into the patient's lymph nodes, sites rich in T-cells and APC. We believe that this delivery method ensures that T-cells are exposed to greater concentrations of antigen for a longer period of time than would occur after administration by other routes, since cells within lymph nodes are ultimately responsible for the induction, amplification and regulation of an immune response. In our preclinical studies, we have observed that intra-lymph node injection was superior to other routes of administration, producing a much larger number of specific T-cells for a variety of target antigens. In addition, because the plasmid is rapidly degraded, we believe that intranodal administration yields plasmid distribution and uptake that is highly selective for the APC within lymph nodes, thereby improving not only the efficacy but also the safety of DNA plasmid vaccination.

*Potency and duration of response.* Because T-cell responses are transient and relatively limited, the potential window to induce a therapeutic immune response is narrow. Our non-clinical studies indicate that the magnitude of the T-cell response can be modulated by the duration and the protocol for achieving antigen exposure. We found that the most robust T-cell responses were obtained when exposure to antigen persisted in the lymph node and when different immunization regimens (prime-boost approaches) were used. Specifically, repeated administration of the plasmid, followed by the peptides, produced greater proliferation of specific T-cells against PRAME and PSMA than did other immunization schedules. To maintain a therapeutic response, it is anticipated that at least two treatment cycles with MCK1106-PP or -MT will need to be administered in patients with tumors that express these antigens. However, subjects may remain in the clinical trials for up to six additional treatment cycles as long as signs of tumor progression are not exhibited.

*Composition.* In contrast to other approaches based on tumor cells, immune cells, tumor lysates or microbes, our strategy encompasses off-the-shelf, synthetic molecules that are not infective and cannot self-replicate. Both recombinant DNA and peptides can be easily manufactured, characterized and formulated as sterile, stable materials suitable for clinical use.

## **Targeted Drug Therapy**

As part of our effort to develop innovative cancer therapies, we have built a drug discovery group that qualifies targets for high-throughput screening, identifies and optimizes lead compounds and develops initial preclinical data. Potential compounds are further assessed by the pharmacology and toxicology group that supports all of our product development efforts.

Our drug discovery efforts, though focused on cancer targets, are directed at several biochemical signaling pathways that may play a role in a number of diseases, including inflammatory diseases and cancer. One of these pathways is

known as the unfolded protein response, or UPR, a response to stress or changes in cellular conditions during which proteins cease functioning correctly. The UPR is intended to restore the normal function of the cell by halting protein production while molecular chaperones remove improperly folded proteins. When cellular stress continues for an extended period of time, the role of the UPR changes from restoring normal function to initiating programmed cell death, which is also known as apoptosis. In this manner, the improperly functioning cell is removed from the body. However, in myeloma cells and possibly other malignancies, the UPR does not work



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effectively. In these cells, an enzyme known as IRE-1 activates a gene (XBP-1) that enhances molecular chaperone activity and protein degradation. The result is that the tumor cells escape apoptosis.

Using our IRE-1 assay, we have identified a novel lead class of compounds that selectively antagonize IRE-1 in vitro. This class also inhibits XBP-1 activity in tumor cells and animal models. At present, we are optimizing the current lead compounds. In February 2008, we finalized the terms of a research award from the Multiple Myeloma Research Foundation that will help to support our optimization and preclinical studies of an IRE-1 antagonist. Under this award, we will receive up to \$1.0 million over the next two years.

Another signaling pathway that we have studied intensively involves a protein known as ITK, which is found in T-cells and certain other immune cells but not in any other tissue. ITK is activated by receptor molecules on the surface of T-cells and, when activated, triggers a number of intracellular events that lead to the migration and proliferation of T-cells. The fact that ITK mediates these responses, along with its predominant expression in T-cells, makes ITK a potential molecular target for intervention in T-cell leukemias and lymphomas.

Our drug discovery group has identified and optimized a unique class of molecules that selectively inhibit ITK in vitro and in vivo. We have begun to evaluate the nonclinical safety and pharmacology of lead compounds. In March 2008, we finalized the terms of a research award from the Leukemia & Lymphoma Society that will help to support our development of potential ITK clinical candidates. Under this award, we will receive up to \$1.0 million during 2008.

## **OUR STRATEGY**

Our objective is to develop products primarily in the major therapeutic areas of diabetes and cancer. Our strategy is to achieve this objective by doing the following:

*Establish our Technosphere Insulin System as the preferred mealtime therapy within the broad population of people with diabetes.* We believe the advantages in terms of safety, efficacy and convenience of our Technosphere Insulin System, as compared to subcutaneous or other inhaled insulin products, will enable us to capture a significant portion of the existing insulin-using diabetes market. Our target markets also include patients with type 2 diabetes who are currently using conventional therapies other than insulin, including:

patients currently using diet and exercise therapy but who are having difficulty achieving proper blood glucose control and who otherwise would have started non-insulin oral medications; and

patients currently using non-insulin medications.

*Expand our proprietary Technosphere formulation technology for the delivery of other peptide hormones.* We believe that MKC253 represents the first in a series of Technosphere formulations of peptide hormones that have the potential to demonstrate clinical advantages over existing therapeutic options in diabetes, endocrine disorders and obesity.

*Commercialize our Technosphere portfolio with a partner who shares our commitment to improving the lives of patients with diabetes.* We are evaluating potential collaboration opportunities with large pharmaceutical companies in the United States, Europe and Japan to provide marketing, sales and financial resources to commercialize and sell our Technosphere Insulin System. We have not licensed or transferred any of our rights to this product or to our platform technology.

*Develop novel approaches to treating cancer using our immunotherapy and drug discovery platforms.* We are currently conducting a Phase 1 and a Phase 1/2 clinical trial of our investigational cancer immunotherapy

product candidates. Our goal is to continue to evaluate the safety and efficacy of this approach while advancing our targeted drug therapy programs into preclinical development.

## **SALES AND MARKETING**

Our efforts to date have primarily been directed at developing products for a number of different markets. We currently have no sales or distribution capabilities and have no experience as a company in marketing or selling pharmaceutical products. However, we have built a strategic marketing group and are actively engaged in the

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commercial activities that would normally be undertaken in preparation for launch of a pharmaceutical product, such as conducting market research studies. In a quantitative attribute study conducted in 2007, 685 physicians were surveyed, including 401 primary care physicians and 284 endocrinologists. A total of 210 physicians were located in the United States; the remaining participants were located in the United Kingdom, Germany, France, Spain and Italy. The purpose of the study was to understand and quantify the degree to which Technosphere Insulin would be prescribed by primary care physicians and endocrinologists. Technosphere Insulin was not identified by name; instead, it was only described as a dry powder insulin that had the following attributes when compared to a rapid-acting insulin analog:

Faster onset of action, reaching peak blood levels in 12-15 minutes;

Lower total post-meal glucose excursions and lower two-hour post-meal glucose when used in combination with basal insulin;

Comparable reductions in A1C levels;

Lower incidence of hypoglycemia; and

Less weight gain.

Study participants were also told that this product was administered at the start of a meal with a palm-sized inhaler and that the most common adverse event reported during clinical trials was cough, generally mild, non-productive and of a transient nature.

The research confirmed that Technosphere Insulin is seen as a significant therapeutic improvement over existing rapid-acting insulin therapies. If and when this product is made available, the physicians who participated in this study reported that they expected to decrease their use of other insulins (primarily rapid-acting analogs), exenatide and oral agents. In particular, the results obtained from the United States participants indicated:

Over half of these physicians see Technosphere Insulin as an improvement over existing rapid-acting insulin therapies;

37% of the primary care physicians and 31% of the endocrinologists see Technosphere Insulin as an important or major therapeutic improvement over existing rapid-acting insulin therapies; and

Primary care physicians indicated significant interest in using Technosphere Insulin as the second, third or fourth therapeutic intervention, even more so than endocrinologists.

Similar results were obtained from European study participants.

We are continuing to study the market opportunities for innovative diabetes therapies and will be conducting further assessments of the market potential for Technosphere Insulin.

In order to commercially market any of our products, we need either to develop an internal sales team, continue to expand our marketing infrastructure or collaborate with third parties who have greater sales and marketing capabilities and have access to potentially large markets. Although we believe that establishing our own sales and marketing organizations in North America would have substantial advantages, we recognize that this may not be practical for our diabetes products and that collaborating with companies with established sales and marketing capabilities in a particular market or markets may be a more effective alternative for some products. To date, we have retained

worldwide commercialization rights for all of our products, including our lead product, the Technosphere Insulin System. We believe that this will give us flexibility if we enter into collaborations to provide the necessary sales and marketing support.

We are evaluating potential collaboration opportunities to assist us in the development and commercialization of our Technosphere Insulin System in the United States, Europe and Japan, and we may also create parallel in-house sales and marketing operations in certain key markets, particularly in the United States.

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**MANUFACTURING AND SUPPLY**

In November 2007, we entered into a long-term supply agreement with N. V. Organon pursuant to which Organon will manufacture and supply specified quantities of recombinant human insulin to us. The initial term of this supply agreement will end on December 31, 2012 and will be automatically extended for consecutive two-year periods unless (i) we fail to provide a forecast of our insulin requirements for the two-year extension period to Organon at least 24 months before any automatic extension or (ii) either party provides 23-months advance written notice to the other party of its desire to terminate the agreement. We and Organon each have normal and customary termination rights, including (a) for material breach of the agreement by the other party, (b) due to the liquidation or bankruptcy of the other party or (c) upon 90-days advance written notice if the parties are unable to agree after mediation on the consequences of any changes to the product specifications required by any controlling regulatory authority. We may terminate the supply agreement upon 30-days advance written notice to Organon if certain regulatory authorities fail to approve or withdraw approval of our Technosphere Insulin System. If we terminate the supply agreement following failure to obtain or maintain regulatory approval of the Technosphere Insulin System or either party terminates the agreement following the parties inability to agree after any regulatory authority-mandated changes to product specifications that relate specifically to the use of insulin in Technosphere Insulin, we will be required to pay Organon a specified termination fee if Organon is unable to sell certain quantities of insulin to other parties. We believe that Organon has sufficient capacity to provide us with sufficient quantities of insulin to support our needs through the initial stages of commercialization. We must rely on our insulin supplier to maintain compliance with relevant regulatory requirements including current Good Manufacturing Practices, or cGMP.

We have a long-term supply agreement with Vaupell, Inc. for the manufacture and supply of our MedTone inhaler and the cartridges that are inserted into it. We are in the process of qualifying a second manufacturer to supply us with commercial quantities of these components. We rely on our manufacturers to comply with relevant regulatory requirements, including compliance with Quality System Regulations, or QSRs. We believe our manufacturers have the capacity to meet our clinical trial and commercial requirements.

Currently, we obtain the raw material from which we produce Technosphere particles from Evonik Industries (formerly Degussa AG), a major chemical manufacturer with facilities in Europe and North America. We are in the process of evaluating a second manufacturer to supply us with commercial quantities of this raw material. We also have the capability of manufacturing this chemical ourselves in our Danbury, Connecticut facility, which is now treated as a back-up facility. Like us, our third-party manufacturers are subject to extensive governmental regulation.

We formulate and fill the Technosphere Insulin powder into plastic cartridges and blister package the cartridges in a manufacturing suite in our Danbury facility. Although our Danbury facility has adequate capacity to meet our clinical trial needs, we are currently expanding our manufacturing facility in order to increase our filling and packaging capacity. The construction phase is scheduled to be completed in the second half of 2008; equipment installation and validation will continue into 2009. When completed and validated, the expanded facility is expected to have the capacity to supply our anticipated needs for the initial years of commercialization. We believe that our building improvements to date have been adequately validated and that the facility continues to substantially conform with cGMP. As well, during the fourth quarter of 2007, our quality management systems were audited and certified to be in conformance with the ISO 13485 and ISO 9001 standards.

**INTELLECTUAL PROPERTY AND PROPRIETARY TECHNOLOGY**

Our success will depend in large measure on our ability to obtain and enforce our intellectual property rights, effectively maintain our trade secrets and avoid infringing the proprietary rights of third parties. Our policy is to file patent applications on what we deem to be important technological developments that might relate to our product candidates or methods of using our product candidates and to seek intellectual property protection in the

United States, Europe, Japan and selected other jurisdictions for all significant inventions. We have obtained, are seeking, and will continue to seek patent protection on the compositions of matter, methods and devices flowing from our research and development efforts. We have also in-licensed certain technology.

Our Technosphere drug delivery platform, including our Technosphere Insulin product, enjoys patent protection relating to the particles, their manufacture, and their use for pulmonary delivery of drugs. We have additional

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patent coverage relating to the treatment of diabetes using our Technosphere Insulin product. Recently we have been granted patent coverage for our inhaler cartridges, the form in which our insulin product will be sold to the consumer. We have additional pending patent applications, and expect to file further applications, relating to the drug delivery platform, methods of manufacture, the Technosphere Insulin product and its use, MKC253 and other Technosphere-based products, inhalers and inhaler cartridges. Overall we own 29 issued patents and over 135 pending applications in the United States and select jurisdictions around the world related to our Technosphere platform. These include composition and method of treatment patents providing protection for Technosphere Insulin that will remain in force into 2020, as will our inhaler patents, and a patent on inhaler cartridges that that will remain in force into 2023.

In addition, we own or have in-licensed intellectual property relating to several drug targets of interest in the treatment of cancer and other fields. Patents and patent applications in this area are drawn to drug screening methods, methods of treatment, and chemical structures of inhibitors of these targets. Our cancer immunotherapy program is built on proprietary methods for the selection, design and administration of epitopes, as well as the plasmids and peptides that are the active ingredients of our products. Overall we own 13 issued patents and over 155 pending applications in the United States and select jurisdictions around the world related to our immunotherapy program.

The fields of pulmonary drug delivery and cancer therapies are crowded and a substantial number of patents have been issued in these fields. In addition, because patent positions can be highly uncertain and frequently involve complex legal and factual questions, the breadth of claims obtained in any application or the enforceability of issued patents cannot be confidently predicted. Further, there can be substantial delays in commercializing pharmaceutical products, which can partially consume the statutory period of exclusivity through patents.

In addition, the coverage claimed in a patent application can be significantly reduced before a patent is issued, either in the United States or abroad. Statutory differences in patentable subject matter may limit the protection we can obtain on some of our inventions outside of the United States. For example, methods of treating humans are not patentable in many countries outside of the United States. These and other issues may limit the patent protection we will be able to secure internationally. Consequently, we do not know whether any of our pending or future patent applications will result in the issuance of patents or, to the extent patents have been issued or will be issued, whether these patents will be subjected to further proceedings limiting their scope, will provide significant proprietary protection or competitive advantage, or will be circumvented or invalidated. Furthermore, patents already issued to us or our pending applications may become subject to disputes that could be resolved against us. In addition, patent applications in the United States filed before November 29, 2000 are currently maintained in secrecy until the patent issues, although in certain countries, including the United States, for applications filed on or after November 29, 2000, applications are generally published 18 months after the application's priority date. In any event, because publication of discoveries in scientific or patent literature often trails behind actual discoveries, we cannot be certain that we were the first inventor of the subject matter covered by our pending patent applications or that we were the first to file patent applications on such inventions.

Although we own a number of domestic and foreign patents and patent applications relating to our Technosphere-based investigational products and our cancer products under development, we have identified certain third-party patents having claims relating to pulmonary insulin delivery that may trigger an allegation of infringement upon the commercial manufacture and sale of our Technosphere Insulin System. We have also identified third-party patents disclosing methods and compositions of matter related to DNA-based vaccines that also may trigger an allegation of infringement upon the commercial manufacture and sale of our cancer immunotherapy. We believe that we are not infringing any valid claims of any patent owned by a third party. However, if a court were to determine that our inhaled insulin product or cancer immunotherapies were infringing any of these patent rights, we would have to establish with the court that these patents were invalid in order to avoid legal liability for infringement of these patents. Proving patent invalidity can be difficult because issued patents are presumed valid. Therefore, in the event

that we are unable to prevail in an infringement or invalidity action we will either have to acquire the third-party patents outright or seek a royalty-bearing license. Royalty-bearing licenses effectively increase costs and therefore may materially affect product profitability. Furthermore, if the patent holder refuses to either assign or license us the infringed patents, it may be necessary to cease manufacturing the product entirely and/or design around the patents. In either event, our business would be harmed and our profitability could be materially adversely



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impacted. If third parties file patent applications, or are issued patents claiming technology also claimed by us in pending applications, we may be required to participate in interference proceedings in the United States Patent and Trademark Office, or USPTO, to determine priority of invention. We may be required to participate in interference proceedings involving our issued patents and pending applications.

We also rely on trade secrets and know-how, which are not protected by patents, to maintain our competitive position. We require our officers, employees, consultants and advisors to execute proprietary information and invention and assignment agreements upon commencement of their relationships with us. These agreements provide that all confidential information developed or made known to the individual during the course of our relationship must be kept confidential, except in specified circumstances. These agreements also provide that all inventions developed by the individual on behalf of us must be assigned to us and that the individual will cooperate with us in connection with securing patent protection on the invention if we wish to pursue such protection. There can be no assurance, however, that these agreements will provide meaningful protection for our inventions, trade secrets or other proprietary information in the event of unauthorized use or disclosure of such information.

We also execute confidentiality agreements with outside collaborators. However, disputes may arise as to the ownership of proprietary rights to the extent that outside collaborators apply technological information to our projects that are developed independently by them or others, or apply our technology to outside projects, and there can be no assurance that any such disputes would be resolved in our favor. In addition, any of these parties may breach the agreements and disclose our confidential information or our competitors might learn of the information in some other way. If any trade secret, know-how or other technology not protected by a patent were to be disclosed to or independently developed by a competitor, our business, results of operations and financial condition could be adversely affected.

## **COMPETITION**

The pharmaceutical and biotechnology industries are highly competitive and characterized by rapidly evolving technology and intense research and development efforts. We expect to compete with companies, including the major international pharmaceutical companies, and other institutions that have substantially greater financial, research and development, marketing and sales capabilities and have substantially greater experience in undertaking preclinical and clinical testing of products, obtaining regulatory approvals and marketing and selling biopharmaceutical products. We will face competition based on, among other things, product efficacy and safety, the timing and scope of regulatory approvals, product ease of use and price.

### **Diabetes treatments**

We believe our Technosphere Insulin System provides us with important competitive advantages in the delivery of insulin when compared with currently known alternatives. However, new drugs or further developments in alternative drug delivery methods may provide greater therapeutic benefits, or comparable benefits at lower cost, than our Technosphere Insulin System. There can be no assurance that existing or new competitors will not introduce products or processes competitive with or superior to our product candidates.

We have set forth below more detailed information about certain of our competitors. The following is based on information currently available to us.

#### **Inhaled and oral insulin delivery systems**

In January 2006, the FDA and the European Medicines Evaluation Agency approved Exubera<sup>®</sup>, developed by Pfizer, Inc. in collaboration with Nektar Therapeutics, for the treatment of adults with type 1 and type 2 diabetes. Exubera<sup>®</sup>

was slow to gain market acceptance and, in October 2007, Pfizer announced that it was returning the rights to the product to Nektar. Nektar subsequently announced that it was actively seeking to enter into a new partnership for the sales and marketing of Exubera<sup>®</sup> as well as its next generation inhaled insulin. This latter product is currently in Phase 1 trials; Nektar is reportedly targeting approval of this product for 2011.

In January 2008, Novo Nordisk A/S announced that it was halting development of its inhaled insulin product, having reached the conclusion that it did not have adequate commercial potential. Notwithstanding the termination

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of this program, Novo Nordisk stated that it intended to increase research and development activities targeted at inhalation systems for long-acting formulations of insulin and GLP-1.

In March 2008, Eli Lilly and Company announced that it too was terminating the development of its AIR<sup>®</sup> inhaled insulin system. Lilly stated that this decision resulted from increasing uncertainties in the regulatory environment and after a thorough evaluation of the evolving commercial and clinical potential of its product compared to existing medical therapies.

There are also several companies that are pursuing development of products involving the oral delivery of insulin. Biocon Limited is currently in Phase 2 trials of IN-105, a tablet for the oral delivery of insulin. Emisphere Technologies, Inc. has also developed an oral formulation of insulin. A Phase 2 trial of the Emisphere investigational product was completed in the fall of 2006. Other companies are evaluating alternative means of delivering insulin orally. Genex Biotechnology Corporation is currently conducting Phase 3 trials in North America of its liquid formulation of insulin that is sprayed onto the buccal mucosa. This product, Oral-lyn<sup>™</sup>, is currently available for sale in certain countries, including Ecuador and India. Bidel Inc. is currently conducting Phase 1 trials of an oral formulation of insulin (VIAtab<sup>™</sup>) designed to be administered sublingually. We are not aware that the timelines to commercialization for any of these investigational products have been made available publicly.

### **Non-insulin medications**

We expect that our Technosphere Insulin System will compete with currently available non-insulin medications for type 2 diabetes. These products include the following:

Sulfonylureas (including Glucotrol<sup>®</sup>, Diabeta<sup>®</sup>, Glynase<sup>®</sup>, Micronase<sup>®</sup>, and Amaryl<sup>®</sup>), also called oral hypoglycemic agents, prompt the pancreas to secrete insulin. This class of drugs is most effective in individuals whose pancreas still have some working pancreas cells.

Meglitinides (including Prandin<sup>®</sup> and Starlix<sup>®</sup>) are taken with meals and reduce the elevation in blood glucose that generally follows eating. If these drugs are not taken with meals, blood glucose will drop dramatically and inappropriately.

Biguanides (including Glucophage<sup>®</sup>, Glucophage<sup>®</sup> XR, and Fortamet<sup>®</sup>) lower blood glucose by improving the sensitivity of cells to insulin (i.e., by diminishing insulin resistance).

Thiazolidinedione (including Avandia<sup>®</sup> and Actos<sup>®</sup>) improves the uptake of glucose by cells in the body.

Alpha-glucosidase inhibitors (including Prandase<sup>®</sup>, Precose<sup>®</sup> and Glyset<sup>®</sup>) lower the amount of glucose absorbed from the intestines, thereby reducing the rise in blood glucose that occurs after a meal.

Inhibitors of dipeptidyl peptidase IV (Januvia<sup>®</sup>) are a class of drugs that work by blocking the degradation of GLP-1, which is a naturally occurring incretin.

Incretin mimetics (Byetta<sup>®</sup>) work by several mechanisms including stimulating the pancreas to secrete insulin when blood glucose levels are high. This class of drug would also compete directly with MKC253, our proprietary formulation of GLP-1 loaded onto Technosphere particles.

### **Injected insulin**

In the subcutaneous insulin market, our competitors have made considerable efforts in promoting rapid acting injectable insulin formulations. Humalog<sup>®</sup>, which was developed by Eli Lilly and Company, and NovoLog<sup>®</sup>, which was developed by Novo Nordisk A/S, are the two principal injectable insulin formulations with which we expect to compete. Bidel, Inc. is conducting Phase 3 trials of VIAject<sup>™</sup>, its proprietary diluent that is combined with freeze-dried human insulin to create a rapid-acting insulin formulation.

### **Cancer treatments**

For many types of cancer, chemotherapy remains a significant component of the treatment regimen. Increasingly, however, drugs and antibodies that specifically target the damaged mechanisms of malignant cells

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are being used to treat cancer. One such cancer therapy is Rituxan® (Biogen IDEC/Genentech/Roche), an antibody that targets a protein found on B-cell lymphoma cells. Genentech, Inc. and Roche have also partnered to market two other successful antibodies: Avastin®, which targets the new blood vessels that supply tumors, and Herceptin®, which targets a protein expressed in breast tumor cells. Erbitux® (ImClone/Bristol-Myers Squibb/Merck Serono), which targets a growth factor associated with malignant growth, is another antibody that has been approved for the treatment of certain types of cancer.

The armamentarium of cancer treatments has been strengthened in recent years by several drugs that target specific molecular aberrations in tumor cells. One such drug is Gleevec®, developed and marketed by Novartis AG, which was initially approved for use in chronic myeloid leukemia. The drug has subsequently been approved for use in additional types of cancer. Similarly, Tarceva® (OSI Pharmaceuticals/Genentech) was initially approved for non-small cell lung cancer; label-expanding studies later allowed the drug to be indicated for pancreatic cancer. Velcade®, developed by Millenium Pharmaceuticals and Ortho Biotech, acts by inhibiting protein degradation, thereby inducing apoptosis. It was initially approved for use in multiple myeloma; its label now includes an indication for mantle cell lymphoma.

Our cancer therapies may face competition from the products described above as well as from other brands. In addition, our cancer immunotherapy products may face direct competition from one or more therapeutic cancer vaccines that are currently in late-stage development. These immunotherapy products include:

Amolimogene (MGI Pharma, Inc.), a DNA-based therapeutic vaccine that is in Phase 3 trials for the treatment of cervical dysplasia;

GV1001 (Pharmexa A/S), a peptide-based therapeutic vaccine in Phase 3 trials for the treatment of pancreatic cancer (and other solid tumors);

MAGE-A3 Antigen-Specific Cancer Immunotherapeutic (GlaxoSmithKline), a peptide-based product in Phase 3 trials for the treatment of non-small cell lung cancer;

TroVax® (Oxford BioMedica plc), a virus-based vaccine that encodes an antigen found on the surface of many tumor types, now in Phase 3 trials for renal cell carcinoma; and

GVAX™ (Cell Genesys Inc.) is a whole-cell vaccine that uses inactivated prostate tumor cells. This vaccine is being evaluated for the treatment of prostate cancer in a Phase 3 trial.

An approach being evaluated by several immunotherapy developers is to use proteins or whole cells derived from tumors as the basis for a personalized vaccine to treat the cancer. These so-called autologous vaccines are exemplified by:

BIOVAXID™ (Accentia Biopharmaceuticals), Specifid™ (Favrille, Inc.) and MyVax® (Genitope Corporation), each of which in Phase 3 trials for non-Hodgkin's lymphoma, use proteins harvested from tumor cells. Oncophage® (Antigenics Inc.) is also derived from patients' tumor cells. Oncophage has been evaluated in Phase 3 trials in kidney cancer and melanoma; currently, it is being evaluated in a Phase 1/2 trial for recurrent glioma;

OncoVAX® (Vaccinogen, Inc.), a vaccine formed from patients' tumor cells that are irradiated and injected back into the patient;

M-Vax (AVAX Technologies, Inc.) is another autologous vaccine. In this approach, whole melanoma cells are harvested and reformulated into the vaccine. In 2000, M-Vax was approved in Australia for the treatment of

melanoma. Subsequently, it was withdrawn from the market. Currently, it is being evaluated in a Phase 3 trial in the United States;

Provenge<sup>®</sup> (Dendreon Corporation) is a vaccine composed of autologous APC that are loaded with an antigen from prostate tumor cells then re-injected into patients. In May 2007, Dendreon received an approvable letter from the FDA in respect to its application for the approval of Provenge<sup>®</sup> in which the FDA requested that Dendreon provide additional survival data in order to support its claims that Provenge<sup>®</sup> is effective.

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**GOVERNMENT REGULATION AND PRODUCT APPROVAL**

The FDA and comparable regulatory agencies in state, local and foreign jurisdictions impose substantial requirements upon the clinical development, manufacture and marketing of medical devices and new drug products. These agencies, through regulations that implement the Federal Food, Drug, and Cosmetic Act, as amended, or FDCA, and other regulations, regulate research and development activities and the development, testing, manufacture, labeling, storage, shipping, approval, advertising, promotion, sale and distribution of such products. In addition, if our products are marketed abroad, they also are subject to export requirements and to regulation by foreign governments. The regulatory clearance process is generally lengthy, expensive and uncertain. Failure to comply with applicable FDA and other regulatory requirements can result in sanctions being imposed on us or the manufacturers of our products, including hold letters on clinical research, civil or criminal fines or other penalties, product recalls, or seizures, or total or partial suspension of production or injunctions, refusals to permit products to be imported into or exported out of the United States, refusals of the FDA to grant approval of drugs or to allow us to enter into government supply contracts, withdrawals of previously approved marketing applications and criminal prosecutions.

The steps typically required before an unapproved new drug product for use in humans may be marketed in the United States include:

Preclinical studies that include laboratory evaluation of product chemistry and formulation, as well as animal studies to assess the potential safety and efficacy of the product. Certain preclinical tests must be conducted in compliance with good laboratory practice regulations. Violations of these regulations can, in some cases, lead to invalidation of the studies, or requiring such studies to be repeated. In some cases, long-term preclinical studies are conducted while clinical studies are ongoing.

Submission to the FDA of an investigational new drug application, or IND, which must become effective before human clinical trials may commence. The results of the preclinical studies are submitted to the FDA as part of the IND. Unless the FDA objects, the IND becomes effective 30 days following receipt by the FDA.

Approval of clinical protocols by independent institutional review boards, or IRBs, at each of the participating clinical centers conducting a study. The IRBs consider, among other things, ethical factors, the potential risks to individuals participating in the trials and the potential liability of the institution. The IRB also approves the consent form signed by the trial participants.

Adequate and well-controlled human clinical trials to establish the safety and efficacy of the product. Clinical trials involve the administration of the drug to healthy volunteers or to patients under the supervision of a qualified medical investigator according to an approved protocol. The clinical trials are conducted in accordance with protocols that detail the objectives of the study, the parameters to be used to monitor participant safety and efficacy or other criteria to be evaluated. Each protocol is submitted to the FDA as part of the IND. Human clinical trials are typically conducted in the following four sequential phases that may overlap or be combined:

In Phase 1, the drug is initially introduced into a small number of individuals and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion. Phase 1 clinical trials are often conducted in healthy human volunteers and such cases do not provide evidence of efficacy. In the case of severe or life-threatening diseases, the initial human testing is often conducted in patients rather than healthy volunteers. Because these patients already have the target disease, these studies may provide initial evidence of efficacy that would traditionally be obtained in Phase 2 clinical trials. Consequently, these types of trials are frequently referred to as Phase 1/2 clinical trials. The FDA receives reports on the progress of each phase

of clinical testing and it may require the modification, suspension or termination of clinical trials if it concludes that an unwarranted risk is presented to patients or healthy volunteers.

Phase 2 involves clinical trials in a limited patient population to further identify any possible adverse effects and safety risks, to determine the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.



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Phase 3 clinical trials are undertaken to further evaluate dosage, clinical efficacy and to further test for safety in an expanded patient population at geographically dispersed clinical study sites. Phase 3 clinical trials usually include a broader patient population so that safety and efficacy can be substantially established. Phase 3 clinical trials cannot begin until Phase 2 evaluation demonstrates that a dosage range of the product may be effective and has an acceptable safety profile.

Phase 4 clinical trials are performed if the FDA requires, or a company pursues, additional clinical trials after a product is approved. These clinical trials may be made a condition to be satisfied after a drug receives approval. The results of Phase 4 clinical trials can confirm the effectiveness of a product candidate and can provide important safety information to augment the FDA's voluntary adverse drug reaction reporting system.

Concurrent with clinical trials and preclinical studies, companies also must develop information about the chemistry and physical characteristics of the drug and finalize a process for manufacturing the product in accordance with drug cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product and the manufacturer must develop methods for testing the quality, purity, and potency of the final products. Additionally, appropriate packaging must be selected and tested and chemistry stability studies must be conducted to demonstrate that the product does not undergo unacceptable deterioration over its shelf-life.

Submission to the FDA of an NDA based on the clinical trials. The results of pharmaceutical development, preclinical studies, and clinical trials are submitted to the FDA in the form of an NDA for approval of the marketing and commercial shipment of the product. Under the Pediatric Research Equity Act of 2003, or PREA, NDAs are required to include an assessment, generally based on clinical study data, of the safety and efficacy of drugs for all relevant pediatric populations. The statute provides for waivers or deferrals in certain situations but we can make no assurances that such situations will apply to us or our product candidates.

Medical products containing a combination of new drugs, biological products, or medical devices are regulated as combination products in the United States. A combination product generally is defined as a product comprised of components from two or more regulatory categories (*e.g.*, drug/device, device/biologic, drug/biologic). Each component of a combination product is subject to the requirements established by the FDA for that type of component, whether a new drug, biologic, or device. In order to facilitate pre-market review of combination products, the FDA designates one of its centers to have primary jurisdiction for the pre-market review and regulation of the overall product. The determination whether a product is a combination product or two separate products is made by the FDA on a case-by-case basis. We have had discussions with the FDA about the status of our Technosphere Insulin System as a combination product and we have been told that the FDA considers our product a combination drug/device. There have been some indications from the FDA that the review of any future marketing applications for our Technosphere Insulin System will involve reviews within the Division of Metabolism and Endocrinology Products and the Division of Pulmonary and Allergy Products, both within the Center for Drug Evaluation and Research, as well as review within the Center for Devices and Radiological Health, the Center within the FDA that reviews Medical Devices. Although the FDA has not made a final decision in this regard, we currently understand that the Division of Metabolic and Endocrine Products will be the lead group and obtain consulting reviews from the other two FDA groups if we submit an NDA.

The testing and approval process requires substantial time, effort and financial resources. In February 2008, the FDA released a draft guidance document that provides recommendations for the development of drugs and therapeutic biologics for the treatment and prevention of diabetes. We reviewed this draft guidance document as it applies to our programs for Technosphere Insulin and MKC253 and we believe that our clinical development programs are

consistent with this draft guidance. Nonetheless, we cannot be certain that any approval of our products will be granted on a timely basis, if at all. If any of our products are approved for marketing by the FDA, we will be subject to continuing regulation by the FDA, including record-keeping requirements, reporting of adverse experiences with the product, submitting other periodic reports, drug sampling and distribution requirements, notifying the FDA and gaining its approval of certain manufacturing or labeling changes, and complying with certain electronic records and signature requirements. Prior to and following approval, if granted, all manufacturing sites are subject to inspection by the FDA and other national regulatory bodies and must comply with cGMP, QSR

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and other requirements enforced by the FDA and other national regulatory bodies through their facilities inspection program. Foreign manufacturing establishments must comply with similar regulations. In addition, our drug-manufacturing facilities located in Danbury and the facilities of our insulin supplier, the supplier(s) of our Technosphere material and the supplier(s) of our MedTone inhaler and cartridges are subject to federal registration and listing requirements and, if applicable, to state licensing requirements. Failure, including those of our suppliers, to obtain and maintain applicable federal registrations or state licenses, or to meet the inspection criteria of the FDA or the other national regulatory bodies, would disrupt our manufacturing processes and would harm our business. In complying with standards set forth in these regulations, manufacturers must continue to expend time, money and effort in the area of production and quality control to ensure full compliance. Currently, we believe we are operating under all of the necessary guidelines and permits.

It is not yet clear to what extent we will be subject to regulations governing pre-market approval or clearances of medical devices separate from approval requirements governing drugs. We currently expect that our inhaler will be approved as part of the NDA for our Technosphere Insulin System. No assurances exist that we will not be required to obtain separate device clearances or approval for use of our inhaler with our Technosphere Insulin System. This may result in our being subject to medical device review user fees and to other device requirements to market our inhaler and may result in significant delays in commercialization. Even if the device component is approved as part of our NDA for the Technosphere Insulin System, numerous device regulatory requirements still apply to the device part of the drug-device combination. These include:

- product labeling regulations;

- general prohibition against promoting products for unapproved or off-label uses;

- corrections and removals (e.g., recalls);

- establishment registration and device listing;

- general prohibitions against the manufacture and distribution of adulterated and misbranded devices; and

- the Medical Device Reporting regulation, which requires that manufacturers report to the FDA if their device may have caused or contributed to a death or serious injury or malfunctioned in a way that would likely cause or contribute to a death or serious injury if it were to recur.

Further, the company we have contracted to manufacture our MedTone inhaler and cartridges will be subject to the QSR, which requires manufacturers to follow elaborate design, testing, control, documentation and other quality assurance procedures during the manufacturing process of medical devices, among other requirements.

Failure to adhere to regulatory requirements at any stage of development, including the preclinical and clinical testing process, the review process, or at any time afterward, including after approval, may result in various adverse consequences. These consequences include action by the FDA or another national regulatory body that has the effect of delaying approval or refusing to approve a product; suspending or withdrawing an approved product from the market; seizing or recalling a product; or imposing criminal penalties against the manufacturer. In addition, later discovery of previously unknown problems may result in restrictions on a product, its manufacturer, or the NDA holder, or market restrictions through labeling changes or product withdrawal. Also, new government requirements may be established or they may change at any time that could delay or prevent regulatory approval of our products under development. For example, in response to recent events regarding questions about the safety of certain approved prescription products, including the lack of adequate warnings, the FDA and Congress are currently considering new regulatory and legislative approaches to advertising, monitoring and assessing the safety of marketed drugs, including

legislation providing the FDA with authority to mandate labeling changes for approved pharmaceutical products, particularly those related to safety. We also cannot be sure that the current Congressional and FDA initiatives pertaining to ensuring the safety of marketed drugs or other developments pertaining to the pharmaceutical industry will not adversely affect our operations. We cannot predict the likelihood, nature or extent of adverse governmental regulation that might arise from future legislative or administrative action, either in the United States or abroad.

In addition, the FDA imposes a number of complex regulations on entities that advertise and promote drugs, which include, among other requirements, standards for and regulations of direct-to-consumer advertising, off-label

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promotion, industry sponsored scientific and educational activities, and promotional activities involving the Internet. Such advertising and promotional activities are also being scrutinized by the FDA and Congress as a result of recent concerns that have been raised about the safety of marketed drugs. The FDA has very broad enforcement authority under the FDCA, and failure to comply with these regulations can result in penalties, including the issuance of a warning letter directing us to correct deviations from FDA standards, a requirement that future advertising and promotional materials be pre-cleared by the FDA, and state and federal civil and criminal investigations and prosecutions.

Products manufactured in the United States and marketed outside the United States are subject to certain FDA regulations, as well as regulation by the country in which the products are to be sold. We also would be subject to foreign regulatory requirements governing clinical trials and drug product sales if products are marketed abroad. Whether or not FDA approval has been obtained, approval of a product by the comparable regulatory authorities of foreign countries usually must be obtained prior to the marketing of the product in those countries. The approval process varies from jurisdiction to jurisdiction and the time required may be longer or shorter than that required for FDA approval.

Product development and approval within this regulatory framework take a number of years, involve the expenditure of substantial resources and are uncertain. Many drug products ultimately do not reach the market because they are not found to be safe or effective or cannot meet the FDA's other regulatory requirements. In addition, there can be no assurance that the current regulatory framework will not change or that additional regulation will not arise at any stage of our product development that may affect approval, delay the submission or review of an application or require additional expenditures by us. There can be no assurance that we will be able to obtain necessary regulatory clearances or approvals on a timely basis, if at all, for any of our product candidates under development, and delays in receipt or failure to receive such clearances or approvals, the loss of previously received clearances or approvals, or failure to comply with existing or future regulatory requirements could have a material adverse effect on our business and results of operations.

Under European Union regulatory systems, marketing authorizations may be submitted either under a centralized or decentralized procedure. The centralized procedure provides for the grant of a single marketing authorization that is valid for all European Union member states. The decentralized procedure provides for mutual recognition of national approval decisions. Under this latter procedure, the holder of a national marketing authorization may submit an application to the remaining member states. Within 90 days of receiving the application and assessment report, each member state must decide whether to recognize approval. We plan to choose the appropriate route of European regulatory filing in an attempt to accomplish the most rapid regulatory approvals. However, the chosen regulatory strategy may not secure regulatory approvals or approvals of the chosen product indications. In addition, these approvals, if obtained, may take longer than anticipated.

We cannot provide assurance that any of our product candidates will prove to be safe or effective, will receive regulatory approvals, or will be successfully commercialized.

In addition to the foregoing, we are subject to numerous federal, state and local laws relating to such matters as laboratory practices, the experimental use of animals, the use and disposal of hazardous or potentially hazardous substances, controlled drug substances, safe working conditions, manufacturing practices, environmental protection and fire hazard control. We may incur significant costs to comply with those laws and regulations now or in the future.

**Patent restoration and marketing exclusivity**

The Drug Price Competition and Patent Term Restoration Act of 1984, known as the Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act, permits the FDA to approve abbreviated NDAs, or ANDAs, for generic versions of innovator drugs and also provides certain patent restoration and market exclusivity protections to innovator drug manufacturers. The ANDA process permits competitor companies to obtain marketing approval for a new drug with the same active ingredient for the same uses, dosage form and strength as an innovator drug but does not require the conduct and submission of preclinical or clinical studies demonstrating safety and efficacy for that product. Instead of providing completely new safety and efficacy data, the ANDA

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applicant only need to submit manufacturing information and clinical data demonstrating that the copy is bioequivalent to the innovator's product in order to gain marketing approval from the FDA.

Another type of marketing application allowed by the Hatch-Waxman Amendments, a Section 505(b)(2) application, may be permitted where a company does not own or have a right to reference all the data required for approval. Section 505(b)(2) NDAs are often submitted for drug products that contain the same active ingredient as those in first approved drug products and where additional studies are required for approval, such as for changes in routes of administration or dosage forms.

Once an NDA is approved, the product covered thereby becomes a listed drug which can, in turn, be cited by potential competitors in support of approval of an ANDA or a 505(b)(2) application.

The Hatch-Waxman Amendments provide for a period of three years exclusivity following approval of a listed drug that contains previously approved active ingredients but is approved in a new dosage, dosage form, route of administration or combination, or for a new use, the approval of which was required to be supported by new clinical trials conducted by or for the sponsor. During this period of exclusivity, FDA cannot grant effective approval of an ANDA or a 505(b)(2) application based on that listed drug.

The Hatch-Waxman Amendments also provide a period of five years exclusivity following approval of a drug containing no previously approved active ingredients. During this period of exclusivity, ANDAs or 505(b)(2) applications based upon those drugs cannot be submitted unless the submission accompanies a challenge to a listed patent, in which case the submission may be made four years following the original product approval.

Additionally, in the event that the sponsor of the listed drug has informed FDA of patents covering its listed drug and FDA lists those patents in the Orange Book, applicants submitting an ANDA or a 505(b)(2) application referencing that drug are required to certify whether they intend to market their generic products prior to expiration of those patents. If an ANDA applicant certifies that it believes one or more listed patents is invalid or not infringed, it is required to provide notice of its filing to the NDA sponsor and the patent holder. If either party then initiates a suit for patent infringement against the ANDA sponsor within 45 days of receipt of the notice, FDA cannot grant effective approval of the ANDA until either 30 months has passed or there has been a court decision holding that the patent in question is invalid or not infringed. If the ANDA applicant certifies that it does not intend to market its generic product before some or all listed patents on the listed drug expire, then FDA cannot grant effective approval of the ANDA until those patents expire. The first ANDA applicant submitting substantially complete applications certifying that listed patents for a particular product are invalid or not infringed may qualify for a period of 180 days after a court decision of invalidity or non-infringement or after it begins marketing its product, whichever occurs first. During this 180 day period, subsequently submitted ANDAs cannot be granted effective approval.

The FDA Modernization Act of 1997 included a pediatric exclusivity provision that was extended by the Best Pharmaceuticals for Children Act of 2002. Pediatric exclusivity is designed to provide an incentive to manufacturers for conducting research about the safety and efficacy of their products in children. Pediatric exclusivity, if granted, provides an additional six months of market exclusivity in the United States for new or currently marketed drugs if certain pediatric studies requested by the FDA are completed by the applicant and the applicant has other existing patent or exclusivity protection for the drug. To obtain this additional six months of exclusivity, it would be necessary for us to first receive a written request from the FDA to conduct pediatric studies and then to conduct the requested studies according to a previously agreed timeframe and submit the report of the study. There can be no assurances that we would receive a written request from the FDA and if so that we would complete the studies in accordance with the requirements for this six-month exclusivity. The current pediatric exclusivity provision is scheduled to end on October 1, 2012, and there can be no assurances that it will be reauthorized.

**EMPLOYEES**

As of December 31, 2007, we had 609 full-time employees. 106 of these employees were engaged in research and development, 182 in manufacturing, 208 in clinical, regulatory affairs and quality assurance and 113 in administration, finance, management, information systems, marketing, corporate development and human resources. 60 of these employees have a Ph.D. degree and/or M.D. degree and are engaged in activities relating



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to research and development, manufacturing, quality assurance and business development. None of our employees is subject to a collective bargaining agreement. We believe relations with our employees are good.

**SCIENTIFIC ADVISORS**

We seek advice from a number of leading scientists and physicians on scientific, technical and medical matters. These advisors are leading scientists in the areas of pharmacology, chemistry, immunology and biology. Our scientific advisors are consulted regularly to assess, among other things:

- our research and development programs;
- the design and implementation of our clinical programs;
- our patent and publication strategies;
- market opportunities from a clinical perspective;
- new technologies relevant to our research and development programs; and
- specific scientific and technical issues relevant to our business.

Our diabetes program is supported by the following scientific advisors (and their primary affiliations):

<b>Name</b>	<b>Primary Affiliation</b>
Stephanie Amiel, MD, FRCP	King's College London School of Medicine
Richard Bergenstal, MD	International Diabetes Center, Park Nicollet Institute
Geremia Bolli	University of Perugia
Alan D. Cherrington, PhD	Vanderbilt University Medical Center
David D. Alessio, MD	University of Cincinnati
Steven Edelman, MD	University of California, San Diego
Alexander Fleming, MD	Kinexum Box LLC
Brian Frier, MD, FECP, BS	Edinburgh Royal Infirmary
Irl B. Hirsch, MD	University of Washington Medical Center
Edward Horton, MD	Joslin Diabetes Center
Lois Jovanovic, MD	Sansum Medical Research Institute
Steven Kahn, MB, ChB	University of Washington
David Klonoff, MD	Dorothy L. & James E. Frank Diabetes Research Institute
Harold E. Lebovitz, MD, FACE	State University of New York, Brooklyn
Daniel Lorber, MD	Diabetes Care & Information Center of New York
Sten Madsbad	Hvidovre University Hospital, Copenhagen
Chantal Mathieu, MD, PhD	Laboratorium voor Experimentele Geneeskunde en Endocrinologie
Mark Peyrot, MD	Loyola College Center
Daniel Porte, MD	University of California, San Diego
Philip Raskin, MD, FACE, FACP	University of Texas
Julio Rosenstock, MD	Dallas Diabetes and Endocrinology Center

Jesse Roth, MD, FACP  
Richard Rubin, PhD, CDE  
Robert Sherwin, MD  
Jay Skyler, MD, MACP

North Shore-Long Island Jewish Health System  
Johns Hopkins University School of Medicine  
Yale University School of Medicine  
University of Miami, Diabetes Research Institute

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Our cancer program is supported by the following scientific advisors (and their primary affiliations):

<b>Name</b>	<b>Primary Affiliation</b>
Paul A. Bartlett, Ph.D.	University of California, Berkeley
Philippe Bey, Ph.D.	Pharmaceutical consultant
Jeffrey Bluestone, Ph.D.	University of California, San Francisco
Roger Cone, Ph.D.	Oregon Health & Science University
Richard Dalby, Ph.D.	University of Maryland
Frank Douglas, Ph.D.	Puretech Ventures
W. Martin Kast, Ph.D.	University of Southern California
Antoni Ribas, M.D.	University of California, Los Angeles
Owen Witte, M.D.	University of California, Los Angeles

**EXECUTIVE OFFICERS**

The following table sets forth our current executive officers and their ages as of December 31, 2007:

<b>Name</b>	<b>Age</b>	<b>Position(s)</b>
Alfred E. Mann	82	Chairman of the Board of Directors and Chief Executive Officer
Hakan S. Edstrom	57	President, Chief Operating Officer and Director
Richard L. Anderson	68	Corporate Vice President and Chief Financial Officer
Juergen A. Martens, Ph.D.	52	Corporate Vice President, Technical Operations and Chief Technical Officer
Diane M. Palumbo	54	Corporate Vice President, Human Resources
Dr. Peter C. Richardson	48	Corporate Vice President and Chief Scientific Officer
John R. Riesenberger	59	Corporate Vice President and Chief Commercialization Officer
David Thomson, Ph.D., J.D.	41	Corporate Vice President, General Counsel and Secretary

*Alfred E. Mann* has been one of our directors since April 1999, our Chairman of the Board since December 2001 and our Chief Executive Officer since October 2003. He founded and formerly served as Chairman and Chief Executive Officer of MiniMed, Inc., a publicly traded company focused on diabetes therapy and microinfusion drug delivery that was acquired by Medtronic, Inc. in August 2001. Mr. Mann also founded and, from 1972 through 1992, served as Chief Executive Officer of Pacesetter Systems, Inc. and its successor, Siemens Pacesetter, Inc., a manufacturer of cardiac pacemakers, now the Cardiac Rhythm Management Division of St. Jude Medical Corporation. Mr. Mann founded and since 1993, has served as Chairman and until January 2008 as Co-Chief Executive Officer of Advanced Bionics Corporation, a medical device manufacturer focused on neurostimulation to restore hearing to the deaf and to treat chronic pain and other neural deficits, that was acquired by Boston Scientific Corporation in June 2004. Mr. Mann has also founded and is non-executive Chairman of Second Sight, which is developing a visual prosthesis for the blind and Quallion, which produces batteries for medical products and for the military and aerospace industries. Mr. Mann is also non-executive Chairman of the Alfred Mann Foundation and Alfred Mann Institute at the University of Southern California, and the Alfred Mann Foundation for Biomedical Engineering, which is establishing additional institutes at other research universities. Mr. Mann holds a bachelor's and master's degree in Physics from the University of California at Los Angeles, honorary doctorates from Johns Hopkins University, the University of

Southern California, Western University and the Technion-Israel Institute of Technology and is a member of the National Academy of Engineering.

*Hakan S. Edstrom* has been our President and Chief Operating Officer since April 2001 and has served as one of our directors since December 2001. Mr. Edstrom was with Bausch & Lomb, Inc., a health care product company,

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from January 1998 to April 2001, advancing to the position of Senior Corporate Vice President and President of Bausch & Lomb, Inc. Americas Region. From 1981 to 1997, Mr. Edstrom was with Pharmacia Corporation, where he held various executive positions, including President and Chief Executive Officer of Pharmacia Ophthalmics Inc. Mr. Edstrom is currently a director of Q-Med AB, a biotechnology and medical device company. Mr. Edstrom was educated in Sweden and holds a master's degree in business administration from the Stockholm School of Economics.

*Richard L. Anderson* has been our Corporate Vice President and Chief Financial Officer since October 2002. From January 1997 to September 2002, Mr. Anderson held various executive positions at NeoRx Corporation, a Seattle-based publicly traded biotechnology company, including President, Chief Operating Officer, Chief Financial Officer and Senior Vice President, Finance and Operations. Mr. Anderson holds a master's degree in Management from Johns Hopkins University, a master's degree in solid state physics from the University of Maryland and a bachelor's degree in physics from Bucknell University. Mr. Anderson is currently a director of VIA Pharmaceuticals, a biotechnology company. In December 2007, we entered into an agreement with Mr. Anderson pursuant to which he will transition to the position of Corporate Vice President - Office of the Chairman during the second quarter of 2008 and will retire on March 31, 2009.

*Juergen A. Martens, Ph.D.* has been our Corporate Vice President of Operations and Chief Technology Officer since September 2005. From 2000 to August 2005, he was employed by Nektar Therapeutics, Inc., most recently as Vice President of Pharmaceutical Technology Development. Previously, he held technical management positions at Aerojet Fine Chemicals from 1998 to 2000 and at FMC Corporation from 1996 to 1998. From 1987 to 1996, Dr. Martens held a variety of management positions with increased responsibility in R&D, plant management, and business process development at Lonza, in Switzerland and in the United States. Dr. Martens holds a BS in chemical engineering from the Technical College Mannheim/Germany, a BS/MS in chemistry and a doctorate in physical chemistry from the University of Marburg/Germany.

*Diane M. Palumbo* has been our Corporate Vice President of Human Resources since November 2004. From July 2003 to November 2004, she was President of her own human resources consulting company. From June 1991 to July 2003, Ms. Palumbo held various positions with Amgen, Inc., a California-based biopharmaceutical company, including Senior Director, Human Resources. In addition, Ms. Palumbo has held Human Resources positions with Unisys and Mitsui Bank Ltd. of Tokyo. She holds a master's degree in business administration from St. John's University, NY and a Bachelor of Science degree, magna cum laude, also from St. John's University, NY.

*Dr. Peter C. Richardson* has been our Corporate Vice President and Chief Scientific Officer since October 2005. From 1991 to October 2005, he was employed by Novartis Pharmaceuticals Corporation, which is the U.S. affiliate of Novartis AG, a world leader in healthcare, most recently as Senior Vice President, Global Head of Development Alliances. From 2003 until 2005, he was Senior Vice President and Head of Development of Novartis Pharmaceuticals KK Japan. He earlier practiced as an endocrinologist. Dr. Richardson holds a B.Med.Sci (Hons.) and a BM.BS (Hons.) from University of Nottingham Medical School; an MRCP (UK) from the Royal College of Physicians, UK; a Certificate in Pharmaceutical Medicine from Universities of Freiburg, Strasbourg and Basle; and a Diploma in Pharmaceutical Medicine from the Royal College of Physicians Faculty of Pharmaceutical Medicine.

*John R. Riesenger* has been our Corporate Vice President and Chief Commercialization Officer since January 2008. From 2001 to 2007, he was a Principal and the Executive Vice President of Shaw Science Partners, a pharmaceutical science branding agency. Prior to that position, Mr. Riesenger was with Pharmacia & Upjohn and The Upjohn Company for a total of 28 years, including 15 years in the U.S. organization and 13 years in the international, global and corporate organizations in a diverse range of geographic and functional accountabilities. Before his retirement, he held the position of Vice-President, Business Intelligence, Global Business Management. He currently serves as an Executive-In-Residence at the Eli Broad Graduate School of Business, Michigan State University. Mr. Riesenger holds a Bachelor of Science degree with a dual major in economics and business and a

MBA degree from Hofstra University.

*David Thomson, Ph.D., J.D.* has been our Corporate Vice President, General Counsel and Corporate Secretary since January 2002. Prior to joining us, he practiced corporate/commercial and securities law at the Toronto law firm of Davies Ward Phillips & Vineberg LLP from May 1999 through December 2001, except for a period from

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May to December 2000, when he served as Vice President, Business Development for CTL ImmunoTherapies Corp. From March 1994 to August 1996, Dr. Thomson held a post-doctoral position at the Rockefeller University, where he conducted medical research in the Laboratory of Neurophysiology. Dr. Thomson obtained his bachelor's degree, master's degree and Ph.D. degree from Queens University and obtained his J.D. degree from the University of Toronto.

Executive officers serve at the discretion of our Board of Directors. There are no family relationships between any of our directors and executive officers.

### **Item 1A. Risk Factors**

*You should consider carefully the following information about the risks described below, together with the other information contained in this report, before you decide to buy or maintain an investment in our common stock. We believe the risks described below are the risks that are material to us as of the date of this annual report. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect our business. If any of the following risks actually occur, our business, financial condition, results of operations and future growth prospects would likely be materially and adversely affected. In these circumstances, the market price of our common stock could decline, and you may lose all or part of the money you paid to buy our common stock.*

### **RISKS RELATED TO OUR BUSINESS**

***We have a history of operating losses, we expect to continue to incur losses and we may never become profitable.***

We are a development stage company with no commercial products. All of our product candidates are still being developed, and all but our Technosphere Insulin System are still in early stages of development. Our product candidates will require significant additional development, clinical trials, regulatory clearances and additional investment before they can be commercialized. We anticipate that our Technosphere Insulin System will not be commercially available for at least two years, if at all.

We have never been profitable and, as of December 31, 2007, we had an accumulated deficit of \$1.1 billion. The accumulated deficit has resulted principally from costs incurred in our research and development programs, the write-off of goodwill and general operating expenses. We expect to make substantial expenditures and to incur increasing operating losses in the future in order to further develop and commercialize our product candidates, including costs and expenses to complete clinical trials, seek regulatory approvals and market our product candidates. This accumulated deficit may increase significantly as we expand development and clinical trial efforts.

Our losses have had, and are expected to continue to have, an adverse impact on our working capital, total assets and stockholders' equity. Our ability to achieve and sustain profitability depends upon obtaining regulatory approvals for and successfully commercializing our Technosphere Insulin System, either alone or with third parties. We do not currently have the required approvals to market any of our product candidates, and we may not receive them. We may not be profitable even if we succeed in commercializing any of our product candidates. As a result, we cannot be sure when we will become profitable, if at all.

***If we fail to raise additional capital, our financial condition and business would suffer.***

It is costly to develop therapeutic product candidates and conduct clinical trials for these product candidates. Although we are currently focusing on our Technosphere Insulin System as our lead product candidate, we have begun to conduct clinical trials for additional product candidates. Our existing capital resources will not be sufficient to support the expense of completing development of our Technosphere Insulin System or any of our other product candidates.

In October 2007, we completed the sale of 27,014,686 shares of our common stock resulting in aggregate net proceeds of approximately \$249.8 million after expenses. Also on October 2, 2007, we replaced the \$150.0 million loan arrangement with our principal stockholder with a new loan arrangement that allows us to borrow up to a total of \$350.0 million before January 1, 2010. From April 1, 2008 until September 30, 2008, we can borrow up to \$150.0 million in one or more advances, and from March 1, 2009 until December 31, 2009, we can borrow the



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remaining \$200.0 million plus any amount not previously borrowed in one or more advances. We may not borrow more than one advance in any 12-month period, and each advance must be not less than \$50.0 million.

Based upon our current expectations, we believe that our existing capital resources, including the net proceeds from our sales of common stock and the new loan arrangement with our principal stockholder, will enable us to continue planned operations through the fourth quarter of 2009. However, we cannot assure you that our plans will not change or that changed circumstances will not result in the depletion of our capital resources more rapidly than we currently anticipate. Accordingly, we plan to raise additional capital, either through the sale of equity and/or debt securities, a strategic business collaboration or the establishment of other funding facilities, in order to continue the development and commercialization of our Technosphere Insulin System and other product candidates and to support our other ongoing activities. The amount of additional funds we need will depend on a number of factors, including:

the rate of progress and costs of our clinical trials and research and development activities, including costs of procuring clinical materials and expanding our own manufacturing facilities;

our success in establishing strategic business collaborations and the timing and amount of any payments we might receive from any collaboration we are able to establish;

actions taken by the FDA and other regulatory authorities affecting our products and competitive products;

our degree of success in commercializing our Technosphere Insulin System or our other product candidates;

the emergence of competing technologies and products and other adverse market developments;

the timing and amount of payments we might receive from potential licensees;

the costs of preparing, filing, prosecuting, maintaining and enforcing patent claims and other intellectual property rights or defending against claims of infringement by others; and

the costs of discontinuing projects and technologies or decommissioning existing facilities, if we undertake those activities.

We have raised capital in the past primarily through the sale of equity securities and most currently through the sale of equity and debt securities. We may in the future pursue the sale of additional equity and/or debt securities, or the establishment of other funding facilities. Issuances of additional debt or equity securities or the conversion of any of our currently outstanding convertible debt securities into shares of our common stock could impact your rights as a holder of our common stock and may dilute your ownership percentage. Moreover, the establishment of other funding facilities may impose restrictions on our operations. These restrictions could include limitations on additional borrowing and specific restrictions on the use of our assets, as well as prohibitions on our ability to create liens, pay dividends, redeem our stock or make investments.

We also may seek to raise additional capital by pursuing opportunities for the licensing or sale of certain intellectual property and other assets, including our Technosphere technology platform. We cannot offer assurances, however, that any strategic collaborations, sales of securities or sales or licenses of assets will be available to us on a timely basis or on acceptable terms, if at all. We may be required to enter into relationships with third parties to develop or commercialize products or technologies that we otherwise would have sought to develop independently, and any such relationships may not be on terms as commercially favorable to us as might otherwise be the case.

In the event that sufficient additional funds are not obtained through strategic collaboration opportunities, sales of securities, licensing arrangements and/or asset sales on a timely basis, we may be required to reduce expenses through the delay, reduction or curtailment of our projects, including our Technosphere Insulin System development activities, or further reduction of costs for facilities and administration.

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***We depend heavily on the successful development and commercialization of our lead product candidate, the Technosphere Insulin System, which is in clinical development, and our other product candidates, which are in early clinical or preclinical development.***

To date, we have not completed the development of any product candidates through to commercialization. Our Technosphere Insulin System is currently undergoing clinical trials, while our other product candidates are generally in early clinical or preclinical development. We anticipate that in the near term, our ability to generate revenues will depend solely on the successful development and commercialization of our Technosphere Insulin System.

We have expended significant time, money and effort in the development of our lead product candidate, the Technosphere Insulin System, which has not yet received regulatory approval and which may never be commercialized. Before we can market and sell our Technosphere Insulin System, we will need to complete Phase 3 clinical trials and demonstrate in these trials that our Technosphere Insulin System is safe and effective. Our current development plans call for the completion of our pivotal Phase 3 clinical trials of our Technosphere Insulin System in the third quarter of 2008. We must also receive the necessary approvals from the FDA and similar foreign regulatory agencies before this product candidate can be marketed in the United States or elsewhere. Even if we were to receive regulatory approval, we ultimately may be unable to gain market acceptance of our Technosphere Insulin System for a variety of reasons, including the treatment and dosage regimen, potential adverse effects, the availability of alternative treatments and cost effectiveness. If we fail to commercialize our Technosphere Insulin System, our business, financial condition and results of operations will be materially and adversely affected.

We are seeking to develop and expand our portfolio of product candidates through our internal research programs and through licensing or otherwise acquiring the rights to therapeutics in the areas of cancer and other indications. All of these product candidates will require additional research and development and significant preclinical, clinical and other testing prior to seeking regulatory approval to market them. Accordingly, these product candidates will not be commercially available for a number of years, if at all.

A significant portion of the research that we are conducting involves new and unproven compounds and technologies, including our Technosphere Insulin System, Technosphere platform technology and immunotherapy product candidates. Research programs to identify new product candidates require substantial technical, financial and human resources. Even if our research programs identify candidates that initially show promise, these candidates may fail to progress to clinical development for any number of reasons, including discovery upon further research that these candidates have adverse effects or other characteristics that indicate they are unlikely to be effective. In addition, the clinical results we obtain at one stage are not necessarily indicative of future testing results. If we fail to successfully complete the development and commercialization of our Technosphere Insulin System or develop or expand our other product candidates, or are significantly delayed in doing so, our business and results of operations will be harmed and the value of our stock could decline.

***If we do not achieve our projected development goals in the timeframes we announce and expect, our business would be harmed and the market price of our common stock could decline.***

For planning purposes, we estimate the timing of the accomplishment of various scientific, clinical, regulatory and other product development goals, which we sometimes refer to as milestones. These milestones may include the commencement or completion of scientific studies and clinical trials and the submission of regulatory filings. From time to time, we publicly announce the expected timing of some of these milestones. All of these milestones are based on a variety of assumptions. The actual timing of the achievement of these milestones can vary dramatically compared to our estimates, in many cases for reasons beyond our control, depending on numerous factors, including:

the rate of progress, costs and results of our clinical trial and research and development activities, which will be impacted by the level of proficiency and experience of our clinical staff;

our ability to identify and enroll patients who meet clinical trial eligibility criteria;

our ability to access sufficient, reliable and affordable supplies of components used in the manufacture of our product candidates, including insulin and other materials for our Technosphere Insulin System;

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the costs of expanding and maintaining manufacturing operations, as necessary;

the extent of scheduling conflicts with participating clinicians and clinical institutions;

the receipt of approvals by our competitors and by us from the FDA and other regulatory agencies; and

other actions by regulators.

In addition, if we do not obtain sufficient additional funds through sales of securities, strategic collaborations or the license or sale of certain of our assets on a timely basis, we may be required to reduce expenses by delaying, reducing or curtailing our Technosphere Insulin System or other product development activities, which would impact our ability to meet milestones. If we fail to commence or complete, or experience delays in or are forced to curtail, our proposed clinical programs or otherwise fail to adhere to our projected development goals in the timeframes we announce and expect, our business and results of operations will be harmed and the market price of our common stock may decline.

***We face substantial competition in the development of our product candidates and may not be able to compete successfully, and our product candidates may be rendered obsolete by rapid technological change.***

We face intense competition in the development of our Technosphere Insulin System. In January 2006, the FDA and the European Medicines Evaluation Agency approved Exubera<sup>®</sup>, developed by Pfizer, Inc. in collaboration with Nektar Therapeutics, for the treatment of adults with type 1 and type 2 diabetes. Exubera<sup>®</sup> was slow to gain market acceptance and, in October 2007, Pfizer announced that it was returning rights to the product to Nektar. Nektar subsequently announced that it was actively seeking to enter into a new partnership for the sales and marketing of Exubera<sup>®</sup> as well as its next generation inhaled insulin. This latter product is currently in Phase 1 trials; Nektar is reportedly targeting approval of this product for 2011. In January 2008, Novo Nordisk A/S announced that it was halting development of its inhaled insulin product, having reached the conclusion that it did not have adequate commercial potential. Notwithstanding the termination of this program, Novo Nordisk stated that it intended to increase research and development activities targeted at inhalation systems for long-acting formulations of insulin and GLP-1. In March 2008, Eli Lilly and Company announced that it too was terminating the development of its AIR<sup>®</sup> inhaled insulin system. Lilly stated that this decision resulted from increasing uncertainties in the regulatory environment and after a thorough evaluation of the evolving commercial and clinical potential of its product compared to existing medical therapies. In addition, a number of established pharmaceutical companies have or are developing technologies for the treatment of diabetes. We also face substantial competition for the development of our other product candidates.

Many of our existing or potential competitors have, or have access to, substantially greater financial, research and development, production, and sales and marketing resources than we do and have a greater depth and number of experienced managers. As a result, our competitors may be better equipped than we are to develop, manufacture, market and sell competing products. In addition, gaining favorable reimbursement is critical to the success of Technosphere Insulin. Many of our competitors have existing infrastructure and relationships with managed care organizations and reimbursement authorities which can be used to their advantage.

The rapid rate of scientific discoveries and technological changes could result in one or more of our product candidates becoming obsolete or noncompetitive. Our competitors may develop or introduce new products that render our technology and our Technosphere Insulin System less competitive, uneconomical or obsolete. Our future success will depend not only on our ability to develop our product candidates but to improve them and to keep pace with emerging industry developments. We cannot assure you that we will be able to do so.

We also expect to face increasing competition from universities and other non-profit research organizations. These institutions carry out a significant amount of research and development in the areas of diabetes and cancer. These institutions are becoming increasingly aware of the commercial value of their findings and are more active in seeking patent and other proprietary rights as well as licensing revenues.

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***If we fail to enter into a strategic collaboration with respect to our Technosphere Insulin System, we may not be able to execute on our business model.***

We have held extensive discussions with a number of pharmaceutical companies concerning a potential strategic business collaboration for our Technosphere Insulin System. To date, we have not reached agreement with any of these companies on a collaboration. While we are continuing to engage in such discussions, we believe that we will have to expend significant additional time and effort before we could reach agreement, and we cannot predict when, if ever, we could conclude such an agreement with a partner. There can be no assurance that any such collaboration will be available to us on a timely basis or on acceptable terms, if at all. If we are not able to enter into a collaboration on terms that are favorable to us, we could be required to undertake and fund product development, clinical trials, manufacturing and marketing activities solely at our own expense. We currently estimate that the capital required to continue the development of our Technosphere Insulin System over the next 12 months would be in the range of \$300 to \$400 million. However, this estimate may change based on how the program proceeds. Failure to enter into a collaboration with respect to our Technosphere Insulin System could substantially increase our requirements for capital, which might not be available on favorable terms, if at all. Alternatively, we would have to substantially reduce our development efforts, which would delay or otherwise impede the commercialization of our Technosphere Insulin System.

We will face similar challenges as we seek to develop our other product candidates. Our current strategy for developing, manufacturing and commercializing our other product candidates includes evaluating the potential for collaborating with pharmaceutical and biotechnology companies at some point in the drug development process and for these collaborators to undertake the advanced clinical development and commercialization of our product candidates. It may be difficult for us to find third parties that are willing to enter into collaborations on economic terms that are favorable to us, or at all. Failure to enter into a collaboration with respect to any other product candidate could substantially increase our requirements for capital and force us to substantially reduce our development effort.

***If we enter into collaborative agreements with respect to our Technosphere Insulin System and if our third-party collaborators do not perform satisfactorily or if our collaborations fail, development or commercialization of our Technosphere Insulin System may be delayed and our business could be harmed.***

We currently rely on clinical research organizations and hospitals to conduct, supervise or monitor some or all aspects of clinical trials involving our Technosphere Insulin System. Further, we may also enter into license agreements, partnerships or other collaborative arrangements to support the financing, development and marketing of our Technosphere Insulin System. We may also license technology from others to enhance or supplement our technologies. These various collaborators may enter into arrangements that would make them potential competitors. These various collaborators also may breach their agreements with us and delay our progress or fail to perform under their agreements, which could harm our business.

If we enter into collaborative arrangements, we will have less control over the timing, planning and other aspects of our clinical trials, and the sale and marketing of our Technosphere Insulin System and our other product candidates. We cannot offer assurances that we will be able to enter into satisfactory arrangements with third parties as contemplated or that any of our existing or future collaborations will be successful.

***Testing of our Technosphere Insulin System or another product candidate may not yield successful results, and even if it does, we may still be unable to commercialize that product candidate.***

Our research and development programs are designed to test the safety and efficacy of our Technosphere Insulin System and our other product candidates through extensive nonclinical and clinical testing. We may experience numerous unforeseen events during, or as a result of, the testing process that could delay or prevent





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commercialization of our Technosphere Insulin System or any of our other product candidates, including the following:

safety and efficacy results obtained in our nonclinical and initial clinical testing may be inconclusive or may not be predictive of results obtained in later-stage clinical trials or following long-term use, and we may as a result be forced to stop developing product candidates that we currently believe are important to our future;

the data collected from clinical trials of our product candidates may not be sufficient to support FDA or other regulatory approval;

after reviewing test results, we or any potential collaborators may abandon projects that we previously believed were promising; and

our product candidates may not produce the desired effects or may result in adverse health effects or other characteristics that preclude regulatory approval or limit their commercial use if approved.

We are nearing completion of a pivotal Phase 3 safety study of our Technosphere Insulin System to evaluate pulmonary function over a period of two years. Our Technosphere Insulin System is intended for multiple uses per day. Due to the size and timeframe over which existing and planned clinical trials are conducted, the results of clinical trials, including our existing Phase 3 trials, may not be indicative of the effects of the use of our Technosphere Insulin System over longer terms. If use of our Technosphere Insulin System results in adverse health effects or reduced efficacy or both, the FDA or other regulatory agencies may terminate our ability to market and sell our Technosphere Insulin System, may narrow the approved indications for use or otherwise require restrictive product labeling or marketing, or may require further clinical trials, which may be time-consuming and expensive and may not produce favorable results.

As a result of any of these events, the FDA, other regulatory authorities, any collaborator or we may suspend or terminate clinical trials or marketing of our Technosphere Insulin System at any time. Any suspension or termination of our clinical trials or marketing activities may harm our business and results of operations and the market price of our common stock may decline.

***If we are unable to transition successfully from an early-stage development company to a company that commercializes therapeutics, our operations would suffer.***

We are at a critical juncture in our development, having transitioned from an early-stage development company to one with multiple Phase 3 clinical trials. Phase 3 development of our Technosphere Insulin System is far more complex than the earlier phases. Overall, we plan to support a significant number of studies in the near term. We have not previously implemented the range of studies contemplated for our Phase 3 clinical program. Moreover, as a company, we have no previous experience in the Phase 3-through-NDA stage of product development.

We require a well-structured plan to make this transition. In the past year, we have added a significant number of new executive personnel, particularly in clinical development, regulatory and manufacturing production, including personnel with significant Phase 3-to-commercialization experience. We have aligned our management structure to accommodate the increasing complexity of our operations, and we are implementing the following measures, among others, to accommodate our transition, complete development of our Technosphere Insulin System and successfully implement our commercialization strategy for our Technosphere Insulin System:

expand our manufacturing capabilities;

develop comprehensive and detailed commercialization, clinical development and regulatory plans; and implement standard operating procedures, including those for protocol development.

If we are unable to accomplish these measures in a timely manner, we would be at considerable risk of failing to:

complete our Phase 3 clinical trial program in a deliberate fashion, on time and within budget; and

develop through our Phase 3 trials the key clinical data needed to obtain regulatory approval and compete successfully in the marketplace.

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***If our suppliers fail to deliver materials and services needed for the production of our Technosphere Insulin System in a timely and sufficient manner, or they fail to comply with applicable regulations, our business and results of operations would be harmed and the market price of our common stock could decline.***

For our Technosphere Insulin System to be commercially viable, we need access to sufficient, reliable and affordable supplies of insulin, our MedTone inhaler, the related cartridges and other materials. In November 2007, we entered into a long-term supply agreement with N.V. Organon, which is currently our sole supplier for insulin. We are aware of several other suppliers of bulk insulin, but to date we have not entered into a commercial relationship with any of them. Currently we obtain our Technosphere pre-cursor raw material from Evonik Industries, a major chemical manufacturer with facilities in Europe and North America. We are in the process of evaluating a second manufacturer to supply us with commercial quantities of this raw material. We also utilize our in-house chemical manufacturing plant as a back up facility. We believe Evonik Industries has the capacity to supply our current clinical and future commercial requirements. We entered into a long-term supply agreement with Vaupell, Inc., the supplier of our MedTone inhaler and cartridges. We are in the process of qualifying a second manufacturer to supply us with commercial quantities of these components. We must rely on our suppliers to comply with relevant regulatory and other legal requirements, including the production of insulin in accordance with cGMP and the production of MedTone inhaler and related cartridges in accordance with device QSR. The supply of all of these materials may be limited or the manufacturer may not meet relevant regulatory requirements, and if we are unable to obtain these materials in sufficient amounts, in a timely manner and at reasonable prices, or if we should encounter delays or difficulties in our relationships with manufacturers or suppliers, the development or manufacturing of our Technosphere Insulin System may be delayed. Any such events would delay the submission of our Technosphere Insulin System for regulatory approval or market introduction and subsequent sales and, if so, our business and results of operations will be harmed and the market price of our common stock may decline.

***We have never manufactured our Technosphere Insulin System or any other product candidate in commercial quantities, and if we fail to develop an effective manufacturing capability for our product candidates or to engage third-party manufacturers with this capability, we may be unable to commercialize these products.***

We currently obtain our Technosphere precursor raw material primarily from Evonik Industries. We use our Danbury, Connecticut facility to formulate Technosphere Insulin, fill plastic cartridges with Technosphere Insulin and blister package the cartridges for our clinical trials. We presently intend to increase our formulation, fill and finishing capabilities at Danbury in order to accommodate our activities through initial commercialization. This expansion will involve a number of third-party suppliers of equipment and materials as well as engineering and construction services. Our suppliers may not deliver all of the required equipment, materials and services in a timely manner or at reasonable prices. If we encounter difficulties in our relationships with these suppliers, or if a supplier becomes unable to provide us with goods or services at the agreed-upon terms or schedule, our facilities expansion could be delayed or its costs increased.

We have never manufactured our Technosphere Insulin System or any other product candidate in commercial quantities. As our product candidates move through the regulatory process, we will need to either develop the capability of manufacturing on a commercial scale or engage third-party manufacturers with this capability, and we cannot offer assurances that we will be able to do either successfully. The manufacture of pharmaceutical products requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of pharmaceutical products often encounter difficulties in production, especially in scaling up initial production. These problems include difficulties with production costs and yields, quality control and assurance and shortages of qualified personnel, as well as compliance with strictly enforced federal, state and foreign regulations. In addition, before we would be able to produce commercial quantities of Technosphere Insulin at our Danbury facility, it would have to undergo a pre-approval inspection by the FDA. The

expansion process and preparation for the FDA's pre-approval inspection for commercial production at the Danbury facility could take an additional six months or longer. If we use a third-party supplier to formulate Technosphere Insulin or produce raw material, the transition could also require significant start-up time to qualify

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and implement the manufacturing process. If we engage a third-party manufacturer, our third-party manufacturer may not perform as agreed or may terminate its agreement with us.

Additionally, if we manufacture commercial material at a different facility than the site of manufacture of clinical trial materials or if we manufacture commercial material on a significantly larger production scale than the production scale for clinical trial materials, we may be required by the FDA to establish that the results obtained from the clinical trials may reasonably be extrapolated to such commercial material.

Any of these factors could cause us to delay or suspend clinical trials, regulatory submissions, required approvals or commercialization of our product candidates, entail higher costs and result in our being unable to effectively commercialize our products. Furthermore, if we or a third-party manufacturer fail to deliver the required commercial quantities of any product on a timely basis, and at commercially reasonable prices and acceptable quality, and we were unable to promptly find one or more replacement manufacturers capable of production at a substantially equivalent cost, in substantially equivalent volume and quality on a timely basis, we would likely be unable to meet demand for such products and we would lose potential revenues.

***We deal with hazardous materials and must comply with environmental laws and regulations, which can be expensive and restrict how we do business.***

Our research and development work involves the controlled storage and use of hazardous materials, including chemical, radioactive and biological materials. In addition, our manufacturing operations involve the use of CBZ-lysine, which is stable and non-hazardous under normal storage conditions, but may form an explosive mixture under certain conditions. Our operations also produce hazardous waste products. We are subject to federal, state and local laws and regulations governing how we use, manufacture, store, handle and dispose of these materials. Moreover, the risk of accidental contamination or injury from hazardous materials cannot be completely eliminated, and in the event of an accident, we could be held liable for any damages that may result, and any liability could fall outside the coverage or exceed the limits of our insurance. Currently, our general liability policy provides coverage up to \$1 million per occurrence and \$2 million in the aggregate and is supplemented by an umbrella policy that provides a further \$4 million of coverage; however, our insurance policy excludes pollution coverage and we do not carry a separate hazardous materials policy. In addition, we could be required to incur significant costs to comply with environmental laws and regulations in the future. Finally, current or future environmental laws and regulations may impair our research, development or production efforts.

When we purchased the facilities located in Danbury, Connecticut in 2001, there was a soil cleanup plan in process. As part of the purchase, we obtained an indemnification from the seller related to the remediation of the soil for all known environmental conditions that existed at the time the seller acquired the property. The seller is, in turn, indemnified for these known environmental conditions by the previous owner. We initiated the final stages of the soil cleanup plan which we estimate will cost approximately \$1.5 million to complete by the end of the third quarter of 2008. We also received an indemnification from the seller for environmental conditions created during its ownership of the property and for environmental problems unknown at the time that the seller acquired the property. These additional indemnities are limited to the purchase price that we paid for the Danbury facilities. In the event that any cleanup costs are imposed on us and we are unable to collect the full amount of these costs and expenses from the seller or the party responsible for the contamination, we may be required to pay these costs and our business and results of operations may be harmed.

***If we fail to enter into collaborations with third parties, we would be required to establish our own sales, marketing and distribution capabilities, which could impact the commercialization of our products and harm our business.***

A broad base of physicians, including primary care physicians, internists and endocrinologists, treat patients with diabetes. A large sales force will be required in order to educate and support these physicians. Therefore, we plan to enter into collaborations with one or more pharmaceutical companies to market, distribute and sell our Technosphere Insulin System, if it is approved. If we fail to enter into collaborations, we would be required to establish our own direct sales, marketing and distribution capabilities. Establishing these capabilities can be time-consuming and expensive. We estimate that establishing a specialty sales force would cost in excess of \$35 million.

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To further expand the potential of our Technosphere Insulin System and to reach the majority of physicians treating patients with diabetes, it will be necessary to establish a primary-care sales force. Because we lack experience in selling pharmaceutical products to the diabetes market, we would be at a disadvantage to our potential competitors, all of whom have substantially more resources and experience than we do. For example, our competitors have existing sales forces in excess of 1,000 representatives targeting primary care physicians. We, acting alone, would not initially be able to field a sales force as large as our competitors or provide the same degree of market research or marketing support.

In addition, our competitors would have a greater ability to devote research resources toward expansion of the indications for their products. We cannot assure you that we will succeed in entering into acceptable collaborations, that any such collaboration will be successful or, if not, that we will successfully develop our own sales, marketing and distribution capabilities.

***If any product that we may develop does not become widely accepted by physicians, patients, third-party payers and the healthcare community, we may be unable to generate significant revenue, if any.***

Technosphere Insulin System and our other product candidates are new and unproven. Even if any of our product candidates obtain regulatory approvals, it may not gain market acceptance among physicians, patients, third-party payers and the healthcare community. Failure to achieve market acceptance would limit our ability to generate revenue and would adversely affect our results of operations.

The degree of market acceptance of our Technosphere Insulin System and our other product candidates will depend on many factors, including the:

- claims for which FDA approval can be obtained, including superiority claims;
- perceived advantages and disadvantages of competitive products;
- willingness and ability of patients and the healthcare community to adopt new technologies;
- ability to manufacture the product in sufficient quantities with acceptable quality and at an acceptable cost;
- perception of patients and the healthcare community, including third-party payers, regarding the safety, efficacy and benefits of the product compared to those of competing products or therapies;
- convenience and ease of administration of the product relative to existing treatment methods;
- pricing and reimbursement of the product relative to existing treatment therapeutics and methods; and
- marketing and distribution support for the product.

Physicians will not recommend a product until clinical data or other factors demonstrate the safety and efficacy of the product as compared to other treatments. Even if the clinical safety and efficacy of our product candidates is established, physicians may elect not to recommend these product candidates for a variety of factors, including the reimbursement policies of government and third-party payers and the effectiveness of our competitors in marketing their therapies. Because of these and other factors, any product that we may develop may not gain market acceptance, which would materially harm our business, financial condition and results of operations.

***If third-party payers do not reimburse customers for our products, our products might not be used or purchased, which would adversely affect our revenues.***

Our future revenues and potential for profitability may be affected by the continuing efforts of governments and third-party payers to contain or reduce the costs of healthcare through various means. For example, in certain foreign markets the pricing of prescription pharmaceuticals is subject to governmental control. In the United States, there has been, and we expect that there will continue to be, a number of federal and state proposals to implement similar governmental controls. We cannot be certain what legislative proposals will be adopted or what actions federal, state or private payers for healthcare goods and services may take in response to any healthcare reform proposals or legislation. Such reforms may make it difficult to complete the development and testing of our Technosphere Insulin System and our other product candidates, and therefore may limit our ability to generate



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revenues from sales of our product candidates and achieve profitability. Further, to the extent that such reforms have a material adverse effect on the business, financial condition and profitability of other companies that are prospective collaborators for some of our product candidates, our ability to commercialize our product candidates under development may be adversely affected.

In the United States and elsewhere, sales of prescription pharmaceuticals still depend in large part on the availability of reimbursement to the consumer from third-party payers, such as governmental and private insurance plans. Third-party payers are increasingly challenging the prices charged for medical products and services. In addition, because each third-party payer individually approves reimbursement, obtaining these approvals is a time-consuming and costly process. We would be required to provide scientific and clinical support for the use of any product to each third-party payer separately with no assurance that approval would be obtained. This process could delay the market acceptance of any product and could have a negative effect on our future revenues and operating results. Even if we succeed in bringing one or more products to market, we cannot be certain that any such products would be considered cost-effective or that reimbursement to the consumer would be available, in which case our business and results of operations would be harmed and the market price of our common stock could decline.

***If product liability claims are brought against us, we may incur significant liabilities and suffer damage to our reputation.***

The testing, manufacturing, marketing and sale of our Technosphere Insulin System and our other product candidates expose us to potential product liability claims. A product liability claim may result in substantial judgments as well as consume significant financial and management resources and result in adverse publicity, decreased demand for a product, injury to our reputation, withdrawal of clinical trial volunteers and loss of revenues. We currently carry worldwide liability insurance in the amount of \$10 million. We believe these limits are reasonable to cover us from potential damages arising from current and previous clinical trials of our Technosphere Insulin System. In addition, we carry local policies per trial in each country in which we conduct clinical trials that require us to carry coverage based on local statutory requirements. We intend to obtain product liability coverage for commercial sales in the future if our Technosphere Insulin System is approved. However, we may not be able to obtain insurance coverage that will be adequate to satisfy any liability that may arise, and because insurance coverage in our industry can be very expensive and difficult to obtain, we cannot assure you that we will be able to obtain sufficient coverage at an acceptable cost, if at all. If losses from such claims exceed our liability insurance coverage, we may ourselves incur substantial liabilities. If we are required to pay a product liability claim, we may not have sufficient financial resources to complete development or commercialization of any of our product candidates and, if so, our business and results of operations would be harmed and the market price of our common stock may decline.

***If we lose any key employees or scientific advisors, our operations and our ability to execute our business strategy could be materially harmed.***

In order to commercialize our product candidates successfully, we will be required to expand our work force, particularly in the areas of manufacturing, clinical trials management, regulatory affairs, business development, and sales and marketing. These activities will require the addition of new personnel, including management, and the development of additional expertise by existing personnel. We face intense competition for qualified employees among companies in the biotechnology and biopharmaceutical industries. Our success depends upon our ability to attract, retain and motivate highly skilled employees. We may be unable to attract and retain these individuals on acceptable terms, if at all.

The loss of the services of any principal member of our management and scientific staff could significantly delay or prevent the achievement of our scientific and business objectives. All of our employees are at will and we currently do not have employment agreements with any of the principal members of our management or scientific staff, and we do

not have key person life insurance to cover the loss of any of these individuals. Replacing key employees may be difficult and time-consuming because of the limited number of individuals in our industry with the skills and experience required to develop, gain regulatory approval of and commercialize our product candidates successfully.

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We have relationships with scientific advisors at academic and other institutions to conduct research or assist us in formulating our research, development or clinical strategy. These scientific advisors are not our employees and may have commitments to, and other obligations with, other entities that may limit their availability to us. We have limited control over the activities of these scientific advisors and can generally expect these individuals to devote only limited time to our activities. Failure of any of these persons to devote sufficient time and resources to our programs could harm our business. In addition, these advisors are not prohibited from, and may have arrangements with, other companies to assist those companies in developing technologies that may compete with our product candidates.

***If our Chief Executive Officer is unable to devote sufficient time and attention to our business, our operations and our ability to execute our business strategy could be materially harmed.***

Alfred Mann, our Chairman and Chief Executive Officer, is also serving as the Chairman of Advanced Bionics Corporation. Mr. Mann is involved in many other business and charitable activities. As a result, the time and attention Mr. Mann devotes to the operation of our business varies, and he may not expend the same time or focus on our activities as other, similarly situated chief executive officers. If Mr. Mann is unable to devote the time and attention necessary to running our business, we may not be able to execute our business strategy and our business could be materially harmed.

***Our facilities that are located in Southern California may be affected by man-made or natural disasters.***

Our headquarters and some of our research and development activities are located in Southern California, where they are subject to a risk of man-made disasters, terrorism, and an enhanced risk of natural and other disasters such as fires, power and telecommunications failures, mudslides, and earthquakes. An act of terrorism, fire, earthquake or other catastrophic loss that causes significant damage to our facilities or interruption of our business could harm our business. We do not carry insurance to cover losses caused by earthquakes, and the insurance coverage that we carry for fire damage and for business interruption may be insufficient to compensate us for any losses that we may incur.

***If our internal controls over financial reporting are not considered effective, our business and stock price could be adversely affected.***

Section 404 of the Sarbanes-Oxley Act of 2002 requires us to evaluate the effectiveness of our internal controls over financial reporting as of the end of each fiscal year, and to include a management report assessing the effectiveness of our internal controls over financial reporting in our annual report on Form 10-K for that fiscal year. Section 404 also requires our independent registered public accounting firm to attest to, and report on, our internal controls over financial reporting. Our management determined, as of the quarter ended June 30, 2007, that we had a material weakness in identifying and recording clinical trial costs, principally from the failure of our controls to detect an overstatement of clinical trial liabilities. As of December 31, 2007, we completed the execution of our remediation plan and our management has concluded that our internal control over financial reporting was effective as of December 31, 2007.

Our management, including our Chief Executive Officer and Chief Financial Officer, does not expect that our internal controls over financial reporting will prevent all error and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. Further, the design of a control system must reflect the fact that there are resource constraints, and the benefits of controls must be considered relative to their costs. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud involving a company have been, or will be, detected. The design of any system of controls is based in part on certain assumptions about the likelihood of future events, and we cannot assure you that any design will succeed in achieving its stated goals under all potential future conditions. Over time, controls may become inadequate because of changes in

conditions or deterioration in the degree of compliance with policies or procedures. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and not be detected. We cannot assure you that we or our independent registered public accounting firm will not identify a material weakness in our internal controls in the future. A material weakness in our internal controls over financial

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reporting would require management and our independent registered public accounting firm to evaluate our internal controls as ineffective. If our internal controls over financial reporting are not considered effective, we may experience a loss of public confidence, which could have an adverse effect on our business and on the market price of our common stock.

## **RISKS RELATED TO REGULATORY APPROVALS**

*Our product candidates must undergo rigorous nonclinical and clinical testing and we must obtain regulatory approvals, which could be costly and time-consuming and subject us to unanticipated delays or prevent us from marketing any products.*

Our research and development activities, as well as the manufacturing and marketing of our product candidates, including our Technosphere Insulin System, are subject to regulation, including regulation for safety, efficacy and quality, by the FDA in the United States and comparable authorities in other countries. FDA regulations and the regulation of comparable foreign regulatory authorities are wide-ranging and govern, among other things:

product design, development, manufacture and testing;

product labeling;

product storage and shipping;

pre-market clearance or approval;

advertising and promotion; and

product sales and distribution.

Clinical testing can be costly and take many years, and the outcome is uncertain and susceptible to varying interpretations. Based on our discussions with the FDA and on our understanding of the interactions between the FDA and other pharmaceutical companies developing inhaled insulin delivery systems, we expect, among other requirements, that we will need safety data covering at least two years from patients treated with our Technosphere Insulin System and that we must complete an additional six-month carcinogenicity study of Technosphere Insulin in rodents in order to obtain approval. We cannot be certain when or under what conditions we will undertake further clinical trials. The clinical trials of our product candidates may not be completed on schedule, the FDA or foreign regulatory agencies may order us to stop or modify our research, or these agencies may not ultimately approve any of our product candidates for commercial sale. The data collected from our clinical trials may not be sufficient to support regulatory approval of our various product candidates, including our Technosphere Insulin System. Two of our three pivotal trials (studies 009 and 030) are being conducted under Special Protocol Assessments and the third (study 102) is very similar to study 009. Nonetheless, even if we believe the data collected from our clinical trials are sufficient, the FDA has substantial discretion in the approval process and may disagree with our interpretation of the data. For example, even if we meet the statistical criteria for non-inferiority with respect to the primary endpoint in a pivotal clinical study (study 102) of our Technosphere Insulin System, the FDA may deem the results uninterpretable because of issues related to the open-label, non-inferiority design of the study. Our failure to adequately demonstrate the safety and efficacy of any of our product candidates would delay or prevent regulatory approval of our product candidates, which could prevent us from achieving profitability.

The requirements governing the conduct of clinical trials and manufacturing and marketing of our product candidates, including our Technosphere Insulin System, outside the United States vary widely from country to country. Foreign

approvals may take longer to obtain than FDA approvals and can require, among other things, additional testing and different clinical trial designs. Foreign regulatory approval processes include all of the risks associated with the FDA approval processes. Some of those agencies also must approve prices of the products. Approval of a product by the FDA does not ensure approval of the same product by the health authorities of other countries. In addition, changes in regulatory policy in the United States or in foreign countries for product approval during the period of product development and regulatory agency review of each submitted new application may cause delays or rejections.

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The process of obtaining FDA and other required regulatory approvals, including foreign approvals, is expensive, often takes many years and can vary substantially based upon the type, complexity and novelty of the products involved. We are not aware of any precedent for the successful commercialization of products based on our technology. On January 26, 2006, the FDA approved the first pulmonary insulin product, Exubera. This approval has had an impact on and, notwithstanding the voluntary withdrawal of the product from the market by its manufacturer, could still impact the development and registration of our Technosphere Insulin System in different ways, including: Exubera may be used as a reference for safety and efficacy evaluations of our Technosphere Insulin System, and the approval standards set for Exubera may be applied to other products that follow including our Technosphere Insulin System. The FDA has advised us that it will regulate our Technosphere Insulin System as a combination product because of the complex nature of the system that includes the combination of a new drug (Technosphere Insulin) and a new medical device (the MedTone inhaler used to administer the insulin). The FDA indicated that the review of a future drug marketing application for our Technosphere Insulin System will involve three separate review groups of the FDA: (1) the Metabolic and Endocrine Drug Products Division; (2) the Pulmonary Drug Products Division; and (3) the Center for Devices and Radiological Health within the FDA that reviews medical devices. We currently understand that the Metabolic and Endocrine Drug Products Division will be the lead group and will obtain consulting reviews from the other two FDA groups. The FDA has not made an official final decision in this regard, however, and we can make no assurances at this time about what impact FDA review by multiple groups will have on the review and approval of our product or whether we are correct in our understanding of how our Technosphere Insulin System will be reviewed and approved.

Also, questions that have been raised about the safety of marketed drugs generally, including pertaining to the lack of adequate labeling, may result in increased cautiousness by the FDA in reviewing new drugs based on safety, efficacy, or other regulatory considerations and may result in significant delays in obtaining regulatory approvals. Such regulatory considerations may also result in the imposition of more restrictive drug labeling or marketing requirements as conditions of approval, which may significantly affect the marketability of our drug products. FDA review of our Technosphere Insulin System as a combination product therapy may lengthen the product development and regulatory approval process, increase our development costs and delay or prevent the commercialization of our Technosphere Insulin System.

We are developing our Technosphere Insulin System as a new treatment for diabetes utilizing unique, proprietary components. As a combination product, any changes to either the MedTone inhaler, the Technosphere material or the insulin, including new suppliers, could possibly result in FDA requirements to repeat certain clinical studies. This means, for example, that switching to an alternate delivery system could require us to undertake additional clinical trials and other studies, which could significantly delay the development and commercialization of our Technosphere Insulin System. Our product candidates that are currently in development for the treatment of cancer also face similar obstacles and costs.

We currently expect that our inhaler will be reviewed for approval as part of the NDA for our Technosphere Insulin System. No assurances exist that we will not be required to obtain separate device clearances or approval for use of our inhaler with our Technosphere Insulin System. This may result in our being subject to medical device review user fees and to other device requirements to market our inhaler and may result in significant delays in commercialization. Even if the device component is approved as part of our NDA for our Technosphere Insulin System, numerous device regulatory requirements still apply to the device part of the drug-device combination.

***We have only limited experience in filing and pursuing applications necessary to gain regulatory approvals, which may impede our ability to obtain timely approvals from the FDA or foreign regulatory agencies, if at all.***

We will not be able to commercialize our Technosphere Insulin System or any other product candidates until we have obtained regulatory approval. We have no experience as a company in late-stage regulatory filings, such as preparing

and submitting NDAs, which may place us at risk of delays, overspending and human resources inefficiencies. Any delay in obtaining, or inability to obtain, regulatory approval could harm our business.



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***If we do not comply with regulatory requirements at any stage, whether before or after marketing approval is obtained, we may be subject to criminal prosecution, fined or forced to remove a product from the market or experience other adverse consequences, including restrictions or delays in obtaining regulatory marketing approval.***

Even if we comply with regulatory requirements, we may not be able to obtain the labeling claims necessary or desirable for product promotion. We may also be required to undertake post-marketing trials. In addition, if we or other parties identify adverse effects after any of our products are on the market, or if manufacturing problems occur, regulatory approval may be withdrawn and a reformulation of our products, additional clinical trials, changes in labeling of, or indications of use for, our products and/or additional marketing applications may be required. If we encounter any of the foregoing problems, our business and results of operations will be harmed and the market price of our common stock may decline.

***Even if we obtain regulatory approval for our product candidates, such approval may be limited and we will be subject to stringent, ongoing government regulation.***

Even if regulatory authorities approve any of our product candidates, they could approve less than the full scope of uses or labeling that we seek or otherwise require special warnings or other restrictions on use or marketing or could require potentially costly post-marketing follow-up clinical trials. Regulatory authorities may limit the segments of the diabetes population to which we or others may market our Technosphere Insulin System or limit the target population for our other product candidates. Based on currently available clinical studies, we believe that our Technosphere Insulin System may have certain advantages over currently approved insulin products including its approximation of the natural early insulin secretion normally seen in healthy individuals following the beginning of a meal. Nonetheless, there are no assurances that these and other advantages, if any, of our Technosphere Insulin System have clinical significance or can be confirmed in head-to-head clinical trials against appropriate approved comparator insulin drug products. Such comparative clinical trials are required to make these types of superiority claims in labeling or advertising. These aforementioned observations and others may therefore not be capable of substantiation in comparative clinical trials prior to our NDA submission, if at all, or otherwise may not be suitable for inclusion in product labeling or advertising and, as a result, our Technosphere Insulin System may not have competitive advantages when compared to other insulin products.

The manufacture, marketing and sale of these product candidates will be subject to stringent and ongoing government regulation. The FDA may also withdraw product approvals if problems concerning safety or efficacy of the product occur following approval. In response to questions that have been raised about the safety of certain approved prescription products, including the lack of adequate warnings, the FDA and United States Congress are currently considering new regulatory and legislative approaches to advertising, monitoring and assessing the safety of marketed drugs, including legislation providing the FDA with authority to mandate labeling changes for approved pharmaceutical products, particularly those related to safety. We also cannot be sure that the current FDA and United States Congressional initiatives pertaining to ensuring the safety of marketed drugs or other developments pertaining to the pharmaceutical industry will not adversely affect our operations.

We also are required to register our establishments and list our products with the FDA and certain state agencies. We and any third-party manufacturers or suppliers must continually adhere to federal regulations setting forth requirements, known as cGMP (for drugs) and QSR (for medical devices), and their foreign equivalents, which are enforced by the FDA and other national regulatory bodies through their facilities inspection programs. If our facilities, or the facilities of our manufacturers or suppliers, cannot pass a preapproval plant inspection, the FDA will not approve the marketing of our product candidates. In complying with cGMP and foreign regulatory requirements, we and any of our potential third-party manufacturers or suppliers will be obligated to expend time, money and effort in production, record-keeping and quality control to ensure that our products meet applicable specifications and other

requirements. QSR requirements also impose extensive testing, control and documentation requirements. State regulatory agencies and the regulatory agencies of other countries have similar requirements. In addition, we will be required to comply with regulatory requirements of the FDA, state regulatory agencies and the regulatory agencies of other countries concerning the reporting of adverse events and device malfunctions, corrections and removals (e.g., recalls), promotion and advertising and general prohibitions against the manufacture and distribution of adulterated and misbranded devices. Failure to comply with these regulatory requirements could

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result in civil fines, product seizures, injunctions and/or criminal prosecution of responsible individuals and us. Any such actions would have a material adverse effect on our business and results of operations.

***Our insulin supplier does not yet supply human recombinant insulin for an FDA-approved product and will likely be subject to an FDA preapproval inspection before the agency will approve a future marketing application for our Technosphere Insulin System.***

Our insulin supplier sells its product outside of the United States. However, we can make no assurances that our insulin supplier will be acceptable to the FDA. If we were required to find a new or additional supplier of insulin, we would be required to evaluate the new supplier's ability to provide insulin that meets our specifications and quality requirements, which would require significant time and expense and could delay the manufacturing and future commercialization of our Technosphere Insulin System. We also depend on suppliers for other materials that comprise our Technosphere Insulin System, including our MedTone inhaler and cartridges. All of our device suppliers must comply with relevant regulatory requirements including QSR. It also is likely that major suppliers will be subject to FDA preapproval inspections before the agency will approve a future marketing application for our Technosphere Insulin System. At the present time our insulin supplier is certified to the ISO9001:2000 Standard. There can be no assurance, however, that if the FDA were to conduct a preapproval inspection of our insulin supplier or other suppliers, that the agency would find that the supplier substantially comply with the QSR or cGMP requirements, where applicable. If we or any potential third-party manufacturer or supplier fails to comply with these requirements or comparable requirements in foreign countries, regulatory authorities may subject us to regulatory action, including criminal prosecutions, fines and suspension of the manufacture of our products.

***Reports of side effects or safety concerns in related technology fields or in other companies' clinical trials could delay or prevent us from obtaining regulatory approval or negatively impact public perception of our product candidates.***

At present, there are a number of clinical trials being conducted by us and other pharmaceutical companies involving insulin delivery systems. If we discover that our lead product candidate is associated with a significantly increased frequency of adverse events, or if other pharmaceutical companies announce that they observed frequent adverse events in their trials involving the pulmonary delivery of insulin, we could encounter delays in the timing of our clinical trials or difficulties in obtaining the approval of our Technosphere Insulin System. As well, the public perception of our lead product candidates might be adversely affected, which could harm our business and results of operations and cause the market price of our common stock to decline, even if the concern relates to another company's products or product candidates.

There are also a number of clinical trials being conducted by other pharmaceutical companies involving compounds similar to, or competitive with, our other product candidates. Adverse results reported by these other companies in their clinical trials could delay or prevent us from obtaining regulatory approval or negatively impact public perception of our product candidates, which could harm our business and results of operations and cause the market price of our common stock to decline.

## **RISKS RELATED TO INTELLECTUAL PROPERTY**

***If we are unable to protect our proprietary rights, we may not be able to compete effectively, or operate profitably.***

Our commercial success depends, in large part, on our ability to obtain and maintain intellectual property protection for our technology. Our ability to do so will depend on, among other things, complex legal and factual questions, and it should be noted that the standards regarding intellectual property rights in our fields are still evolving. We attempt to protect our proprietary technology through a combination of patents, trade secrets and confidentiality agreements.

We own a number of domestic and international patents, have a number of domestic and international patent applications pending and have licenses to additional patents. We cannot assure you that our patents and licenses will successfully preclude others from using our technologies, and we could incur substantial costs in seeking enforcement of our proprietary rights against infringement. Even if issued, the patents may not give us an advantage over competitors with similar alternative technologies.

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Moreover, the issuance of a patent is not conclusive as to its validity or enforceability and it is uncertain how much protection, if any, will be afforded by our patents. A third party may challenge the validity or enforceability of a patent after its issuance by various proceedings such as oppositions in foreign jurisdictions or re-examinations in the United States. If we attempt to enforce our patents, they may be challenged in court where they could be held invalid, unenforceable, or have their breadth narrowed to an extent that would destroy their value.

We also rely on unpatented technology, trade secrets, know-how and confidentiality agreements. We require our officers, employees, consultants and advisors to execute proprietary information and invention and assignment agreements upon commencement of their relationships with us. We also execute confidentiality agreements with outside collaborators. There can be no assurance, however, that these agreements will provide meaningful protection for our inventions, trade secrets, know-how or other proprietary information in the event of unauthorized use or disclosure of such information. If any trade secret, know-how or other technology not protected by a patent were to be disclosed to or independently developed by a competitor, our business, results of operations and financial condition could be adversely affected.

***If we become involved in lawsuits to protect or enforce our patents or the patents of our collaborators or licensors, we would be required to devote substantial time and resources to prosecute or defend such proceedings.***

Competitors may infringe our patents or the patents of our collaborators or licensors. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that a patent of ours is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover its technology. A court may also decide to award us a royalty from an infringing party instead of issuing an injunction against the infringing activity. An adverse determination of any litigation or defense proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly and could put our patent applications at risk of not issuing.

Interference proceedings brought by the USPTO may be necessary to determine the priority of inventions with respect to our patent applications or those of our collaborators or licensors. Litigation or interference proceedings may fail and, even if successful, may result in substantial costs and be a distraction to our management. We may not be able, alone or with our collaborators and licensors, to prevent misappropriation of our proprietary rights, particularly in countries where the laws may not protect such rights as fully as in the United States. We may not prevail in any litigation or interference proceeding in which we are involved. Even if we do prevail, these proceedings can be very expensive and distract our management.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, during the course of this kind of litigation, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, the market price of our common stock may decline.

***If our technologies conflict with the proprietary rights of others, we may incur substantial costs as a result of litigation or other proceedings and we could face substantial monetary damages and be precluded from commercializing our products, which would materially harm our business.***

Over the past three decades the number of patents issued to biotechnology companies has expanded dramatically. As a result it is not always clear to industry participants, including us, which patents cover the multitude of biotechnology product types. Ultimately, the courts must determine the scope of coverage afforded by a patent and the courts do not always arrive at uniform conclusions.

A patent owner may claim that we are making, using, selling or offering for sale an invention covered by the owner's patents and may go to court to stop us from engaging in such activities. Such litigation is not uncommon in our industry. For example, in August 2006, Novo Nordisk filed a lawsuit against Pfizer claiming that Pfizer's product Exubera infringes certain patents owned by Novo Nordisk that cover inhaled insulin treatment for diabetes.

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Patent lawsuits can be expensive and would consume time and other resources. There is a risk that a court would decide that we are infringing a third party's patents and would order us to stop the activities covered by the patents, including the commercialization of our products. In addition, there is a risk that we would have to pay the other party damages for having violated the other party's patents (which damages may be increased, as well as attorneys' fees ordered paid, if infringement is found to be willful), or that we will be required to obtain a license from the other party in order to continue to commercialize the affected products, or to design our products in a manner that does not infringe a valid patent. We may not prevail in any legal action, and a required license under the patent may not be available on acceptable terms or at all, requiring cessation of activities that were found to infringe a valid patent. We also may not be able to develop a non-infringing product design on commercially reasonable terms, or at all.

Although we own a number of domestic and foreign patents and patent applications relating to our Technosphere Insulin System and cancer vaccine products under development, we have identified certain third-party patents having claims relating to chemical compositions of matter and pulmonary insulin delivery that may trigger an allegation of infringement upon the commercial manufacture and sale of our Technosphere Insulin System. We have also identified third-party patents disclosing methods of use and compositions of matter related to DNA-based vaccines that also may trigger an allegation of infringement upon the commercial manufacture and sale of our cancer therapy. If a court were to determine that our insulin products or cancer therapies were infringing any of these patent rights, we would have to establish with the court that these patents were invalid or unenforceable in order to avoid legal liability for infringement of these patents. However, proving patent invalidity or unenforceability can be difficult because issued patents are presumed valid. Therefore, in the event that we are unable to prevail in an infringement or invalidity action we will have to either acquire the third-party patents outright or seek a royalty-bearing license. Royalty-bearing licenses effectively increase production costs and therefore may materially affect product profitability. Furthermore, should the patent holder refuse to either assign or license us the infringed patents, it may be necessary to cease manufacturing the product entirely and/or design around the patents, if possible. In either event, our business would be harmed and our profitability could be materially adversely impacted.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, during the course of this kind of litigation, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, the market price of our common stock may decline.

In addition, patent litigation may divert the attention of key personnel and we may not have sufficient resources to bring these actions to a successful conclusion. At the same time, some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. An adverse determination in a judicial or administrative proceeding or failure to obtain necessary licenses could prevent us from manufacturing and selling our products or result in substantial monetary damages, which would adversely affect our business and results of operations and cause the market price of our common stock to decline.

***We may not obtain trademark registrations for our potential trade names.***

We have not selected trade names for some of our products and product candidates; therefore, we have not filed trademark registrations for our potential trade names for our products in all jurisdictions, nor can we assure that we will be granted registration of those potential trade names for which we have filed. Although we intend to defend any opposition to our trademark registrations, no assurance can be given that any of our trademarks will be registered in the United States or elsewhere or that the use of any of our trademarks will confer a competitive advantage in the marketplace. Furthermore, even if we are successful in our trademark registrations, the FDA has its own process for drug nomenclature and its own views concerning appropriate proprietary names. It also has the power, even after granting market approval, to request a company to reconsider the name for a product because of evidence of confusion

in the marketplace. We cannot assure you that the FDA or any other regulatory authority will approve of any of our trademarks or will not request reconsideration of one of our trademarks at some time in the future.



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**RISKS RELATED TO OUR COMMON STOCK**

***Our stock price is volatile.***

The stock market, particularly in recent years, has experienced significant volatility particularly with respect to pharmaceutical and biotechnology stocks, and this trend may continue. The volatility of pharmaceutical and biotechnology stocks often does not relate to the operating performance of the companies represented by the stock. Our business and the market price of our common stock may be influenced by a large variety of factors, including:

the progress and results of our clinical trials;

announcements by us or our competitors concerning clinical trial results, acquisitions, strategic alliances, technological innovations, newly approved commercial products, product discontinuations, or other developments;

the availability of critical materials used in developing and manufacturing our Technosphere Insulin System or other product candidates;

developments or disputes concerning our patents or proprietary rights;

the expense and time associated with, and the extent of our ultimate success in, securing regulatory approvals;

announcements by us concerning our financial condition or operating performance;

changes in securities analysts' estimates of our financial condition or operating performance;

general market conditions and fluctuations for emerging growth and pharmaceutical market sectors;

sales of large blocks of our common stock, including sales by our executive officers, directors and significant stockholders;

discussion of our Technosphere Insulin System, our other product candidates, competitors' products, or our stock price by the financial and scientific press, the healthcare community and online investor communities such as chat rooms; and

general economic, political or stock market conditions.

Any of these risks, as well as other factors, could cause the market price of our common stock to decline.

***If other biotechnology and biopharmaceutical companies or the securities markets in general encounter problems, the market price of our common stock could be adversely affected.***

Public companies in general and companies included on the Nasdaq Global Market in particular have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of those companies. There has been particular volatility in the market prices of securities of biotechnology and other life sciences companies, and the market prices of these companies have often fluctuated because of problems or successes in a given market segment or because investor interest has shifted to other segments. These broad market and industry factors may cause the market price of our common stock to decline, regardless of our operating performance. We have no control over this volatility and can only focus our efforts on our own operations, and even

these may be affected due to the state of the capital markets.

In the past, following periods of large price declines in the public market price of a company's securities, securities class action litigation has often been initiated against that company. Litigation of this type could result in substantial costs and diversion of management's attention and resources, which would hurt our business. Any adverse determination in litigation could also subject us to significant liabilities.

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***Our Chief Executive Officer and principal stockholder can individually control our direction and policies, and his interests may be adverse to the interests of our other stockholders. After his death, his stock will be left to his funding foundations for distribution to various charities, and we cannot assure you of the manner in which those entities will manage their holdings.***

At March 10, 2008, Mr. Mann beneficially owned approximately 48.1% of our outstanding shares of capital stock. We believe members of Mr. Mann's family beneficially owned at least an additional 1% of our outstanding shares of common stock, although Mr. Mann does not have voting or investment power with respect to these shares. By virtue of his holdings, Mr. Mann can and will continue to be able to effectively control the election of the members of our board of directors, our management and our affairs and prevent corporate transactions such as mergers, consolidations or the sale of all or substantially all of our assets that may be favorable from our standpoint or that of our other stockholders or cause a transaction that we or our other stockholders may view as unfavorable.

Subject to compliance with United States federal and state securities laws, Mr. Mann is free to sell the shares of our stock he holds at any time. Upon his death, we have been advised by Mr. Mann that his shares of our capital stock will be left to the Alfred E. Mann Medical Research Organization, or AEMMRO, and AEM Foundation for Biomedical Engineering, or AEMFBE, not-for-profit medical research foundations that serve as funding organizations for Mr. Mann's various charities, including the Alfred Mann Foundation, or AMF, and the Alfred Mann Institute at the University of Southern California, the Technion-Israel Institute of Technology, and at Purdue University, and that may serve as funding organizations for any other charities that he may establish. The AEMMRO is a membership foundation consisting of six members, including Mr. Mann, his wife, three of his children and Dr. Joseph Schulman, the chief scientist of the AEMFBE. The AEMFBE is a membership foundation consisting of five members, including Mr. Mann, his wife, and the same three of his children. Although we understand that the members of AEMMRO and AEMFBE have been advised of Mr. Mann's objectives for these foundations, once Mr. Mann's shares of our capital stock become the property of the foundations, we cannot assure you as to how those shares will be distributed or how they will be voted.

***The future sale of our common stock or the conversion of our senior convertible notes into common stock could negatively affect our stock price.***

Substantially all of the outstanding shares of our common stock are available for public sale, subject in some cases to volume and other limitations or delivery of a prospectus. If our common stockholders sell substantial amounts of common stock in the public market, or the market perceives that such sales may occur, the market price of our common stock may decline. Likewise the issuance of additional shares of our common stock upon the conversion of some or all of our senior convertible notes could adversely affect the trading price of our common stock. In addition, the existence of these notes may encourage short selling of our common stock by market participants. Furthermore, if we were to include in a company-initiated registration statement shares held by our stockholders pursuant to the exercise of their registrations rights, the sale of those shares could impair our ability to raise needed capital by depressing the price at which we could sell our common stock.

In addition, we will need to raise substantial additional capital in the future to fund our operations. If we raise additional funds by issuing equity securities or additional convertible debt, the market price of our common stock may decline and our existing stockholders may experience significant dilution.

***Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.***

We are incorporated in Delaware. Certain anti-takeover provisions under Delaware law and in our certificate of incorporation and amended and restated bylaws, as currently in effect, may make a change of control of our company more difficult, even if a change in control would be beneficial to our stockholders. Our anti-takeover provisions include provisions such as a prohibition on stockholder actions by written consent, the authority of our board of directors to issue preferred stock without stockholder approval, and supermajority voting requirements for specified actions. In addition, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which generally prohibits stockholders owning 15% or more of our outstanding voting stock

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from merging or combining with us in certain circumstances. These provisions may delay or prevent an acquisition of us, even if the acquisition may be considered beneficial by some of our stockholders. In addition, they may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for appointing the members of our management.

***Because we do not expect to pay dividends in the foreseeable future, you must rely on stock appreciation for any return on your investment.***

We have paid no cash dividends on any of our capital stock to date, and we currently intend to retain our future earnings, if any, to fund the development and growth of our business. As a result, we do not expect to pay any cash dividends in the foreseeable future, and payment of cash dividends, if any, will also depend on our financial condition, results of operations, capital requirements and other factors and will be at the discretion of our board of directors. Furthermore, we may in the future become subject to contractual restrictions on, or prohibitions against, the payment of dividends. Accordingly, the success of your investment in our common stock will likely depend entirely upon any future appreciation. There is no guarantee that our common stock will appreciate in value after the offering or even maintain the price at which you purchased your shares, and you may not realize a return on your investment in our common stock.

### **Item 1B. *Unresolved Staff Comments.***

Not applicable.

### **Item 2. *Properties***

In 2001, we acquired a facility in Danbury, Connecticut that included two buildings comprising approximately 190,000 square feet encompassing 17.5 acres. In 2007, we commenced construction of approximately 140,000 square feet of new manufacturing space. When the expansion is completed in 2008, our facility will have two buildings with a total of approximately 328,000 square feet, housing our research and development, administrative and manufacturing functions, primarily for Technosphere Insulin formulation, filling and packaging. We believe the Danbury facility will have sufficient space to satisfy potential commercial demand for the launch of our Technosphere Insulin System and, with the expansion completed, the first few years thereafter for our Technosphere Insulin System and other Technosphere-related products.

We own and occupy approximately 147,000 square feet of laboratory, office and manufacturing space in Valencia, California. The facility contains our principal executive offices and houses our research and development laboratories for our cancer and other programs. We also use this facility to provide support for the development of our Technosphere programs.

We lease approximately 59,000 square feet of office space in Paramus, New Jersey pursuant to a lease that ends in May 2010, with an option to extend the lease through May 2012.

### **Item 3. *Legal Proceedings***

None.

### **Item 4. *Submission of Matters to a Vote of Security Holders***

No matters were submitted to a vote of our security holders during the quarter ended December 31, 2007.



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Our common stock has been traded on the Nasdaq Global Market (and its predecessor the Nasdaq National Market) under the symbol MNKD since July 28, 2004. The following table sets forth for the quarterly periods indicated, the high and low sales prices for our common stock as reported by the Nasdaq Global Market.

	<b>High</b>	<b>Low</b>
Year ended December 31, 2006		
First quarter	\$ 22.00	\$ 11.05
Second quarter	\$ 21.74	\$ 16.42
Third quarter	\$ 21.48	\$ 15.50
Fourth quarter	\$ 21.68	\$ 15.73
Year ended December 31, 2007		
First quarter	\$ 17.24	\$ 14.30
Second quarter	\$ 15.47	\$ 10.47
Third quarter	\$ 13.57	\$ 8.21
Fourth quarter	\$ 11.93	\$ 7.58

The closing sales price of our common stock on the Nasdaq Global Market was \$4.99 on March 10, 2008 and there were 192 registered holders of record as of that date.

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**Performance Measurement Comparison**

*The material in this section is not soliciting material, is not deemed filed with the SEC and shall not be incorporated by reference by any general statement incorporating by reference this Annual Report on Form 10-K into any of our filings under the Securities Act of 1933, as amended, or the Securities Act, or the Exchange Act of 1934, as amended, or the Exchange Act, except to the extent we specifically incorporate this section by reference.*

**Performance Measurement Comparison**

The following graph illustrates a comparison of the cumulative total stockholder return (change in stock price plus reinvested dividends) of our common stock with (i) the Nasdaq Composite Index and (ii) the Nasdaq Biotechnology Index. The comparisons in the graph are required by the SEC and are not intended to forecast or be indicative of possible future performance of our common stock.

Assumes a \$100 investment, on July 28, 2004, in (i) our common stock, (ii) the securities comprising the Nasdaq Composite Index and (iii) the securities comprising the Nasdaq Biotechnology Index.

**Dividend Policy**

We have never declared or paid any cash dividends on our common stock. We currently intend to retain all available funds and any future earnings for use in the operation and expansion of our business. Accordingly, we do not anticipate paying any cash dividends on our common stock in the foreseeable future. Any future determination to pay dividends will be at the discretion of our board of directors.

**Recent Sales of Unregistered Securities**

Not applicable.



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None.

**Item 6. Selected Financial Data**

The following selected consolidated financial data should be read in conjunction with our consolidated financial statements and notes thereto and with Management's Discussion and Analysis of Financial Condition and Results of Operations, which are included elsewhere in this Annual Report on Form 10-K.

Statement of Operations Data:	Year Ended December 31,				
	2003	2004	2005	2006	2007
	(In thousands, except per share amounts)				
Revenue	\$	\$	\$	\$ 100	\$ 10
Operating expenses:					
Research and development	45,613	59,406	95,347	191,796	256,844
General and administrative	20,699	17,743	22,775	42,001	50,523
Total operating expenses	66,312	77,149	118,122	233,797	307,367
Loss from operations	(66,312)	(77,149)	(118,122)	(233,697)	(307,357)
Other income (expense)	36	226	78	208	(197)
Interest expense on note payable to principal stockholder				(1,511)	
Interest expense on senior convertible notes				(222)	(3,408)
Interest income	398	932	3,707	4,679	17,775
Loss before provision for income taxes	(65,878)	(75,991)	(114,337)	(230,543)	(293,187)
Income tax	(1)	(1)	(1)	(5)	(3)
Net loss	(65,879)	(75,992)	(114,338)	(230,548)	(293,190)
Deemed dividends related to beneficial conversion feature of convertible preferred stock	(1,017)	(19,822)			
Accretion on redeemable preferred stock	(253)	(60)			
Net loss applicable to common stockholders	\$ (67,149)	\$ (95,874)	\$ (114,338)	\$ (230,548)	\$ (293,190)
Basic and diluted net loss per share	\$ (3.63)	\$ (3.80)	\$ (2.87)	\$ (4.52)	\$ (3.66)
Shares used to compute basic and diluted net loss per share	18,488	25,221	39,871	50,970	80,038



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<b>Balance Sheet Data:</b>	<b>As of December 31,</b>				
	<b>2003</b>	<b>2004</b>	<b>2005</b>	<b>2006</b>	<b>2007</b>
	<b>(In thousands)</b>				
Cash, cash equivalents and marketable securities	\$ 55,945	\$ 90,533	\$ 145,634	\$ 436,479	\$ 368,285
Working capital	49,097	82,837	128,507	404,588	311,154
Total assets	125,876	163,483	228,371	539,737	543,443
Deferred compensation and other liabilities	404	76	29	24	24
Senior convertible notes				111,267	111,761
Redeemable convertible preferred stock	5,188				
Deficit accumulated during the development stage	(366,971)	(442,963)	(557,301)	(787,849)	(1,081,039)
Total stockholders' equity	111,577	150,363	206,977	383,487	364,100

**Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations**

The following discussion of our financial condition and results of operations should be read in conjunction with our consolidated financial statements and notes thereto included in this Annual Report on Form 10-K.

**OVERVIEW**

We are a biopharmaceutical company focused on the discovery, development and commercialization of therapeutic products for diseases such as diabetes and cancer. Our lead investigational product candidate, the Technosphere Insulin System, is currently in Phase 3 clinical trials in the United States, Europe and Latin America to study its safety and efficacy in the treatment of diabetes. This dry powder therapy consists of our proprietary Technosphere particles onto which insulin molecules are loaded. These loaded particles are then aerosolized and inhaled into the deep lung using our proprietary MedTone inhaler. We believe that the performance characteristics, unique kinetics, convenience and ease of use of the Technosphere Insulin System may have the potential to change the way diabetes is treated. Currently, we are conducting clinical trials to evaluate the safety and efficacy of another Technosphere-based product for the treatment of diabetes and are developing additional formulations of active compounds loaded onto Technosphere particles. We are also developing therapies for the treatment of different types of cancer. Our other product candidates are at the research stage or in pre-clinical development.

We are a development stage enterprise and have incurred significant losses since our inception in 1991. As of December 31, 2007, we have incurred a cumulative net loss of \$1.1 billion. To date, we have not generated any product revenues and have funded our operations primarily through the sale of equity securities.

We do not expect to record sales of any product prior to regulatory approval and commercialization of our Technosphere Insulin System. We currently do not have the required approvals to market any of our product candidates, and we may not receive such approvals. We may not be profitable even if we succeed in commercializing any of our product candidates. We expect to make substantial and increasing expenditures and to incur additional operating losses for at least the next several years as we:

continue the clinical development of our Technosphere Insulin System for the treatment of diabetes;

expand our manufacturing operations for our Technosphere Insulin System to meet our currently anticipated commercial production needs;

expand our other research, discovery and development programs;

expand our proprietary Technosphere platform technology and develop additional applications for the pulmonary delivery of other drugs; and

enter into sales and marketing collaborations with other companies, if available on commercially reasonable terms, or develop these capabilities ourselves.

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Our business is subject to significant risks, including but not limited to the risks inherent in our ongoing clinical trials and the regulatory approval process, the results of our research and development efforts, competition from other products and technologies and uncertainties associated with obtaining and enforcing patent rights.

### **RESEARCH AND DEVELOPMENT EXPENSES**

Our research and development expenses consist mainly of costs associated with the clinical trials of our product candidates that have not yet received regulatory approval for marketing and for which no alternative future use has been identified. This includes the salaries, benefits and stock-based compensation of research and development personnel, laboratory supplies and materials, facility costs, costs for consultants and related contract research, licensing fees, and depreciation of laboratory equipment. We track research and development costs by the type of cost incurred. We partially offset research and development expenses with the recognition of estimated amounts receivable from the State of Connecticut pursuant to a program under which we can exchange qualified research and development income tax credits for cash.

Our research and development staff conducts our internal research and development activities, which include research, product development, clinical development, manufacturing and related activities. This staff is located in our facilities in Valencia, California; Paramus, New Jersey; and Danbury, Connecticut. We expense the majority of research and development costs as we incur them.

Clinical development timelines, likelihood of success and total costs vary widely. We are focused primarily on advancing the Technosphere Insulin System through Phase 3 clinical trials and regulatory filings. Based on the results of preclinical studies, we plan to develop additional applications of our Technosphere technology. Additionally, we anticipate that we will continue to determine which research and development projects to pursue, and how much funding to direct to each project, on an ongoing basis, in response to the scientific and clinical success of each product candidate. We cannot be certain when any revenues from the commercialization of our products will commence.

At this time, due to the risks inherent in the clinical trial process and given the early stage of development of our product candidates other than the Technosphere Insulin System, we are unable to estimate with any certainty the costs that we will incur in the continued development of our product candidates for commercialization. The costs required to complete the development of our Technosphere Insulin System will be largely dependent on the scope of our clinical trials, the cost and efficiency of our manufacturing process and discussions with the FDA on its requirements.

### **GENERAL AND ADMINISTRATIVE EXPENSES**

Our general and administrative expenses consist primarily of salaries, benefits and stock-based compensation for administrative, finance, business development, human resources, legal and information systems support personnel. In addition, general and administrative expenses include professional service fees and business insurance costs.

### **CRITICAL ACCOUNTING POLICIES**

We have based our discussion and analysis of our financial condition and results of operations on our financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities and expenses. We evaluate our estimates and judgments on an ongoing basis. We base our estimates on historical experience and on various assumptions that we believe to be reasonable under the circumstances, the results of which form the basis for making estimates of expenses such as stock option expenses and judgments about the carrying values of assets and liabilities. Actual results may differ from these estimates under

different assumptions or conditions. The significant accounting policies that are critical to the judgments and estimates used in the preparation of our financial statements are described in more detail below.

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### **Impairment of long-lived assets**

Assessing long-lived assets for impairment requires us to make assumptions and judgments regarding the carrying value of these assets. We evaluate long-lived assets for impairment whenever events or changes in circumstances indicate that the carrying value of an asset may not be recoverable. The assets are considered to be impaired if we determine that the carrying value may not be recoverable based upon our assessment of the following events or changes in circumstances:

- significant changes in our strategic business objectives and utilization of the assets;
- a determination that the carrying value of such assets cannot be recovered through undiscounted cash flows;
- loss of legal ownership or title to the assets; or
- the impact of significant negative industry or economic trends.

If we believe our assets to be impaired, the impairment we recognize is the amount by which the carrying value of the assets exceeds the fair value of the assets. Any write-downs would be treated as permanent reductions in the carrying amount of the asset and an operating loss would be recognized. In addition, we base the useful lives and related amortization or depreciation expense on our estimate of the useful lives of the assets. If a change were to occur in any of the above-mentioned factors or estimates, our reported results could materially change.

To date, we have had recurring operating losses, and the recoverability of our long-lived assets is contingent upon executing our business plan. If we are unable to execute our business plan, we may be required to write down the value of our long-lived assets in future periods.

### **Clinical trial expenses**

Our clinical trial accrual process seeks to account for expenses resulting from our obligations under contract with vendors, consultants, and clinical site agreements in connection with conducting clinical trials. The financial terms of these contracts are subject to negotiations which vary from contract to contract and may result in payment flows that do not match the periods over which materials or services are provided to us under such contracts. Our objective is to reflect the appropriate trial expenses in our financial statements by matching period expenses with period services and efforts expended. We account for these expenses according to the progress of the trial as measured by patient progression and the timing of various aspects of the trial. We determine accrual estimates through discussions with internal clinical personnel and outside service providers as to the progress or state of completion of trials, or the services completed. Service provider status is then compared to the contractual obligated fee to be paid for such services. During the course of a clinical trial, we adjust our rate of clinical expense recognition if actual results differ from our estimates. In the event that we do not identify certain costs that have begun to be incurred or we underestimate or overestimate the level of services performed or the costs of such services, our reported expenses for a period would be too low or too high. The date on which certain services commence, the level of services performed on or before a given date and the cost of the services are often judgmental. We make these judgments based upon the facts and circumstances known to us in accordance with generally accepted accounting principles.

### **Stock-based compensation**

On January 1, 2006, the Company adopted the provisions of SFAS No. 123R, which is a revision of SFAS No. 123, *Accounting for Stock-Based Compensation* ( SFAS No. 123 ). Prior to January 1, 2006, the Company accounted for employee stock options and the employee stock purchase plan using the intrinsic value method in accordance with

Accounting Principles Board ( APB ) Opinion No. 25 ( APB No. 25 ), *Accounting for Stock Issued to Employees*, and adopted the disclosure only alternative of SFAS No. 123. SFAS No. 123R eliminated the intrinsic value method of accounting for stock options which the Company followed until December 31, 2005. Further, SFAS No. 123R requires all share-based payments to employees, including grants of stock options and the compensatory elements of employee stock purchase plans, to be recognized in the income statement based upon the fair value of the awards at the grant date.



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Upon adoption of SFAS No. 123R, the Company selected the modified prospective transition method whereby unvested awards at the date of adoption, as well as awards that are granted, modified or settled after the date of adoption, will be measured and accounted for in accordance with SFAS No. 123R. Measurement and attribution of compensation cost for awards unvested as of January 1, 2006 is based on the same estimate of the grant-date or modification-date fair value and the same attribution method (straight-line) used previously under SFAS No. 123. Our consolidated financial statements as of and for the years ended December 31, 2007 and 2006 reflect the impact of SFAS No. 123R. In accordance with the modified prospective transition method, our consolidated financial statements for prior periods have not been restated to reflect, and do not include, the impact of SFAS 123R.

### **Accounting for income taxes**

We must make significant management judgments when determining our provision for income taxes, our deferred tax assets and liabilities and any valuation allowance recorded against our net deferred tax assets. At December 31, 2007, we have established a valuation allowance of \$387.5 million against all of our net deferred tax asset balance, due to uncertainties related to our deferred tax assets as a result of our history of operating losses. The valuation allowance is based on our estimates of taxable income by jurisdiction in which we operate and the period over which our deferred tax assets will be recoverable. In the event that actual results differ from these estimates or we adjust these estimates in future periods, we may need to change the valuation allowance, which could materially impact our financial position and results of operations.

In July 2006, the FASB issued FASB Interpretation No. 48, *Accounting for Uncertainty in Income Taxes – an interpretation of FASB Statement No. 109* ( FIN 48 ), which clarifies the accounting and disclosure for uncertainty in tax positions, as defined. FIN 48 seeks to reduce the diversity in practice associated with certain aspects of the recognition and measurement related to accounting for income taxes. We are subject to the provisions of FIN 48 as of January 1, 2007. We believe that our income tax filing positions and deductions will be sustained on audit and do not anticipate any adjustments that will result in a material change to our financial position. Therefore, no reserves for uncertain income tax positions have been recorded pursuant to FIN 48. The cumulative effect, if any, of applying FIN 48 is to be reported as an adjustment to the opening balance of retained earnings in the year of adoption. Our adoption of FIN 48 did not result in a cumulative effect adjustment to retained earnings. Tax years since 1992 remain subject to examination by the major tax jurisdictions in which we are subject to tax.

## **RESULTS OF OPERATIONS**

### **Years ended December 31, 2007 and 2006**

#### **Revenues**

During the years ended December 31, 2007 and 2006, the Company recognized \$10,000 and \$100,000, respectively, in revenue under a license agreement. We do not anticipate sales of any product prior to regulatory approval and commercialization of our Technosphere Insulin System.

#### **Research and Development Expenses**

The following table provides a comparison of the research and development expense categories for the years ended December 31, 2007 and 2006 (dollars in thousands):

**Year Ended  
December 31,**

	<b>2007</b>	<b>2006</b>	<b>\$ Change</b>	<b>% Change</b>
Clinical	\$ 124,655	\$ 110,623	\$ 14,032	13%
Manufacturing	86,473	40,656	45,817	113%
Research	36,720	33,962	2,758	8%
Research and development tax credit	(753)	(585)	(168)	29%
Stock-based compensation expense	9,749	7,140	2,609	37%
Research and development expenses	\$ 256,844	\$ 191,796	\$ 65,048	34%

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The increase in research and development expenses for the year ended December 31, 2007, as compared to the year ended December 31, 2006, was primarily due to increases in manufacturing costs, including clinical supplies, for Technosphere Insulin and increased costs associated with the expanded clinical development of our Technosphere Insulin System and the continuation of other preclinical studies. We anticipate that our research and development expenses will increase slightly in 2008 as we complete our pivotal Technosphere Insulin trials, continue preparation for commercial scale manufacturing of Technosphere Insulin, expand our Technosphere platform technology, and continue to pursue cancer therapies. Specifically, we anticipate increased expenses related to the expansion, qualification and validation of our commercial manufacturing processes and facilities.

The research and development tax credit recognized for the years ended December 31, 2007 and 2006 partially offsets our research and development expenses. The State of Connecticut provides an opportunity to exchange certain research and development income tax credit carryforwards for cash in exchange for forgoing the carryforward of the research and development credits. Estimated amounts receivable under the program are recorded as a reduction of research and development expenses. During the years ended December 31, 2007 and 2006, research and development expenses were offset by \$0.8 million and \$0.6 million, respectively, in connection with the program.

**General and Administrative Expenses**

The following table provides a comparison of the general and administrative expense categories for the years ended December 31, 2007 and 2006 (dollars in thousands):

	<b>Year Ended December 31,</b>			<b>% Change</b>
	<b>2007</b>	<b>2006</b>	<b>\$ Change</b>	
Salaries, employee related and other general expenses	\$ 42,627	\$ 34,474	\$ 8,153	24%
Stock-based compensation expense	7,896	7,527	369	5%
General and administrative expenses	\$ 50,523	\$ 42,001	\$ 8,522	20%

The increase in general and administrative expenses for the year ended December 31, 2007, as compared to the year ended December 31, 2006, was primarily due to increased headcount and professional service fees. We expect general and administrative expenses to increase slightly in 2008 as a result of increased salary related expenses and professional service fees.

**Interest Income and Expense**

Interest income for the year ended December 31, 2007 increased \$13.1 million as compared to the year ended December 31, 2006 primarily due to higher cash balances resulting from the sale by the Company of common stock and convertible notes in December 2006. Interest expense for the year ended December 31, 2007 was related to the convertible notes issued in December 2006 and amortization of the debt issuance costs, partially offset by capitalized interest related to construction in progress. Interest expense for the year ended December 31, 2006 was related to amounts borrowed under the loan arrangement with our principal stockholder in August 2006.

**Years ended December 31, 2006 and 2005****Revenues**

During the year ended December 31, 2006, the Company recognized \$100,000 in revenue under a license agreement. No revenues were recorded for the year ended December 31, 2005.

**Table of Contents****Research and Development Expenses**

The following table provides a comparison of the research and development expense categories for the years ended December 31, 2006 and 2005 (dollars in thousands):

	<b>Year Ended December 31,</b>			<b>% Change</b>
	<b>2006</b>	<b>2005</b>	<b>\$ Change</b>	
Clinical	\$ 110,623	\$ 49,483	\$ 61,140	124%
Manufacturing	40,656	25,401	15,255	60%
Research	33,962	22,449	11,513	51%
Research and development tax credit	(585)	(1,666)	1,081	(65)%
Stock-based compensation expense (benefit)	7,140	(320)	7,460	
Research and development expenses	\$ 191,796	\$ 95,347	\$ 96,449	101%

The increase in research and development expenses for the year ended December 31, 2006, as compared to the year ended December 31, 2005, was primarily due to increased costs associated with the expanded clinical development of our Technosphere Insulin System and the continuation of other preclinical studies; increased salaries and related expenses driven by higher headcount; increases in consulting services and technology agreements; and increases in stock-based compensation expense. The increase in stock-based compensation expense was due to the adoption of SFAS 123R on January 1, 2006 and the stock-based compensation benefit in 2005 resulting from the fluctuation of our stock price on the stock options that were repriced in November 2003.

The research and development tax credit recognized for the years ended December 31, 2006 and 2005 partially offsets our research and development expenses. The State of Connecticut provides an opportunity to exchange certain research and development income tax credit carryforwards for cash in exchange for forgoing the carryforward of the research and development credits. Estimated amounts receivable under the program are recorded as a reduction of research and development expenses. During the years ended December 31, 2006 and 2005, research and development expenses were offset by \$0.6 million and \$1.7 million, respectively, in connection with the program.

**General and administrative expenses**

The following table provides a comparison of the general and administrative expense categories for the years ended December 31, 2006 and 2005 (dollars in thousands):

	<b>Year Ended December 31,</b>			<b>% Change</b>
	<b>2006</b>	<b>2005</b>	<b>\$ Change</b>	
Salaries, employee related and other general expenses	\$ 34,474	\$ 24,183	\$ 10,291	43%
Stock-based compensation expense (benefit)	7,527	(1,408)	8,935	
General and administrative expenses	\$ 42,001	\$ 22,775	\$ 19,226	84%

General and administrative expenses for the year ended December 31, 2006 increased as compared to the year ended December 31, 2005. Salaries, employee related and other general expenses increased primarily due to increased headcount and administrative services. The increase in stock-based compensation expense was due to the adoption of SFAS 123R on January 1, 2006 as compared to the stock-based compensation benefit in 2005 that resulted from the fluctuation of our stock price on stock options that were repriced in November 2003.

## **LIQUIDITY AND CAPITAL RESOURCES**

We have funded our operations primarily through the sale of equity securities. In October 2007, we issued and sold a total of 27,014,686 shares of our common stock. Of this total, 15,940,489 shares were sold to our principal stockholder at a price per share of \$9.41 and 11,074,197 shares were sold to other investors at a price per share of \$9.03. The resulting aggregate net proceeds were approximately \$249.8 million after expenses. In December 2006,

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we issued and sold 23,000,000 shares of our common stock at a price of \$17.42 per share in an underwritten public offering. The resulting aggregate net proceeds to us from this common stock offering were approximately \$384.7 million after expenses. In December 2006, we also sold \$115.0 million aggregate principal amount of 3.75% Senior Convertible Notes due 2013. The resulting aggregate net proceeds to us from this note offering were approximately \$111.3 million after expenses.

In August 2006, we entered into a \$150.0 million loan arrangement with our principal stockholder, which was amended on August 1, 2007 and replaced with a new loan arrangement on October 2, 2007. Under the new loan arrangement, we can borrow up to a total of \$350.0 million before January 1, 2010. From April 1, 2008 until September 30, 2008, we can borrow up to \$150.0 million in one or more advances, and from March 1, 2009 until December 31, 2009, we can borrow the remaining \$200.0 million plus any amount not previously borrowed in one or more advances. We may not borrow more than one advance in any 12-month period, and each advance must be not less than \$50.0 million. Interest will accrue on each outstanding advance at a fixed rate equal to the one-year LIBOR rate as reported by the *Wall Street Journal* on the date of such advance plus 3% per annum and will be payable quarterly in arrears. Principal repayment is due on December 31, 2011. At any time after January 1, 2010, our principal stockholder can require us to prepay up to \$200.0 million in advances that have been outstanding for at least 12 months. If our principal stockholder exercises this right, we will have until the earlier of 180 days after our principal stockholder provides written notice or December 31, 2011 to prepay such advances. In the event of a default, all unpaid principal and interest either becomes immediately due and payable or may be accelerated at our principal stockholder's option, and the interest rate will increase to the one-year LIBOR rate calculated on the date of the initial advance or in effect on the date of default, whichever is greater, plus 5% per annum. Any borrowings under the loan arrangement will be unsecured. The loan arrangement contains no financial covenants. There are no warrants associated with the loan arrangement, nor are advances convertible into our common stock.

During the year ended December 31, 2007, we used \$245.1 million of cash for our operations compared to using \$189.8 million for our operations in the year ended December 31, 2006. We had a net loss of \$293.2 million for the year ended December 31, 2007, of which \$27.6 million consisted of non-cash charges such as depreciation and amortization, stock-based compensation, and other stock-based charges pursuant to a research agreement. We expect our negative operating cash flow to continue at least until we obtain regulatory approval and achieve commercialization of our Technosphere Insulin System.

We generated \$38.7 million of cash for investing activities during the year ended December 31, 2007, compared to using \$48.3 million for the year ended December 31, 2006. Cash provided by investing activities was primarily from net sales of marketable securities of \$116.9 million partially offset by \$78.3 million in machinery and equipment purchases used to expand our manufacturing operations and quality systems in support of our expansion of clinical trials for Technosphere Insulin System. We expect to make significant purchases of equipment in the foreseeable future.

Our financing activities provided cash of \$255.2 million for the year ended December 31, 2007 compared to \$501.6 million for 2006. Cash from financing activities in 2007 was primarily from the equity offering in October 2007 and the exercise of stock options throughout the year. For 2006, cash from financing activities was primarily from the equity and convertible note offerings in December 2006, as well as the exercise of stock options.

As of December 31, 2007, we had \$368.3 million in cash and cash equivalents. Although we believe our existing cash resources, including the expanded \$350.0 million loan arrangement with our principal stockholder, will be sufficient to fund our anticipated cash requirements through the fourth quarter of 2009, we will require significant additional financing in the future to fund our operations. Accordingly, we expect that we will need to raise additional capital, either through the sale of equity and/or debt securities, a strategic business collaboration with a pharmaceutical or biotechnology company or the establishment of other funding facilities, in order to continue the development and

commercialization of our Technosphere Insulin System and other product candidates and to support our other ongoing activities.

We intend to use our capital resources to continue the development of our Technosphere Insulin System and to develop additional applications for our proprietary Technosphere platform technology. In addition, portions of our capital resources will be devoted to expanding our other product development programs for the treatment of different types of cancers. We are expending a portion of our capital to scale up our manufacturing capabilities in



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our Danbury facilities. We also intend to use our capital resources for general corporate purposes, which may include in-licensing or acquiring additional technologies.

We have held extensive discussions with a number of pharmaceutical companies concerning a potential strategic business collaboration for our Technosphere Insulin System. To date, we have not reached agreement with any of these companies on a collaboration. While we are continuing to engage in such discussions, we believe that we will have to expend significant additional time and effort before we could reach agreement, and we cannot predict when, if ever, we could conclude such an agreement with a partner. There can be no assurance that any such collaboration will be available to us on a timely basis or on acceptable terms, if at all.

If we enter into a strategic business collaboration with a pharmaceutical or biotechnology company, we would expect, as part of the transaction, to receive additional capital. In addition, we expect to pursue the sale of equity and/or debt securities, or the establishment of other funding facilities. Issuances of debt or additional equity could impact the rights of our existing stockholders, dilute the ownership percentages of our existing stockholders and may impose restrictions on our operations. These restrictions could include limitations on additional borrowing, specific restrictions on the use of our assets as well as prohibitions on our ability to create liens, pay dividends, redeem our stock or make investments. We also may seek to raise additional capital by pursuing opportunities for the licensing, sale or divestiture of certain intellectual property and other assets, including our Technosphere technology platform. There can be no assurance, however, that any strategic collaboration, sale of securities or sale or license of assets will be available to us on a timely basis or on acceptable terms, if at all. If we are unable to raise additional capital, we may be required to enter into agreements with third parties to develop or commercialize products or technologies that we otherwise would have sought to develop independently, and any such agreements may not be on terms as commercially favorable to us.

However, we cannot provide assurances that our plans will not change or that changed circumstances will not result in the depletion of our capital resources more rapidly than we currently anticipate. If planned operating results are not achieved or we are not successful in raising additional equity financing or entering a business collaboration, we may be required to reduce expenses through the delay, reduction or curtailment of our projects, including our Technosphere Insulin System development activities, or further reduction of costs for facilities and administration.

**Off-Balance Sheet Arrangements**

As of December 31, 2007, we did not have any off-balance sheet arrangements.

**COMMITMENTS AND CONTINGENCIES**

Our contractual obligations represent future cash commitments and liabilities under agreements with third parties, and exclude contingent liabilities for which we cannot reasonably predict future payments. Accordingly, the table below excludes contractual obligations relating to milestone and royalty payments due to third parties, all of which are contingent upon certain future events. The expected timing of payment of the obligations presented below is estimated based on current information. Future payments relate to operating lease obligations (including facility leases executed in March 2005 and November 2005), the senior convertible notes, and open purchase order and supply commitments consisted of the following at December 31, 2007 (in thousands):

Contractual Obligations	Less Than One Year	Payments Due in			Total
		1-3 Years	3-5 Years	More Than 5 Years	

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Open purchase order and supply commitments(1)	\$ 191,276	\$ 36,951	\$ 84,980	\$	\$ 313,207
Senior Convertible Note Obligations(2)	4,384	8,745	8,757	119,372	141,258
Operating lease obligations	1,693	2,651			4,344
Total contractual obligations	\$ 197,353	\$ 48,347	\$ 93,737	\$ 119,372	\$ 458,809

(1) The amounts included in open purchase order and supply commitments are subject to performance under the purchase order or contract by the supplier of the goods or services and do not become our obligation until such

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performance is rendered. The amount shown is principally for the purchase of materials for our clinical trials, the acquisition of manufacturing equipment, and commitments related to the expansion of our manufacturing plant and the purchase of raw materials under long-term supply agreements.

- (2) The senior convertible note obligation amounts include future interest payments at a fixed rate of 3.75% and payment of the notes in full upon maturity in 2013.

## **RELATED PARTY TRANSACTIONS**

For a description of our related party transactions see Note 16 Related Party Transactions in the notes to our financial statements.

## **RECENT ACCOUNTING PRONOUNCEMENTS**

In December 2007, the FASB ratified the EITF consensus on EITF Issue No. 07-1, *Accounting for Collaborative Arrangements*, that discusses how parties to a collaborative arrangement (which does not establish a legal entity within such arrangement) should account for various activities. The consensus indicates that costs incurred and revenues generated from transactions with third parties (i.e. parties outside of the collaborative arrangement) should be reported by the collaborators on the respective line items in their income statements pursuant to EITF Issue No. 99-19, *Reporting Revenue Gross as a Principal Versus Net as an Agent*. Additionally, the consensus provides that income statement characterization of payments between the participants in a collaborative arrangement should be based upon existing authoritative pronouncements; analogy to such pronouncements if not within their scope; or a reasonable, rational, and consistently applied accounting policy election. EITF Issue No. 07-1 is effective beginning January 1, 2009 and is to be applied retrospectively to all periods presented for collaborative arrangements existing as of the date of adoption. We are evaluating the impact, if any, the adoption of this consensus will have on our results of operations, financial position or cash flows.

In December 2007, the FASB issued SFAS No. 141(R), *Business Combinations* and SFAS No. 160, *Accounting and Reporting of Noncontrolling Interests to Consolidated Financial Statements – an amendment of ARB No. 51* ( SFAS No. 160 ). These standards will significantly change the accounting and reporting for business combination transactions and noncontrolling (minority) interests in consolidated financial statements, including capitalizing at the acquisition date the fair value of acquired IPR&D, and remeasuring and writing down the assets, if necessary, in subsequent periods during their development. These new standards will be applied prospectively for business combinations that occur on or after January 1, 2009, except that presentation and disclosure requirements of SFAS No. 160 regarding noncontrolling interests shall be applied retrospectively.

In September 2007, the FASB ratified EITF 07-3, *Accounting for Advance Payments for Goods or Services to Be Used in Future Research and Development Activities*. EITF 07-3 requires that nonrefundable advance payments for future research and development activities be deferred and capitalized. EITF 07-3 is effective as of the beginning of an entity's first fiscal year that begins after December 15, 2007. We are evaluating the impact, if any, the adoption of EITF 07-3 will have on our results of operations, financial position or cash flows.

In February 2007, the FASB issued SFAS No. 159, *The Fair Value Option for Financial Assets and Financial Liabilities*, which permits entities to choose to measure many financial instruments and certain other items at fair value. SFAS No. 159 also includes an amendment to SFAS No. 115, *Accounting for Certain Investments in Debt and Equity Securities* which applies to all entities with available-for-sale and trading securities. This Statement is effective as of the beginning of an entity's first fiscal year that begins after November 15, 2007. We are evaluating the impact, if any, the adoption of this Statement will have on our results of operations, financial position or cash flows.

In September 2006, the FASB issued SFAS No. 157, *Fair Value Measurements*, which defines fair value, establishes a framework for consistently measuring fair value for accounting purposes, and expands disclosures about fair value measurements. SFAS No. 157 is effective for us beginning January 1, 2008, and the provisions of SFAS No. 157 will be applied prospectively as of that date. In February 2008, FASB Staff Position ( FSP ) No. 157-2 was issued. FSP No. 157-2 delays the implementation of certain aspects of SFAS No. 157 to January 1, 2009. We are evaluating the impact, if any, the adoption of this Statement will have on our results of operations, financial position or cash flows.

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### **Item 7A. *Quantitative and Qualitative Disclosures About Market Risk***

We have not used derivative financial instruments in the past to hedge market risk. We are exposed to market risk related to changes in interest rates impacting our cash investment portfolio as well as the interest rate on our credit facility. The interest rate on our credit facility is a fixed rate equal to the one-year LIBOR rate as reported by the *Wall Street Journal* on the date of such advance plus 3% per annum. Our current policy requires us to maintain a highly liquid short-term investment portfolio consisting mainly of U.S. money market funds and investment-grade corporate, government and municipal debt. None of these investments is entered into for trading purposes. Our cash is deposited in and invested through highly rated financial institutions in North America. We do not have any short-term investments at December 31, 2007. If we were to draw the available amount on our \$350 million credit facility and interest rates were to increase from levels at December 31, 2007 we could experience a higher level of interest expense than assumed in our current operating plan.

### **Item 8. *Financial Statements and Supplementary Data***

The information required by this Item is included in Items 15(a)(1) and (2) of Part IV of this Annual Report on Form 10-K.

### **Item 9. *Changes in and Disagreements with Accountants on Accounting and Financial Disclosure***

None.

### **Item 9A. *Controls and Procedures***

#### **Conclusion Regarding the Effectiveness of Disclosure Controls and Procedures**

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in our reports filed under the Exchange Act, is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms and that such information is accumulated and communicated to our management, including our chief executive officer and chief financial officer, as appropriate, to allow for timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives, and management is required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Our chief executive officer and chief financial officer performed an evaluation under the supervision and with the participation of our management, of our disclosure controls and procedures (as defined in Rule 13a-15(b) of the Exchange Act) as of December 31, 2007. Based on that evaluation, our chief executive officer and chief financial officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level.

#### **Management's Report on Internal Control Over Financial Reporting**

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Exchange Act Rule 13a-15(f). Under the supervision and with the participation of our management, including our chief executive officer and chief financial officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting based on the framework set forth in *Internal Control Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on our evaluation under the framework set forth in *Internal Control Integrated Framework*, our management concluded that our internal control over financial reporting was effective as of December 31, 2007. Deloitte & Touche LLP, the

independent registered public accounting firm that audited the financial statements included in this 2007 Form 10-K, has issued an attestation report on our internal control over financial reporting as of December 31, 2007, which is included herein.

**Remediation of Material Weakness**

As of June 30, 2007, our management concluded that we had a material weakness in the operation of controls for identifying and recording clinical trial costs, principally from the failure of our controls to detect an

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overstatement of clinical trial liabilities. The following is a summary of control deficiencies that contributed to the material weakness:

Certain balance sheet accounts relating primarily to accrued vendor invoices and clinical trial costs were not adequately analyzed or reconciled to supporting documentation.

Controls designed to ensure that these accounts and the supporting analysis were reviewed by knowledgeable personnel did not operate effectively.

Personnel responsible for the preparation of these accruals were not adequately trained.

During the latter part of 2007, we implemented a remediation plan to address the control deficiencies that contributed to this material weakness. As of December 31, 2007, we completed the execution of our remediation plan which included recruiting, hiring and training additional accounting staff with technical expertise for identifying and recording clinical trial costs. Additionally, we implemented revised policies and procedures and enhanced our review of the balance sheet accounts relating to clinical trial costs. We anticipate making additional improvements and changes in future periods, however, except as described herein, there were no other changes in our internal control over financial reporting during the fourth quarter of 2007, that materially affected, or are reasonably likely to materially effect, our internal control over financial reporting.

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**Report of Independent Registered Public Accounting Firm**

To the Board of Directors and Stockholders of MannKind Corporation  
Valencia, California

We have audited the internal control over financial reporting of MannKind Corporation and subsidiaries (the Company ) as of December 31, 2007, based on criteria established in *Internal Control – Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission. The Company’s management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying Management’s Report on Internal Control Over Financial Reporting. Our responsibility is to express an opinion on the Company’s internal control over financial reporting based on our audit.

We conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

A company’s internal control over financial reporting is a process designed by, or under the supervision of, the company’s principal executive and principal financial officers, or persons performing similar functions, and effected by the company’s board of directors, management, and other personnel to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company’s internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company’s assets that could have a material effect on the financial statements.

Because of the inherent limitations of internal control over financial reporting, including the possibility of collusion or improper management override of controls, material misstatements due to error or fraud may not be prevented or detected on a timely basis. Also, projections of any evaluation of the effectiveness of the internal control over financial reporting to future periods are subject to the risk that the controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

In our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2007, based on the criteria established in *Internal Control – Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission.

We have also audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the consolidated financial statements as of and for the year ended December 31, 2007 of the Company and our report dated March 14, 2008 expressed an unqualified opinion on those financial statements and included an



explanatory paragraph regarding a change in the manner in which the Company accounts for share-based compensation in 2006.

/s/ DELOITTE & TOUCHE LLP

Los Angeles, California  
March 14, 2008

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**Item 9B. *Other Information.***

None.

**PART III**

Certain information required by Part III is omitted from this Annual Report on Form 10-K because we will file our Proxy Statement within 120 days after the end of our fiscal year pursuant to Regulation 14A for our 2008 Annual Meeting of Stockholders, and the information included in the Proxy Statement is incorporated herein by reference.

**Item 10. *Directors and Executive Officers of the Registrant.***

(a) *Executive Officers* For information regarding the identification and business experience of our executive officers, see *Executive Officers* in Part I, Item 1 of this Annual Report on Form 10-K.

(b) *Directors* The information required by this Item regarding the identification and business experience of our directors and corporate governance matters is contained in the section entitled *Proposal 1 Election of Directors* and *Corporate Governance Principles and Board and Committee Matters* in the Proxy Statement, and is incorporated herein by reference.

Additional information required by this Item is incorporated by reference to the section entitled *Section 16(a) Beneficial Ownership Reporting Compliance* in the Proxy Statement.

We have adopted a Code of Business Conduct and Ethics Policy that applies to our directors and employees (including our principal executive officer, principal financial officer, principal accounting officer and controller), and have posted the text of the policy on our website ([www.mannkindcorp.com](http://www.mannkindcorp.com)) in connection with *Investor Relations* materials. In addition, we intend to promptly disclose on our website (i) the nature of any amendment to the policy that applies to our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions and (ii) the nature of any waiver, including an implicit waiver, from a provision of the policy that is granted to one of these specified individuals, the name of such person who is granted the waiver and the date of the waiver on our website in the future.

**Item 11. *Executive Compensation***

The information under the caption *Executive Compensation* in the Proxy Statement is incorporated herein by reference.

**Item 12. *Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters***

The information under the captions *Security Ownership of Certain Beneficial Owners and Management* and *Executive Compensation Securities Authorized for Issuance under Equity Compensation Plans* in the Proxy Statement is incorporated herein by this reference.

**Item 13. *Certain Relationships, Related Transactions and Director Independence***

The information under the caption *Certain Transactions* and *Corporate Governance Principles and Board and Committee Matters* in the Proxy Statement is incorporated herein by reference. With the exception of the information specifically incorporated by reference from the Proxy Statement in this Annual Report on Form 10-K, the Proxy Statement shall not be deemed to be filed as part of this report. Without limiting the foregoing, the information under

the captions Report of the Audit Committee of the Board of Directors and Report of the Compensation Committee of the Board of Directors in the Proxy Statement is not incorporated by reference.

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**Item 14. *Principal Accounting Fees and Services***

The information under the caption *Principal Accounting Fees and Services* in the Proxy Statement is incorporated herein by reference.

**PART IV**

**Item 15. *Exhibits and Financial Statement Schedules***

(a) The following documents are filed as part of, or incorporated by reference into, this Annual Report on Form 10-K:

(1)(2) Financial Statements and Financial Statement Schedules. The following Financial Statements of MannKind Corporation, Financial Statement Schedules and Report of Independent Registered Public Accounting Firm are included in a separate section of this report beginning on page F-2:

Report of Independent Registered Public Accounting Firm	71
Consolidated Balance Sheets	72
Statements of Operations	73
Statements of Stockholders' Equity (Deficit)	74
Statements of Cash Flows	78
Notes to Financial Statements	80

All financial statement schedules have been omitted because the required information is not applicable or not present in amounts sufficient to require submission of the schedule, or because the information required is included in the consolidated financial statements or the notes thereto.

(3) Exhibits. The exhibits listed under Item 15(c) hereof are filed with, or incorporated by reference into, this Annual Report on Form 10-K. Each management contract or compensatory plan or arrangement is identified separately in Item 15(c) hereof.

(c) Exhibits. The following exhibits are filed as part of, or incorporated by reference into, this Annual Report on Form 10-K:

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<b>Exhibit Number</b>	<b>Description of Document</b>
3.1(1)	Restated Certificate of Incorporation.
3.2(13)	Certificate of Amendment of Amended and Restated Certificate of Incorporation.
3.2(10)	Amended and Restated Bylaws.
4.1(11)	Indenture, by and between MannKind and Wells Fargo Bank, N.A., dated November 1, 2006.
4.2(4)	First Supplemental Indenture, by and between MannKind and Wells Fargo Bank, N.A., dated December 12, 2006.
4.3(4)	Form of 3.75% Senior Convertible Note due 2013.
4.4(1)	Form of common stock certificate.
4.5(1)	Registration Rights Agreement, dated October 15, 1998 by and among CTL ImmunoTherapies Corp., Medical Research Group, LLC, McLean Watson Advisory Inc. and Alfred E. Mann, as amended.
10.1(2)	Promissory Note made by MannKind in favor of Alfred E. Mann dated October 3, 2007.
10.2(13)	Agreement, dated September 13, 2006, between MannKind and Torcon, Inc.
10.3(3)	Securities Purchase Agreement, dated August 2, 2005 by and among MannKind and the purchasers listed on Exhibit A thereto.
10.4 (5)	Supply Agreement, dated December 31, 2004, between MannKind and Vaupell, Inc.
10.5 (1)	Supply Agreement, dated January 1, 2000, between Diosynth B.V. and Pharmaceutical Discovery Corporation.
10.6*(1)	Form of Indemnity Agreement entered into between MannKind and each of its directors and officers.
10.7*(9)	Description of Officers Incentive Program.
10.8*(6)	Description of 2006 executive officer salaries.
10.9*(6)	Description of 2006 non-employee director compensation.
10.9*(12)	Executive Severance Agreement, dated October 10, 2007, between MannKind and Hakan Edstrom.
10.10*(12)	Executive Severance Agreement, dated October 10, 2007, between MannKind and David Thomson.
10.11*(12)	Executive Severance Agreement, dated October 10, 2007, between MannKind and Richard Anderson.
10.12*(12)	Executive Severance Agreement, dated October 10, 2007, between MannKind and Peter Richardson.
10.13*(12)	Executive Severance Agreement, dated October 10, 2007, between MannKind and Juergen Martens.
10.14*(12)	Executive Severance Agreement, dated October 10, 2007, between MannKind and Diane Palumbo.
10.15*(12)	Change of Control Agreement, dated October 10, 2007, between MannKind and Hakan Edstrom.
10.16*(12)	Change of Control Agreement, dated October 10, 2007, between MannKind and David Thomson.
10.17*(12)	Change of Control Agreement, dated October 10, 2007, between MannKind and Richard Anderson.
10.18*(12)	Change of Control Agreement, dated October 10, 2007, between MannKind and Peter Richardson.
10.19*(12)	Change of Control Agreement, dated October 10, 2007, between MannKind and Juergen Martens.
10.20*(12)	Change of Control Agreement, dated October 10, 2007, between MannKind and Diane Palumbo.
10.21*(8)	2004 Equity Incentive Plan and form of stock option agreement there under.
10.22*(7)	Form of Phantom Stock Award Agreement under the 2004 Equity Incentive Plan.
10.23*(9)	2004 Non-Employee Directors Stock Option Plan and form of stock option agreement there under.
10.24*(1)	2004 Employee Stock Purchase Plan and form of offering document there under.
10.25*(1)	Pharmaceutical Discovery Corporation 1991 Stock Option Plan.
10.26*(1)	Pharmaceutical Discovery Corporation 1999 Stock Plan and form of stock option plan there under.
10.27*(1)	AlleCure Corp. 2000 Stock Option and Stock Plan.
10.28*(1)	CTL Immunotherapies Corp. 2000 Stock Option and Stock Plan.
10.29*(1)	2001 Stock Awards Plan.
10.30**	Supply Agreement, dated November 16, 2007, between MannKind and N.V. Organon.

23.1 Consent of Independent Registered Public Accounting Firm

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<b>Exhibit Number</b>	<b>Description of Document</b>
31.1	Certification of the Chief Executive Officer pursuant to Rules 13a-14(a) and 15d-14(a) of the Securities Exchange Act of 1934, as amended.
31.2	Certification of the Chief Financial Officer pursuant to Rules 13a-14(a) and 15d-14(a) of the Securities Exchange Act of 1934, as amended.
32	Certifications of the Chief Executive Officer and Chief Financial Officer pursuant to Rules 13a-14(b) and 15d-14(b) of the Securities Exchange Act of 1934, as amended and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. § 1350)

\* Indicates management contract or compensatory plan.

\*\* Confidential treatment has been requested with respect to certain portions of this exhibit. Omitted portions have been filed separately with the SEC.

Confidential treatment has been granted with respect to certain portions of this exhibit. Omitted portions have been filed separately with the SEC.

- (1) Incorporated by reference to MannKind s registration statement on Form S-1 (File No. 333-115020), filed with the SEC on April 30, 2004, as amended.
- (2) Incorporated by reference to MannKind s Current Report on Form 8-K filed with the SEC on October 3, 2007.
- (3) Incorporated by reference to MannKind s current report on Form 8-K filed with the SEC on August 5, 2005.
- (4) Incorporated by reference to MannKind s current report on Form 8-K filed with the SEC on December 12, 2006.
- (5) Incorporated by reference to MannKind s current report on Form 8-K filed with the SEC on February 23, 2005.
- (6) Incorporated by reference to MannKind s current report on Form 8-K filed with the SEC on February 22, 2006.
- (7) Incorporated by reference to MannKind s current report on Form 8-K filed with the SEC on December 14, 2005.
- (8) Incorporated by reference to MannKind s Current Report on Form 8-K filed with the SEC on May 31, 2006.
- (9) Incorporated by reference to MannKind s Annual Report on Form 10-K filed with the SEC on March 16, 2006.
- (10) Incorporated by reference to MannKind s Current Report on Form 8-K filed with the SEC on November 19, 2007.
- (11) Incorporated by reference to MannKind s Registration Statement on Form S-3 (File No. 333-138373) filed with the SEC on November 2, 2006.
- (12)

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Incorporated by reference to MannKind's Current Report on Form 8-K, as amended, filed with the SEC on October 16, 2007.

- (13) Incorporated by reference to MannKind's Quarterly Report on Form 10-Q filed with the SEC on August 9, 2007.



**Table of Contents****SIGNATURES**

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Mannkind Corporation

By: /s/ Alfred E. Mann

Alfred E. Mann  
Chief Executive Officer

Dated: March 14, 2008

**POWER OF ATTORNEY**

KNOW ALL BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Hakan S. Edstrom, Richard L. Anderson and David Thomson, and each of them, as his or her true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for him or her and in his or her name, place, and stead, in any and all capacities, to sign any and all amendments to this Report, and any other documents in connection therewith, and to file the same, with all exhibits thereto, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or any of them or their or his substitute or substituted, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this Report has been signed below by the following persons on behalf of the Registrant and in the capacities and on the dates indicated.

<b>Signature</b>	<b>Title</b>	<b>Date</b>
/s/ Alfred E. Mann Alfred E. Mann	Chief Executive Officer and chairman of the Board of Directors <i>(Principal Executive Officer)</i>	March 14, 2008
/s/ Hakan S. Edstrom Hakan S. Edstrom	President, Chief Operating Officer and Director	March 14, 2008
/s/ Richard L. Anderson Richard L. Anderson	Corporate Vice President and Chief Financial Officer <i>(Principal Financial and Accounting Officer)</i>	March 14, 2008
/s/ A. E. Cohen A. E. Cohen	Director	March 14, 2008

/s/ Ronald J. Consiglio	Director	March 14, 2008
Ronald J. Consiglio		
/s/ Michael Friedman, M.D.	Director	March 14, 2008
Michael Friedman, M.D.		

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<b>Signature</b>	<b>Title</b>	<b>Date</b>
/s/ Kent Kresa Kent Kresa	Director	March 14, 2008
/s/ David H. MacCallum David H. MacCallum	Director	March 14, 2008
/s/ Heather Hay Murren Heather Hay Murren	Director	March 14, 2008
/s/ Henry L. Nordhoff Henry L. Nordhoff	Director	March 14, 2008

**MANNKIND CORPORATION AND SUBSIDIARIES**  
**(A Development Stage Company)**

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**Report of Independent Registered Public Accounting Firm**

To the Board of Directors and Stockholders of MannKind Corporation  
Valencia, California

We have audited the accompanying consolidated balance sheets of MannKind Corporation and subsidiaries (a development stage company) (the Company) as of December 31, 2006 and 2007 and the related statements of operations, stockholders' equity (deficit), and cash flows for each of the three years in the period ended December 31, 2007 and for the period from February 14, 1991 (date of inception) to December 31, 2007. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, such consolidated financial statements present fairly, in all material respects, the financial position of MannKind Corporation and subsidiaries as of December 31, 2006 and 2007, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2007 and for the period from February 14, 1991 (date of inception) to December 31, 2007, in conformity with accounting principles generally accepted in the United States of America.

As discussed in Note 2 to the consolidated financial statements, the Company changed the manner in which it accounts for share-based compensation in 2006.

We have also audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the Company's internal control over financial reporting as of December 31, 2007, based on the criteria established in *Internal Control - Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated March 14, 2008 expressed an unqualified opinion on the Company's internal control over financial reporting.

/s/ DELOITTE & TOUCHE LLP

Los Angeles, California  
March 14, 2008

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**MANNKIND CORPORATION AND SUBSIDIARIES**  
**(A Development Stage Company)**

**CONSOLIDATED BALANCE SHEETS**

	<b>December 31,</b>	
	<b>2006</b>	<b>2007</b>
	<b>(In thousands, except share data)</b>	
<b>ASSETS</b>		
Current assets:		
Cash and cash equivalents	\$ 319,555	\$ 368,285
Marketable securities	116,924	
State research and development credit exchange receivable current	2,418	831
Prepaid expenses and other current assets	10,650	9,596
Total current assets	449,547	378,712
Property and equipment net	88,328	162,683
State research and development credit exchange receivable net of current portion	1,500	1,500
Other assets	362	548
Total	\$ 539,737	\$ 543,443
<b>LIABILITIES AND STOCKHOLDERS EQUITY</b>		
Current liabilities:		
Accounts payable	\$ 10,715	\$ 35,463
Accrued expenses and other current liabilities	34,244	32,095
Total current liabilities	44,959	67,558
Senior convertible notes	111,267	111,761
Other liabilities	24	24
Total liabilities	156,250	179,343
Commitments and contingencies		
Stockholders equity:		
Undesignated preferred stock, \$0.01 par value 10,000,000 shares authorized; no shares issued or outstanding at December 31, 2006 and 2007		
Common stock, \$0.01 par value 90,000,000 and 150,000,000 shares authorized at December 31, 2006 and 2007, respectively; 73,360,154 and 101,380,823 shares issued and outstanding at December 31, 2006 and 2007, respectively	734	1,014
Additional paid-in capital	1,170,602	1,444,125
Deficit accumulated during the development stage	(787,849)	(1,081,039)
Total stockholders equity	383,487	364,100

Total	\$ 539,737	\$ 543,443
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See notes to financial statements.

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**MANNKIND CORPORATION AND SUBSIDIARIES**  
**(A Development Stage Company)**

**STATEMENTS OF OPERATIONS**

	Year Ended December 31,			Cumulative
	2005	2006	2007	Period from February 14, 1991 (Date of Inception) to December 31, 2007
	(In thousands, except per share data)			
Revenue	\$	\$ 100	\$ 10	\$ 2,968
Operating expenses:				
Research and development	95,347	191,796	256,844	747,040
General and administrative	22,775	42,001	50,523	190,499
In-process research and development costs				19,726
Goodwill impairment				151,428
Total operating expenses	118,122	233,797	307,367	1,108,693
Loss from operations	(118,122)	(233,697)	(307,357)	(1,105,725)
Other income (expense)	78	208	(197)	(1,881)
Interest expense on note payable to principal stockholder		(1,511)		(1,511)
Interest expense on senior convertible notes		(222)	(3,408)	(3,630)
Interest income	3,707	4,679	17,775	31,732
Loss before provision for income taxes	(114,337)	(230,543)	(293,187)	(1,081,015)
Income taxes	(1)	(5)	(3)	(24)
Net loss	(114,338)	(230,548)	(293,190)	(1,081,039)
Deemed dividend related to beneficial conversion feature of convertible preferred stock				(22,260)
Accretion on redeemable preferred stock				(952)
Net loss applicable to common stockholders	\$ (114,338)	\$ (230,548)	\$ (293,190)	\$ (1,104,251)
Net loss per share applicable to common stockholders basic and diluted	\$ (2.87)	\$ (4.52)	\$ (3.66)	
Shares used to compute basic and diluted net loss per share applicable to common stockholders	39,871	50,970	80,038	

See notes to financial statements.







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Issuance of common stock for cash and services	36		1,805		1,805
Collection of stock subscription				400	400
Net loss				(2,004)	(2,004)
<b>BALANCE, DECEMBER 31, 1994</b>	<b>1,126</b>	<b>11</b>	<b>4,528</b>	<b>(5,246)</b>	<b>(707)</b>
Issuance of common stock for services			8		8
Exercise of stock options	1		22		22
Stock compensation			384		384
Net loss				(2,815)	(2,815)
<b>BALANCE, DECEMBER 31, 1995</b>	<b>1,127</b>	<b>11</b>	<b>4,942</b>	<b>(8,061)</b>	<b>(3,108)</b>
Issuance of common stock for cash and services	1		59		59
Exercise of stock options	3		12		12
Stock compensation			126		126
Net loss				(2,570)	(2,570)
<b>BALANCE, DECEMBER 31, 1996</b>	<b>1,131</b>	<b>11</b>	<b>5,139</b>	<b>(10,631)</b>	<b>(5,481)</b>
Issuance of common stock for cash and services	548	6	190		196
Stock compensation			2		2
Exercise of stock options	27		135		135
Conversion of notes payable	12		60		60
Net loss				(2,280)	(2,280)
<b>BALANCE, DECEMBER 31, 1997</b>	<b>1,718</b>	<b>17</b>	<b>5,526</b>	<b>(12,911)</b>	<b>(7,368)</b>
Issuance of common stock for cash and services	2,253	23	12,703		12,726

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Stock compensation			150		150
Exercise of stock options	68	1	24		25
Conversion of notes payable	215	2	1,200		1,202
Net loss				(3,331)	(3,331)
<b>BALANCE, DECEMBER 31, 1998</b>	4,254	43	19,603	(16,242)	3,404
Issuance of common stock	162	2	532		534
Conversion of notes payable	80	1	994		995
Net loss				(5,679)	(5,679)
	74				

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received for common							
be issued							
of common stock							
es			3		60		
of stock options			1		13		
interest on notes						(189)	
on notes							
e						28	
to redemption							
Series A							
le convertible							
stock					(239)		
ed compensation					1,565		
of put option by							
ler					(2,949)		
merger of entities					171,154		
							(48,245)
CE, DECEMBER							
193	15,000		12,305	123	317,117	(2,395)	(94,827)
of common stock							
			3,922	40	58,775		
of common stock							
already received			234	2	(2)		
of stock award to							
			3		84		
received for common							
able					98		
interest on notes						(229)	
on notes							
e						1,314	
l conversion							
Series B							
le preferred stock					1,421		
dividend related to							
l conversion							
Series B							
le preferred stock					(1,421)		
to redemption							
Series A							
le convertible							
stock					(251)		
ed compensation					268		
n redemption by							
ler					1,921		
							(206,265)

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**MANNKIND CORPORATION AND SUBSIDIARIES**  
**(A Development Stage Company)**

**STATEMENTS OF STOCKHOLDERS EQUITY (DEFICIT) (Continued)**

Series B		Series C		Series C	Series C	Common Stock		Additional	Notes	Notes	Acc
Convertible Preferred Shares	Stock Amount	Convertible Preferred Shares	Stock Amount	Convertible Preferred Stock Issuable	Convertible Preferred Stock Subscriptions Receivable	Shares	Amount	Paid-In Capital	Receivable from Stockholders	Receivable from Officers	De
(In thousands)											
193	15,000					16,464	165	378,010	(1,310)		
				50,000	(50,000)						
					31,847						
						3,494	35	49,965			
									70		
						17					
								225	(102)	(225)	(3)
								1,017			
								(1,017)			
								(253)			
								4,501			

								623		
193	15,000		50,000	(18,153)	19,975	200	433,141	(1,412)	(228)	
		356	18,153	(18,153)	18,153					
		624	31,847	(31,847)						
					86		1,079			
					4		46		(107)	
							(225)			228
					(90)	(1)	(1,518)	1,519		
					891	9	5,239			
(193)	(15,000)				811	8	14,992			
		(980)	(50,000)		4,464	45	49,955			
					22					
					36		430			
					6,557	66	83,110			
							19,822			
							(19,822)			
							(60)			
							6,810			







Change in number of common shares outstanding					
Change in number of common shares due to research and development	100	1	2,073		2,173
Change in number of common shares due to equity-based compensation			14,667		14,667
Change in number of common shares due to loss of common shares				(230,548)	(230,548)
<b>CHANGE, DECEMBER 31, 2006</b>	<b>73,360</b>	<b>734</b>	<b>1,170,602</b>	<b>(787,849)</b>	<b>383,777</b>
Change in number of common shares due to Employee Stock Purchase Plan	124	1	1,064		1,189
Change in number of common shares due to exercise of stock options	607	6	4,917		5,524
Change in number of common shares due to awards to consultants	30		123		153
Change in number of common shares due to purchase of stock for cash	27,014	270	249,480		276,764
Change in number of common shares due to the release of restricted stock units	146	2	(526)		(378)
Change in number of common shares due to research and development	100	1	943		1,044
Change in number of common shares due to equity-based compensation			17,522		17,522
Change in number of common shares due to loss of common shares				(293,190)	(293,190)
<b>CHANGE, DECEMBER 31, 2007</b>	<b>101,381</b>	<b>1,014</b>	<b>1,444,125</b>	<b>(1,081,039)</b>	<b>364,361</b>

See notes to financial statements.

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**MANNKIND CORPORATION AND SUBSIDIARIES**  
**(A Development Stage Company)**

**STATEMENTS OF CASH FLOWS**

	Years Ended December 31,			Cumulative
	2005	2006	2007	Period from
	(In thousands)			February 14,
				1991 (Date of
				Inception) to
				December 31,
				2007
<b>CASH FLOWS FROM OPERATING</b>				
<b>ACTIVITIES:</b>				
Net loss	\$ (114,338)	\$ (230,548)	\$ (293,190)	\$ (1,081,039)
Adjustments to reconcile net loss to net cash used in operating activities:				
Depreciation and amortization	7,391	8,517	8,973	48,127
Stock-based compensation (benefit) expense	(1,728)	14,667	17,645	54,830
Stock expense for shares issued pursuant to research agreement		2,074	944	3,018
Loss on sale, abandonment/disposal or impairment of property and equipment	16	79	7,047	10,493
Accrued interest on investments, net of amortization of premiums	(146)	204		58
In-process research and development				19,726
Discount on stockholder notes below market rate				241
Non-cash compensation expense of officer resulting from stockholder contribution				70
Accrued interest expense on notes payable to stockholders				1,538
Non-cash interest expense				3
Accrued interest on notes receivable				(747)
Goodwill impairment				151,428
Loss on available-for-sale securities				229
Changes in assets and liabilities:				
State research and development credit exchange receivable	(695)	(693)	1,587	(2,331)
Prepaid expenses and other current assets	221	(7,606)	2,654	(7,996)
Other assets	(224)	(77)	(186)	(548)
Accounts payable	509	7,168	16,265	26,980
Accrued expenses and other current liabilities	9,185	16,426	(6,885)	27,359
Other liabilities	(47)	(5)		22
Payment of deferred compensation	(1,373)			
Net cash used in operating activities	(101,229)	(189,794)	(245,146)	(748,539)

**CASH FLOWS FROM INVESTING  
ACTIVITIES:**

Purchase of marketable securities	(258,150)	(154,431)	(169,801)	(726,950)
Sales of marketable securities	180,245	126,900	286,725	726,665
Purchase of property and equipment	(17,169)	(20,773)	(78,262)	(209,404)
Proceeds from sale of property and equipment	90	32		214
Restricted cash	583			

Net cash (used in) provided by investing activities	(94,401)	(48,272)	38,662	(209,475)
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**CASH FLOWS FROM FINANCING  
ACTIVITIES:**

Issuance of common stock and warrants	172,680	390,657	255,738	1,139,646
Collection of Series C convertible preferred stock subscriptions receivable				50,000
Issuance of Series B convertible preferred stock for cash				15,000

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**MANNKIND CORPORATION AND SUBSIDIARIES**  
**(A Development Stage Company)**

**STATEMENTS OF CASH FLOWS (Continued)**

	Years Ended December 31,			Cumulative Period from February 14, 1991 (Date of Inception) to December 31, 2007
	2005	2006	2007	
	(In thousands)			
Cash received for common stock to be issued				3,900
Repurchase of common stock				(1,028)
Put shares sold to majority stockholder				623
Borrowings under lines of credit				4,220
Proceeds from notes receivables				1,742
Borrowings on notes payable from principal stockholder		70,000		70,000
Principal payments on notes payable to principal stockholder		(70,000)		(70,000)
Borrowings on notes payable				3,460
Principal payments on notes payable payable to stockholder				(1,667)
Proceeds from senior convertible notes		111,267		111,267
Payment of employment taxes related to vested restricted stock units		(340)	(524)	(864)
Net cash provided by financing activities	172,680	501,584	255,214	1,326,299
NET (DECREASE) INCREASE IN CASH AND CASH EQUIVALENTS	\$ (22,950)	\$ 263,518	\$ 48,730	\$ 368,285
CASH AND CASH EQUIVALENTS, BEGINNING OF PERIOD	78,987	56,037	319,555	
CASH AND CASH EQUIVALENTS, END OF PERIOD	\$ 56,037	\$ 319,555	\$ 368,285	\$ 368,285
<b>SUPPLEMENTAL CASH FLOWS DISCLOSURES:</b>				
Cash paid for income taxes	\$ 1	\$ 5	\$ 3	\$ 24
Interest paid in cash		1,615	4,348	6,043
Accretion on redeemable convertible preferred stock				(952)
Issuance of common stock upon conversion of notes payable				3,331
				171,154

Increase in additional paid-in capital resulting from merger		
Issuance of common stock for notes receivable		2,758
Issuance of put option by stockholder		(2,949)
Put option redemption by stockholder		1,921
Notes receivable by stockholder issued to officers		
Issuance of Series C convertible preferred stock subscriptions		50,000
Issuance of Series A redeemable convertible preferred stock		4,296
Conversion of Series A redeemable convertible preferred stock		(5,248)
Non-cash construction in progress and property and equipment	13,219	13,219
Non-cash transfer from property and equipment to other current assets	1,600	1,600

In connection with the Company's initial public offering, all shares of Series B and Series C convertible preferred stock, in the amount of \$15.0 million and \$50.0 million, respectively, automatically converted into common stock in August 2004.

See notes to financial statements.

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**MANNKIND CORPORATION AND SUBSIDIARIES  
(A Development Stage Company)**

**NOTES TO FINANCIAL STATEMENTS**

**1. Description of Business and Basis of Presentation**

*Business* MannKind Corporation (the Company) is a biopharmaceutical company focused on the discovery, development and commercialization of therapeutic products for diseases such as diabetes and cancer. The Company's lead investigational product candidate, the Technosphere Insulin System, is currently in Phase 3 clinical trials in the United States, Europe and Latin America to study its safety and efficacy in the treatment of diabetes. The Technosphere Insulin System consists of the Company's proprietary Technosphere particles onto which insulin molecules are loaded. These loaded particles are then aerosolized and inhaled deep into the lung using the Company's MedTone inhaler.

*Basis of Presentation* The Company is considered to be in the development stage as its primary activities since incorporation have been establishing its facilities, recruiting personnel, conducting research and development, business development, business and financial planning, and raising capital. Since its inception through December 31, 2007 the Company has reported accumulated net losses of \$1.1 billion, which include a goodwill impairment charge of \$151.4 million (see Note 2), and cumulative negative cash flow from operations of \$748.5 million. It is costly to develop therapeutic products and conduct clinical trials for these products. Based upon the Company's current expectations, management believes the Company's existing capital resources will enable it to continue planned operations through the fourth quarter of 2009. However, the Company cannot provide assurances that its plans will not change or that changed circumstances will not result in the depletion of its capital resources more rapidly than it currently anticipates. Accordingly, the Company expects that it will need to raise additional capital, either through the sale of equity and/or debt securities, a strategic business collaboration with a pharmaceutical company or the establishment of other funding facilities, in order to continue the development and commercialization of its Technosphere Insulin System and other product candidates and to support its other ongoing activities.

On December 12, 2001, the stockholders of AlleCure Corp. (AlleCure) and CTL ImmunoTherapies Corp. (CTL) voted to exchange their shares for shares of Pharmaceutical Discovery Corporation (PDC). Upon approval of the merger, PDC then changed its name to MannKind Corporation. PDC was incorporated in the State of Delaware on February 14, 1991. The stockholders of PDC did not vote on the merger. At the date of the merger, Mr. Alfred Mann owned 76% of PDC, 59% of AlleCure and 69% of CTL. Accordingly, only the minority interest of AlleCure and CTL was stepped up to fair value using the purchase method of accounting. As a result of this purchase accounting, in-process research and development of \$19.7 million and goodwill of \$151.4 million were recorded at the entity level. The historical basis of PDC and the historical basis relating to the ownership interests of Mr. Mann in AlleCure and CTL have been reflected in the financial statements. For periods prior to December 12, 2001, the results of operations have been presented on a combined basis. All references in the accompanying financial statements and notes to the financial statements to number of shares, sales price and per share amounts of the Company's capital stock have been retroactively restated to reflect the share exchange ratios for each of the entities that participated in the merger.

For periods subsequent to December 12, 2001, the accompanying financial statements have been presented on a consolidated basis and include the wholly-owned subsidiaries, AlleCure and CTL. On December 31, 2002, AlleCure and CTL merged with and into MannKind and ceased to be separate entities.

*Segment Information* In accordance with Statement of Financial Accounting Standards (SFAS) No. 131, *Disclosures about Segments of an Enterprise and Related Information*, operating segments are identified as components of an



enterprise about which separate discrete financial information is available for evaluation by the chief operating decision-maker in making decisions regarding resource allocation and assessing performance. To date, the Company has viewed its operations and manages its business as one segment operating entirely in the United States of America.

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**MANNKIND CORPORATION AND SUBSIDIARIES  
(A Development Stage Company)**

**NOTES TO FINANCIAL STATEMENTS (Continued)**

**2. Summary of Significant Accounting Policies**

*Financial Statement Estimates* The preparation of financial statements in conformity with accounting principles generally accepted in the United States of America requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. Actual results could differ from those estimates.

*Cash and Cash Equivalents* The Company considers all highly liquid investments with a purchased maturity date of three months or less to be cash equivalents.

*Concentration of Credit Risk* Financial instruments that potentially subject the Company to concentration of credit risk consist of cash and cash equivalents and marketable securities. Cash and cash equivalents consist primarily of interest-bearing accounts and are regularly monitored by management and held in high credit quality institutions. Marketable securities consist of highly liquid short-term investment securities such as government and investment-grade corporate debt.

*Marketable Securities* The Company accounts for marketable securities as available for sale, in accordance with SFAS No. 115, *Accounting for Certain Debt and Equity Securities*. Unrealized holding gains and losses for available-for-sale securities are reported as a separate component of stockholders' equity until realized. The Company reviews the portfolio for other than temporary impairment in accordance with Emerging Issues Task Force (EITF) Issue No. 03-01, *The Meaning of Other-Than-Temporary Impairment and Its Application to Certain Investments* and Financial Accounting Standards Board (FASB) Staff Position No. 115-1, *The Meaning of Other-Than-Temporary Impairment and Its Application to Certain Investments*.

*State Research and Development Credit Exchange Receivable* The State of Connecticut provides certain companies with the opportunity to exchange certain research and development income tax credit carryforwards for cash in exchange for foregoing the carryforward of the research and development credits. The program provides for an exchange of research and development income tax credits for cash equal to 65% of the value of corporation tax credit available for exchange. Estimated amounts receivable under the program are recorded as a reduction of research and development expenses.

*Fair Value of Financial Instruments* The carrying amounts of financial instruments, which include cash equivalents, marketable securities, accounts payable and payable to stockholder, approximate their fair values due to their relatively short maturities. The carrying amounts of the notes receivable from stockholders through the dates when they were settled reflect market rates of interest for similar loans of similar amounts and terms available from a third party (see Note 7). The carrying amounts of the senior convertible notes reflect market rates of interest for similar loans of similar amounts and terms to a third party (see Note 9). The senior convertible notes had a carrying value of \$111.3 million and \$111.8 million and a fair value of \$118.8 million and \$95.2 million as of December 31, 2006 and 2007, respectively.

*Goodwill and Identifiable Intangibles* As a result of the merger with AlleCure and CTL on December 12, 2001, as described in Note 1, goodwill of \$151.4 million was recorded at the entity level in 2001. Upon adoption of SFAS No. 142, *Goodwill and Other Intangible Assets*, the Company adopted a policy of testing goodwill and intangible assets with indefinite lives for impairment at least annually, as of December 31, with any related

impairment losses being recognized in earnings when identified. In December 2002 the Company concluded that the major AlleCure product development program should be terminated and that the clinical trials of the CTL product should be halted and returned to the research stage. As a result of this determination, the Company closed the CTL facility and reduced headcount for AlleCure and CTL by approximately 50%. In connection with the annual test for impairment of goodwill as of December 31, 2002, the Company determined that on the basis of the internal study, the goodwill recorded for the AlleCure and CTL units was potentially impaired. The Company performed the second step of the annual impairment test as of December 31, 2002 for each of the potentially

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**MANNKIND CORPORATION AND SUBSIDIARIES  
(A Development Stage Company)**

**NOTES TO FINANCIAL STATEMENTS (Continued)**

impaired reporting units and estimated the fair value of the AlleCure and CTL programs using the expected present value of future cash flows which were expected to be negligible. Accordingly, the goodwill balance of \$151.4 million was determined to be fully impaired and an impairment loss was recorded in 2002. Subsequent to December 31, 2002, the Company had no goodwill or intangibles with indefinite lives included on its balance sheet.

*Property and Equipment* Property and equipment are recorded at cost and depreciated using the straight-line method over the estimated useful lives of the related assets. Leasehold improvements are amortized over the term of the lease or the service lives of the improvements, whichever is shorter. Assets under construction are not depreciated until placed into service.

*Impairment of Long-Lived Assets* The Company evaluates long-lived assets for impairment whenever events or changes in circumstances indicate that the carrying value of an asset may not be recoverable in accordance with SFAS No. 144, *Accounting for the Impairment or Disposal of Long Lived-Assets*. Assets are considered to be impaired if the carrying value may not be recoverable based upon management's assessment of the following events or changes in circumstances:

- significant changes in the Company's strategic business objectives and utilization of the assets;
- a determination that the carrying value of such assets can not be recovered through undiscounted cash flows;
- loss of legal ownership or title to the assets; or
- the impact of significant negative industry or economic trends.

If the Company believes an asset to be impaired, the impairment recognized is the amount by which the carrying value of the assets exceeds the fair value of the assets. Any write-downs would be treated as permanent reductions in the carrying amount of the asset and an operating loss would be recognized. For the years ended December 31, 2005 and 2006 the Company did not consider any long-lived assets to be impaired based on management's assessment. During the year ended December 31, 2007, asset impairment of approximately \$6.6 million was recognized as described in Note 5 Property and Equipment.

*Accounts Payable and Accrued Expenses* All liabilities, including accounts payable and accrued expenses, are recorded consistent with the definition of liabilities and accrual accounting as provided by FASB Statement of Financial Accounting Concepts No. 6, *Elements of Financial Statements*.

*Income Taxes* In accordance with SFAS No. 109, *Accounting for Income Taxes*, deferred income tax assets and liabilities are recorded for the expected future tax consequences of temporary differences between the financial statement carrying amounts and the income tax basis of assets and liabilities. A valuation allowance is recorded to reduce net deferred income tax assets to amounts that are more likely than not to be realized.

Income tax positions are considered for uncertainty in accordance with FASB Interpretation No. 48, *Accounting for Uncertainty in Income Taxes - an interpretation of FASB Statement No. 109* (FIN 48). The provisions of FIN 48 are effective beginning January 1, 2007. The Company believes that its income tax filing positions and deductions will be sustained on audit and does not anticipate any adjustments that will result in a material change to its financial position.

Therefore, no reserves for uncertain income tax positions have been recorded pursuant to FIN 48. The cumulative effect, if any, of applying FIN 48 is to be reported as an adjustment to the opening balance of retained earnings in the year of adoption. Our adoption of FIN 48 did not result in a cumulative effect adjustment to retained earnings.

Significant management judgment is involved in determining the provision for income taxes, deferred tax assets and liabilities and any valuation allowance recorded against net deferred tax assets. Due to uncertainties related to deferred tax assets as a result of the history of operating losses, a valuation allowance has been established against the gross deferred tax asset balance. The valuation allowance is based on management's estimates of taxable income by jurisdiction in which the Company operates and the period over which deferred tax assets will be

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recoverable. In the event that actual results differ from these estimates or the Company adjusts these estimates in future periods, a change in the valuation allowance may be needed, which could materially impact the Company's financial position and results of operations.

*Contingencies* Contingencies are recorded in accordance with SFAS No. 5, *Accounting for Contingencies*.

*Stock-Based Compensation* As of December 31, 2007, the Company had three active stock-based compensation plans, which are described more fully in Note 11. On January 1, 2006, the Company adopted the provisions of SFAS No. 123R ( SFAS No. 123R ), *Share-based Payment*, which is a revision of SFAS No. 123 ( SFAS No. 123 ), *Accounting for Stock-Based Compensation*. Prior to January 1, 2006, the Company accounted for employee stock options and the employee stock purchase plan using the intrinsic value method in accordance with Accounting Principles Board ( APB ) Opinion No. 25 ( APB No. 25 ), *Accounting for Stock Issued to Employees*, and adopted the disclosure only alternative of SFAS No. 123. SFAS No. 123R eliminated the intrinsic value method of accounting for stock options which the Company followed until December 31, 2005. Further, SFAS No. 123R requires all share-based payments to employees, including grants of stock options and the compensatory elements of employee stock purchase plans, to be recognized in the income statement based upon the fair value of the awards at the grant date.

Upon adoption of SFAS No. 123R, the Company selected the modified prospective transition method whereby unvested awards at the date of adoption as well as awards that are granted, modified, or settled after the date of adoption will be measured and accounted for in accordance with SFAS No. 123R. Measurement and attribution of compensation cost for awards unvested as of January 1, 2006 is based on the same estimate of the grant-date or modification-date fair value and the same attribution method (straight-line) used previously under SFAS No. 123.

*Warrants* The Company has issued warrants to purchase shares of its common stock. Warrants have been accounted for as equity in accordance with the provisions of EITF Issue No. 00-19: *Accounting for Derivative Financial Instruments Indexed to, and Potentially Settled in, a Company's Own Stock*.

*Research and Development Expenses* Research and development expenses consist primarily of costs associated with the clinical trials of the Company's product candidates, manufacturing supplies and other development materials, compensation and other expenses for research and development personnel, costs for consultants and related contract research, facility costs, and depreciation. Research and development costs, which are net of any tax credit exchange recognized for the Connecticut state research and development credit exchange program, are expensed as incurred consistent with SFAS No. 2, *Accounting for Research and Development Costs*.

*Clinical Trial Expenses* Clinical trial expenses, which are reflected in research and development expenses in the accompanying statements of operations, result from obligations under contracts with vendors, consultants, and clinical site agreements in connection with conducting clinical trials. The financial terms of these contracts are subject to negotiations which vary from contract to contract and may result in payment flows that do not match the periods over which materials or services are provided to the Company under such contracts. The appropriate level of trial expenses are reflected in the Company's financial statements by matching period expenses with period services and efforts expended. These expenses are recorded according to the progress of the trial as measured by patient progression and the timing of various aspects of the trial. Clinical trial accrual estimates are determined through discussions with internal clinical personnel and outside service providers as to the progress or state of completion of trials, or the

services completed. Service provider status is then compared to the contractually obligated fee to be paid for such services. During the course of a clinical trial, the Company may adjust the rate of clinical expense recognized if actual results differ from management's estimates. The date on which certain services commence, the level of services performed on or before a given date and the cost of the services are often judgmental.

*Interest Expense* Interest costs are expensed as incurred, except to the extent such interest is related to construction in progress, in which case interest is capitalized. Interest expense, net, for the years ended December 31, 2006 and 2007 was \$1.7 million and \$3.4 million, respectively. Interest costs capitalized for the years ended

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December 31, 2006 and 2007 were \$0.1 million and \$1.4 million, respectively. No interest was capitalized for the year ended December 31, 2005.

*Net Loss Per Share of Common Stock* Basic net loss per share excludes dilution for potentially dilutive securities and is computed by dividing loss applicable to common stockholders by the weighted average number of common shares outstanding during the period. Diluted net loss per share reflects the potential dilution that could occur if securities or other contracts to issue common stock were exercised or converted into common stock. Potentially dilutive securities are excluded from the computation of diluted net loss per share for all of the periods presented in the accompanying statements of operations because the reported net loss in each of these periods results in their inclusion being antidilutive.

Potentially dilutive securities outstanding are summarized as follows:

	<b>2005</b>	<b>December 31, 2006</b>	<b>2007</b>
Exercise of common stock options	4,985,831	6,216,698	6,886,657
Conversion of senior convertible notes into common stock		5,117,523	5,117,523
Exercise of common stock warrants	3,438,776	2,895,332	2,882,873
Vesting of restricted stock units	164,901	776,653	1,359,662

*Exit or Disposal Activities* SFAS No. 146, *Accounting for Costs Associated with Exit or Disposal Activities*, was effective for exit or disposal activities initiated after December 31, 2002. SFAS No. 146 addresses financial accounting and reporting for the costs associated with exit or disposal activities and EITF Issue No. 94-3, *Liability Recognition for Certain Employee Termination Benefits and Costs to Exit and Disposal Activity (Including Certain Costs Incurred in a Restructuring)*. SFAS No. 146 requires that a liability for costs associated with an exit or disposal activity be recognized when the liability is incurred and establishes that fair value is the objective for initial measurements of the liability.

*Recently Issued Accounting Standards* In December 2007, the FASB ratified the EITF consensus on EITF Issue No. 07-1, *Accounting for Collaborative Arrangements*, that discusses how parties to a collaborative arrangement (which does not establish a legal entity within such arrangement) should account for various activities. The consensus indicates that costs incurred and revenues generated from transactions with third parties (i.e. parties outside of the collaborative arrangement) should be reported by the collaborators on the respective line items in their income statements pursuant to EITF Issue No. 99-19, *Reporting Revenue Gross as a Principal Versus Net as an Agent*. Additionally, the consensus provides that income statement characterization of payments between the participants in a collaborative arrangement should be based upon existing authoritative pronouncements; analogy to such pronouncements if not within their scope; or a reasonable, rational, and consistently applied accounting policy election. EITF Issue No. 07-1 is effective beginning January 1, 2009 and is to be applied retrospectively to all periods presented for collaborative arrangements existing as of the date of adoption. The Company is evaluating the impact, if any, the adoption of this consensus will have on its results of operations, financial position or cash flows.



In December 2007, the FASB issued SFAS No. 141(R), *Business Combinations* and SFAS No. 160, *Accounting and Reporting of Noncontrolling Interests in Consolidated Financial Statements – an amendment of ARB No. 51* ( SFAS No. 160 ). These standards will significantly change the accounting and reporting for business combination transactions and noncontrolling (minority) interests in consolidated financial statements, including capitalizing at the acquisition date the fair value of acquired IPR&D, and remeasuring and writing down these assets, if necessary, in subsequent periods during their development. These new standards will be applied prospectively for business combinations that occur on or after January 1, 2009, except that presentation and disclosure requirements of SFAS No. 160 regarding noncontrolling interests shall be applied retrospectively.

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In September 2007, the FASB ratified EITF Issue No. 07-3 *Accounting for Advance Payments for Goods or Services to Be Used in Future Research and Development Activities* ( EITF 07-3 ). EITF 07-3 requires that nonrefundable advance payments for future research and development activities be deferred and capitalized. EITF 07-3 is effective as of the beginning of an entity's fiscal year that begins after December 15, 2007. The Company is evaluating the impact, if any, the adoption of EITF 07-3 will have on its results of operations, financial position or cash flows.

In February 2007, the FASB issued SFAS No. 159, *The Fair Value Option for Financial Assets and Financial Liabilities*, which permits entities to choose to measure many financial instruments and certain other items at fair value. SFAS No. 159 also includes an amendment to SFAS No. 115, *Accounting for Certain Investments in Debt and Equity Securities* which applies to all entities with available-for-sale and trading securities. This Statement is effective as of the beginning of an entity's first fiscal year that begins after November 15, 2007. The Company is evaluating the impact, if any, the adoption of this Statement will have on its results of operations, financial position or cash flows.

In September 2006, the FASB issued SFAS No. 157, *Fair Value Measurements*, which defines fair value, establishes a framework for consistently measuring fair value for accounting purposes, and expands disclosures about fair value measurements. SFAS No. 157 is effective for the Company beginning January 1, 2008, and the provisions of SFAS No. 157 will be applied prospectively as of that date. In February 2008, FASB Staff Position ( FSP ) No. 157-2 was issued. FSP No. 157-2 delays the implementation of certain aspects of SFAS No. 157 to January 1, 2009. The Company is evaluating the impact, if any, the adoption of this Statement will have on its results of operations, financial position or cash flows.

### 3. Investment in securities

The following is a summary of the available-for-sale securities classified as current assets (in thousands).

	<b>December 31,</b>		<b>December 31,</b>	
	<b>2006</b>		<b>2007</b>	
	<b>Cost Basis</b>	<b>Fair Value</b>	<b>Cost Basis</b>	<b>Fair Value</b>
Auction rate municipal bonds	\$ 116,924	\$ 116,924		

As of December 31, 2007, the Company no longer held any available-for-sale securities. The Company's policy is to maintain a highly liquid short-term investment portfolio. The contractual maturities for auction rate municipal bonds at December 31, 2006 were between 21 and 39 years. Despite the long-term nature of their stated contractual maturities, the Company had the ability to quickly liquidate these securities. Proceeds from the sale and maturities of available-for-sale securities amounted to approximately \$180.2 million, \$126.9 million, and \$286.7 million for the years ended December 31, 2005, 2006, and 2007, respectively. Gross realized gains and losses for available-for-sale securities were insignificant for the years ended December 31, 2005, 2006 and 2007. Gross realized gains and losses for available-for-sale securities are recorded as other income (expense). The cost of securities sold is based on the specific identification method. Unrealized gains and losses for available-for-sale securities for all periods presented in the table above were not material.

**4. State research and development credit exchange receivable**

The State of Connecticut provides certain companies with the opportunity to exchange certain research and development income tax credit carryforwards for cash in exchange for forgoing the carryforward of the research and development income tax credits. The program provides for an exchange of research and development income tax credits for cash equal to 65% of the value of corporation tax credit available for exchange. Estimated amounts receivable under the program are recorded as a reduction of research and development expenses. During the years

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ended December 31, 2005, 2006, and 2007, research and development expenses were offset by \$1.7 million, \$0.6 million, and \$0.8 million, respectively, in connection with the program.

**5. Property and equipment**

Property and equipment consist of the following (dollar amounts in thousands):

	<b>Estimated Useful Life (Years)</b>	<b>December 31,</b>	
		<b>2006</b>	<b>2007</b>
Land		\$ 5,273	\$ 5,273
Buildings	39-40	9,566	9,566
Building improvements	5-40	44,041	52,438
Machinery and equipment	3-10	26,623	30,172
Furniture, fixtures and office equipment	5-10	2,923	3,657
Computer equipment and software	3	5,878	7,559
Leasehold improvements		103	205
Construction in progress		20,164	89,657
Deposits on equipment		6,903	4,882
		121,474	203,409
Less accumulated depreciation and amortization		(33,146)	(40,726)
Property and equipment net		\$ 88,328	\$ 162,683

Leasehold improvements are amortized over four years which is the shorter of the term of the lease or the service lives of the improvements. Depreciation and amortization expense related to property and equipment for the years ended December 31, 2005, 2006 and 2007, and the cumulative period from February 14, 1991 (date of inception) to December 31, 2007 was \$7.4 million, \$8.5 million, \$8.5 million and \$47.6 million, respectively. Capitalized interest during the years ended December 31, 2006 and 2007 was \$0.1 million and \$1.4 million, respectively, and no capitalized interest was recorded during the year ended December 31, 2005.

In December 2007, the Company determined that machinery being built for commercial manufacturing use would no longer be used for this purpose and had no other further alternative use other than for research related to Technosphere Insulin. Accordingly, the Company expensed to research and development the \$5.0 million carrying value of the machinery previously included in construction in progress. Additionally, in November 2007, the Company initiated a plan to sell certain manufacturing machines. A charge in the amount of \$1.6 million is reflected in the research and development expenses in the accompanying statement of operations for the year ended December 31, 2007 to write down the machines being held for sale to their estimated fair value of \$1.6 million. The \$1.6 million carrying value of the machines held for sale are included in the prepaid expenses and other current assets caption in the accompanying

consolidated balance sheet as of December 31, 2007.

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**6. Accrued expenses and other current liabilities**

Accrued expenses and other current liabilities are comprised of the following (in thousands):

	<b>December 31,</b>	
	<b>2006</b>	<b>2007</b>
Salary and related expenses	\$ 7,255	\$ 11,989
Research and clinical trial costs	18,707	11,657
Accrued interest	228	192
Construction in progress	1,929	4,736
Other	6,125	3,521
Accrued expenses and other current liabilities	\$ 34,244	\$ 32,095

**7. Notes receivable from stockholders**

The Company issued 110,000 shares of common stock to an executive of AlleCure in exchange for notes receivable, in the amounts of \$1.2 million during the year ended December 31, 2000 and \$750,000 during the year ended December 31, 2001. The notes bore interest at fixed rates and were payable in five years. The notes were pre-payable at the option of the debtor. The notes were collateralized by the underlying common stock. The executive had no further obligation to the Company under the terms of the stock purchase. During the first quarter of 2003, the executive was terminated by the Company (See Note 13-Commitments and Contingencies - Litigation). The note-for-stock transactions have been accounted for as in-substance stock option grants to an employee. The in-substance stock option grants had no intrinsic value as of the transaction dates. The pre-payment feature of the notes resulted in the exercise price of the in-substance stock option being unknown until the notes were paid in full. Accordingly, the Company was required to measure the intrinsic value of the in-substance stock options on the balance sheet date of each financial reporting period. During 2001, the Company recorded approximately \$815,000 of stock-based compensation expense, which was included in general and administrative expense, relating to the in-substance stock options. This amount was reversed in 2002 because the in-substance stock options had no intrinsic value as of December 31, 2002. There was no stock-based compensation expense recorded for the in-substance options in 2003 because they had no intrinsic value as of December 31, 2003. The Company recorded approximately \$17,000 of stock-based compensation expense relating to the in-substance stock options during the year ended December 31, 2004, which represented the intrinsic value of the in-substance options at year end. This amount was reversed in 2005 because the in-substance stock options had no intrinsic value as of December 31, 2005. In September and October 2005, the principal and interest totaling \$1.6 million on the notes issued in exchange for approximately 78,000 of the 110,000 shares of common stock issued became due and payable. The Company pursued collection and, in January 2006, the debtor tendered 143,949 shares as full repayment of the notes in default and the note issued in exchange for 32,000 shares which would have become due in April 2006. These shares were valued at \$2.6 million on January 31, 2006 and represented principal and interest due through that date on all notes outstanding. The Company received and cancelled 143,949 shares on January 31, 2006.

During the years ended December 31, 2000 and 2001, the Company issued an aggregate 701,333 shares of common stock to various consultants in exchange for notes receivable aggregating approximately \$10.9 million. The notes bore interest at fixed rates and were payable in five years. The notes were pre-payable at the option of the debtors. The notes were collateralized by the underlying common stock. The consultants had no further obligation to the Company under the terms of the stock purchases. The note-for-stock transactions have been accounted for as in-substance stock option grants to non-employees. Since the in-substance stock options were 100% vested and nonforfeitable upon issuance, a measurement date was deemed to have occurred on the issuance date. Accordingly, the Company recorded stock-based compensation expense equal to the estimated fair value of the in-substance options of \$8.4 million in 2000 and \$15,000 in 2001. These amounts were estimated using the Black-Scholes option

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valuation model and the following weighted-average assumptions: volatility of 100%, term of five years, interest rate of 5.06%. Notes issued in exchange for 699,972 of the 701,333 shares aggregating \$10.9 million in principal became due on October 19, 2005. The remaining note for \$32,000 was to become due in September 2006. A total of \$14.6 million in principal and interest became due and payable on October 19, 2005 and the Company pursued collection. On November 21, 2005, the consultants filed a complaint against the Company in the California Superior Court, County of Los Angeles, *Rollins et al. v. MannKind et al*, Case No. BC343381. The complaint alleges causes of action for breach of certain agreements. On January 19, 2006, the parties mediated and settled the case. Under the settlement, the Company repurchased 620,697 shares from the consultants in full satisfaction of the principal and interest on the notes previously accounted for by the Company as in-substance stock options. These shares were tendered and cancelled on February 3, 2006. The Company also agreed to repurchase the remaining 79,275 shares held by the consultants for \$1.4 million in cash. The settlement was reflected as a \$1.4 million charge to general and administrative expense in the fourth quarter of the year ended December 31, 2005 with a corresponding amount payable included in accrued expenses and other current liabilities as of December 31, 2005. On February 21, 2006, the Company received and cancelled the 79,275 shares, and paid the purchase price of \$1.4 million to the consultants. The complaint was dismissed in its entirety with prejudice.

**8. Related-party loan arrangement**

On August 2, 2006, the Company entered into a \$150.0 million loan arrangement with its principal stockholder, which was amended on August 1, 2007 and replaced with a new loan arrangement on October 2, 2007. Under the new arrangement, the Company can borrow up to a total of \$350.0 million before January 1, 2010. From April 1, 2008 until September 30, 2008, the Company can borrow up to \$150.0 million in one or more advances, and from March 1, 2009 until December 31, 2009, the Company can borrow the remaining \$200.0 million plus any amount not previously borrowed in one or more advances. The Company may not borrow more than one advance in any 12-month period, and each advance must be not less than \$50.0 million. Interest will accrue on each outstanding advance at a fixed rate equal to the one-year LIBOR rate as reported by the *Wall Street Journal* on the date of such advance plus 3% per annum and will be payable quarterly in arrears. Principal repayment is due on December 31, 2011. At any time after January 1, 2010, the principal stockholder can require the Company to prepay up to \$200.0 million in advances that have been outstanding for at least 12 months. If the principal stockholder exercises this right, the Company will have until the earlier of 180 days after the principal stockholder provides written notice or December 31, 2011 to prepay such advances. In the event of a default, all unpaid principal and interest either becomes immediately due and payable or may be accelerated at the principal stockholder's option, and the interest rate will increase to the one-year LIBOR rate calculated on the date of the initial advance or in effect on the date of default, whichever is greater, plus 5% per annum. Any borrowings under the loan arrangement will be unsecured. The loan arrangement contains no financial covenants. There are no warrants associated with the loan arrangement, nor are advances convertible into the Company's common stock.

Under the previous loan arrangement, the Company borrowed \$50.0 million on August 2, 2006 and \$20.0 million on November 27, 2006. On December 12, 2006, the Company paid off the total borrowings of \$70.0 million following the completion of concurrent offerings of convertible notes and common stock. As of December 31, 2007, there was no balance outstanding or accrued interest related to the \$350.0 million loan arrangement.

**9. Senior convertible notes**



On December 12, 2006, the Company completed an offering of \$115.0 million aggregate principal amount of 3.75% Senior Convertible Notes due 2013 (the Notes ), including \$15.0 million aggregate principal amount of the Notes sold pursuant to the underwriters' over-allotment option that was exercised in full. The Notes are governed by the terms of an indenture dated as of November 1, 2006 and a First Supplemental Indenture, dated as of December 12, 2006. The Notes bear interest at the rate of 3.75% per year on the principal amount of the Notes,

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payable in cash semi-annually in arrears on June 15 and December 15 of each year, beginning June 15, 2007. As of December 31, 2007, the Company had accrued interest of \$192,000 related to the Notes. The Notes are general, unsecured, senior obligations of the Company and effectively rank junior in right of payment to all of the Company's secured debt, to the extent of the value of the assets securing such debt, and to the debt and all other liabilities of the Company's subsidiaries. The maturity date of the Notes is December 15, 2013 and payment is due in full on that date for unconverted securities. Holders may convert, at any time prior to the close of business on the business day immediately preceding the stated maturity date, any outstanding Notes into shares of the Company's common stock at an initial conversion rate of 44.5002 shares per \$1,000 principal amount of Notes, which is equal to a conversion price of approximately \$22.47 per share, subject to adjustment. Except in certain circumstances, if the Company undergoes a fundamental change: (1) the Company will pay a make-whole premium on the Notes converted in connection with a fundamental change by increasing the conversion rate on such Notes, which amount, if any, will be based on the Company's common stock price and the effective date of the fundamental change, and (2) each holder of the Notes will have the option to require the Company to repurchase all or any portion of such holder's Notes at a repurchase price of 100% of the principal amount of the Notes to be repurchased plus accrued and unpaid interest, if any.

The Company incurred approximately \$3.7 million in debt issuance costs which are recorded as an offset to the debt in the accompanying balance sheet. These costs are being amortized to interest expense using the effective interest method over the term of the Notes.

**10. Common and preferred stock**

*Private Placements* On August 5, 2005, the Company closed a \$175.0 million private placement of common stock and the concurrent issuance of warrants for the purchase of additional shares of common stock to accredited investors including the Company's principal stockholder who purchased \$87.3 million of the private placement. The Company sold 17,132,000 shares of common stock in the private placement, together with warrants to purchase up to 3,426,000 shares of common stock at an exercise price of \$12.228 per share which became exercisable on February 1, 2006 and expire on August 5, 2010. In connection with this private placement, the Company paid \$4.5 million in commissions to the placement agents and incurred \$300,000 in other offering expenses which resulted in net proceeds of approximately \$170.2 million.

On October 2, 2007, the Company sold 15,940,489 shares of the Company's common stock to its principal stockholder at a price per share of \$9.41 and 11,074,197 million shares of common stock to other investors at a price per share of \$9.03. The sales of common stock resulted in aggregate net proceeds to the Company of approximately \$249.8 million after deducting offering expenses.

*Public Equity Offering* On December 12, 2006, the Company closed the sale of 20,000,000 shares of its common stock at a public offering price of \$17.42 per share and on December 19, 2006, closed the sale of an additional 3,000,000 shares of its common stock at a public offering price of \$17.42 per share pursuant to an over-allotment option granted to the underwriters of the offering. Approximately 5.8 million shares were sold to certain of the Company's officers and directors, including 5.75 million shares sold to the principal stockholder. In connection with this offering, the Company paid approximately \$15.0 million in underwriting fees and incurred approximately \$1.1 million in other offering expenses which resulted in net proceeds of approximately \$384.7 million.

*Common Stock* In May 2007, the Company's stockholders approved an increase in the Company's authorized shares of common stock from 90,000,000 to 150,000,000. As of December 31, 2007, 101,380,823 shares of common stock are issued and outstanding.

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The Company had reserved shares of common stock for issuance as follows:

	<b>December 31, 2006</b>	<b>December 31, 2007</b>
Exercise of common stock options	6,216,698	6,886,657
Conversion of senior convertible notes into common stock	5,117,523	5,117,523
Exercise of common stock warrants	2,895,332	2,882,873
Vesting of restricted stock units	776,653	1,359,662
	<b>15,006,206</b>	<b>16,246,715</b>

*Preferred Stock* The Company is authorized to issue 10,000,000 shares of preferred stock. As of December 31, 2007, no shares of preferred stock are issued and outstanding.

*Registration rights* In August 2007, the registration rights of the holders of 17,132,000 shares of common stock together with warrants to purchase up to 2,882,873 shares of common stock, all of which were issued in the August 2005 private placement, expired. All of the warrants remained outstanding as of December 31, 2007.

As of December 31, 2006 the holders of 916,715 shares of the Company's common stock and the holders of warrants to purchase 12,459 shares of the Company's common stock had rights, subject to some conditions, to require the Company to file registration statements covering the resale of their shares or to include their shares in registration statements that the Company may file for itself or other stockholders. All such rights expired on December 1, 2007. Additionally, the warrants to purchase 12,459 shares of common stock all expired, unexercised on December 1, 2007.

## **11. Stock award plans**

As of December 31, 2007, the Company has three active stock-based compensation plans—the 2004 Equity Incentive Plan (the Plan), the 2004 Non-Employee Directors' Stock Option Plan (the NED Plan), and the 2004 Employee Stock Purchase Plan (the ESPP). The Plan provides for the granting of stock awards including stock options and restricted stock units, to employees, directors and consultants. The NED Plan provides for the automatic, non-discretionary grant of options to the Company's non-employee directors. Awards also remain outstanding at December 31, 2007 under the following inactive plans: the 1999 Stock Plan, the CTL Plan, and the Allecure Plan. There are also options outstanding to our principal stockholder at December 31, 2007 that were not granted under any plan; these options were granted during the year ended December 31, 2002, vested over four years, and have an exercise price of \$25.23 per share. The following table summarizes information about our stock-based award plans as of December 31, 2007:

	<b>Outstanding Options</b>	<b>Outstanding Restricted Stock Units</b>	<b>Shares Available for Future Issuance</b>
--	--------------------------------	---	---

2004 Equity Incentive Plan	6,041,576	1,359,662	421,758
2004 Non-Employee Directors Stock Option Plan	447,500		352,500
1999 Stock Plan	122,314		
CTL and Allecure Plan	34,296		
Options outside of any plan granted to principal stockholder	240,972		
Total	6,886,658	1,359,662	774,258

The Company's board of directors determines eligibility, vesting schedules and exercise prices for stock awards granted under the Plan. The NED Plan provides for automatic, non-discretionary grant of options to the

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Company's non-employee directors. Options and other stock awards under the Plan and the NED Plan expire not more than ten years from the date of the grant and are exercisable upon vesting. Stock options generally vest over four years. Current stock option grants vest and become exercisable at the rate of 25% after one year and ratably on a monthly basis over a period of 36 months thereafter. Restricted stock units generally vest at a rate of 25% per year over four years with consideration satisfied by service to the Company. Certain performance-based awards vest upon achieving three pre-determined performance milestones which are expected to occur over periods ranging from 27 months to 42 months. The Plan provides for full acceleration of vesting if an employee is terminated within thirteen months of a change in control, as defined.

In March 2004, the Company's board of directors approved the 2004 Employee Stock Purchase Plan, which became effective upon the closing of the Company's initial public offering. Initially, the aggregate number of shares that could be sold under the plan was 2,000,000 shares of common stock. On January 1 of each year, for a period of ten years beginning January 1, 2005, the share reserve automatically increases by the lesser of: 700,000 shares, 1% of the total number of shares of common stock outstanding on that date, or an amount as may be determined by the board of directors. However, under no event can the annual increase cause the total number of shares reserved under the purchase plan to exceed 10% of the total number of shares of capital stock outstanding on December 31 of the prior year. On January 1, 2006, 2007, and 2008 the purchase plan share reserve was increased by 503,141, 700,000 and 700,000 shares, respectively. In November 2006, the Company's board of directors approved a decrease of 2.6 million shares to the reserve in order to make additional shares available for the Company's December 2006 offerings (see Note 1 Description of Business and Basis of Presentation Public Offerings). As of December 31, 2007, 626,805 shares were available for issuance under the plan. For the years ended December 31, 2005, 2006, and 2007 the Company sold 57,642, 86,093, and 124,011 shares, respectively, of its common stock to employees participating in the plan.

On January 1, 2006, the Company adopted the provisions of SFAS No. 123R ( SFAS No. 123R ), *Share-based Payment*, which is a revision of SFAS No. 123 ( SFAS No. 123 ), *Accounting for Stock-Based Compensation*. Prior to January 1, 2006, the Company accounted for employee stock options and the employee stock purchase plan using the intrinsic value method in accordance with Accounting Principles Board ( APB ) Opinion No. 25 ( APB No. 25 ), *Accounting for Stock Issued to Employees*, and adopted the disclosure only alternative of SFAS No. 123. Accordingly, prior to January 1, 2006, no compensation expense was recorded for options issued to employees with fixed option quantities and fixed exercise prices which were at least equal to the fair value of the Company's common stock at the date of grant. Conversely, when the exercise price for accounting purposes was below fair value of the Company's common stock on the date of grant, a non-cash charge to compensation expense was recorded for the amount equal to the difference between the exercise price and the fair value ratably over the term of the option vesting period. SFAS No. 123R eliminated the intrinsic value method of accounting for stock options which the Company followed until December 31, 2005. Further, SFAS No. 123R requires all share-based payments to employees, including grants of stock options and the compensatory elements of employee stock purchase plans, to be recognized in the income statement based upon the fair value of the awards at the grant date.

Upon adoption of SFAS No. 123R, the Company selected the modified prospective transition method whereby unvested awards at the date of adoption as well as awards that are granted, modified, or settled after the date of adoption will be measured and accounted for in accordance with SFAS No. 123R. Measurement and attribution of compensation cost for awards unvested as of January 1, 2006 is based on the same estimate of the grant-date or modification-date fair value and the same attribution method (straight-line) used previously under SFAS No. 123.

On October 7, 2003, our board of directors approved a repricing program for certain outstanding options to purchase shares of our common stock granted under each of our stock plans. Compensation cost for all options repriced under the repricing program were remeasured on a quarterly basis until the adoption of SFAS No. 123R. For the year ended December 31, 2004, the Company recorded \$4.4 million in stock-based compensation expense

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related to the re-pricing program. For the year ended December 31, 2005, the Company recorded a decrease in stock-based compensation expense of approximately \$2.4 million relating to the re-pricing program.

Upon adoption of SFAS No. 123R, the Company continues to account for non-employee stock-based compensation expense based on the estimated fair value of the options, determined using the Black-Scholes option valuation model, in accordance with EITF No. 96-18, and amortizes such expense on a straight-line basis. In November 2004, pursuant to assignment agreements with two consultants, the Company issued 200 shares of its common stock under its 2004 Equity Incentive Plan. The Company agreed to issue 99,800 additional shares upon the achievement of certain milestones specified in consulting agreements and for the year ended December 31, 2004, the Company recorded approximately \$1.1 million in stock-based compensation expense related to these agreements. In November 2005, 39,800 of the 99,800 shares were issued to the consultants and the Company decreased stock-based compensation expense by approximately \$146,000 based on the fair market value of the shares when issued. In September 2007, the next milestone was considered probable and the Company decreased stock compensation expense by approximately \$115,000 based on the fair market value of the shares. In October 2007, the milestone was met and 30,000 shares were issued. In December 2007, the third milestone was considered probable of achievement and the Company recognized stock compensation expense of approximately \$238,000. In January 2008, the final milestone was met and 30,000 shares were issued. As of December 31, 2007, there were 448,380 options outstanding to consultants.

During the years ended December 31, 2006 and 2007, the Company recorded stock-based compensation expense related to its stock award plans and the ESPP of \$14.7 million and \$17.6 million, respectively. The following table presents stock-based compensation expense included in operating expenses and the pro forma stock-based compensation amounts that would have been included in the statements of operations for the year ended December 31, 2005 had stock-based compensation expense been determined in accordance with the fair value method prescribed by SFAS No. 123 (in thousands, except per share data):

	<b>Year Ended December 31, 2005</b>
Stock-based employee compensation expense determined under the fair value based method for all awards	\$ 13,162
Fair value of discount on employee stock purchase plan	290
Total stock-based employee compensation expense	\$ 13,452
Net loss as reported	\$ 114,338
Stock-based employee compensation benefit included in reported net loss	1,892
Total stock-based employee compensation expense determined under the fair value based method for all awards	13,452
Net loss applicable to common stockholders pro forma	\$ 129,682
Basic and diluted loss applicable to common stockholders per share, as reported	\$ 2.87



Basic and diluted loss applicable to common stockholders per share, pro forma	\$	3.25
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Total stock-based compensation expense/(benefit) recognized in the accompanying statements of operations is as follows (in thousands):

	<b>Year Ended December 31,</b>		
	<b>2005</b>	<b>2006</b>	<b>2007</b>
Employee-related	\$ (1,892)	\$ 14,387	\$ 17,513
Consultant-related	164	280	132
Total	\$ (1,728)	\$ 14,667	\$ 17,645

Total stock-based compensation expense/(benefit) recognized in the accompanying statements of operations is included in the following categories (in thousands):

	<b>Year Ended December 31,</b>		
	<b>2005</b>	<b>2006</b>	<b>2007</b>
Research and development	\$ (320)	\$ 7,140	\$ 9,749
General and administrative	(1,408)	7,527	7,896
Total	\$ (1,728)	\$ 14,667	\$ 17,645

Included in stock compensation expense is approximately \$1.2 million in expense related to the modification of stock awards for five individuals during the year ended December 31, 2007. Under the terms of their modification of stock awards, these individuals' options that were granted during their association with the Company will continue to vest over their respective modification periods. Due to the nature of the modification agreements, one hundred percent of the incremental expense related to the award modifications were expensed during the year ended December 31, 2007.

The Company uses the Black-Scholes option valuation model to estimate the grant date fair value of employee stock options. The expected life of the option is estimated using the simplified method as provided in SEC Staff Accounting Bulletin No. 107 (SAB No. 107). Under this method, the expected life equals the arithmetic average of the vesting term and the original contractual term of the options. The Company also estimates volatility as provided in SAB 107. Under this method, volatility is estimated based on the historical volatility of similar entities whose share prices are publicly available. The Company has selected risk-free interest rates based on U.S. Treasury Securities with an equivalent expected term in effect on the date the options were granted. Additionally, the Company uses historical data and management judgment to estimate stock option exercise behavior and employee turnover rates to estimate the number of stock option awards that will eventually vest. The Company calculated the fair value of employee stock options for the years ended December 31, 2006 and 2007 using the following assumptions:

	<b>Year Ended December 31,</b>			
	<b>2006</b>		<b>2007</b>	
Risk-free interest rate	4.54%	4.96%	4.03%	4.80%
Expected lives	6.1	6.6 years	5.9	6.2 years
Volatility	56%	63%	51%	57%
Dividends				

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Prior to January 1, 2006, under SFAS No. 123, the Company estimated the fair value of each stock option at the grant date or modification date, if any, using the Black-Scholes option valuation model with the following assumptions:

	<b>Year Ended December 31, 2005</b>	
Risk-free interest rate	3.43%	4.49%
Expected lives	4.0 years	
Volatility	100%	
Dividends		

The following table summarizes information about stock options outstanding:

	<b>Number of Shares</b>	<b>Weighted Average Exercise Price per Share</b>	<b>Weighted Average Grant Date Fair Value per Share</b>	<b>Aggregate Intrinsic Value (\$000)</b>
Outstanding at January 1, 2005	4,067,979	\$ 12.19		
Granted	1,634,679	12.03	\$ 8.14	
Exercised	(304,555)	6.42		\$ 1,318
Forfeit	(379,850)	13.04		
Expired	(32,422)	16.02		
Outstanding at December 31, 2005	4,985,831	12.40		
Granted	1,792,525	17.51	\$ 10.41	
Exercised	(262,987)	8.79		\$ 2,523
Forfeit	(250,216)	13.25		
Expired	(48,455)	17.94		
Outstanding at December 31, 2006	6,216,698	13.94		
Granted	1,639,845	10.48	\$ 5.86	
Exercised	(606,833)	8.11		\$ 1,252
Forfeit	(252,016)	14.11		
Expired	(111,036)	12.66		
Outstanding at December 31, 2007	6,886,658	13.64		\$ 381

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Vested or expected to vest at December 31, 2007	6,573,773	13.66	\$	381
Exercisable at December 31, 2007	3,290,292	14.08	\$	381

Cash received from the exercise of options during the years ended December 31, 2005, 2006, and 2007 was approximately \$2.0 million, \$2.3 million, and \$4.9 million respectively. The weighted-average remaining contractual terms for options outstanding, vested or expected to vest, and exercisable at December 31, 2007 was 7.5 years, 7.4, and 6.3 years, respectively.

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A summary of restricted stock units activity for the years ended December 31, 2005, 2006 and 2007 is presented below:

	<b>Number of Shares</b>	<b>Weighted Average Grant Date Fair Value per Share</b>
Outstanding at January 1, 2005		
Granted	165,354	\$ 11.00
Forfeited	(453)	
Outstanding at December 31, 2005	164,901	
Granted	773,713	17.02
Vested	(135,744)	
Forfeited	(26,217)	
Outstanding at December 31, 2006	776,653	16.26
Granted	876,575	9.81
Vested	(202,009)	15.63
Forfeited	(91,557)	13.54
Outstanding at December 31, 2007	1,359,662	12.36

The total fair value of restricted stock units vested during the years ended December 31, 2006 and 2007 was \$2.5 million and \$1.9 million, respectively. The weighted-average remaining contractual terms for restricted stock units outstanding at December 31, 2007 was 9.0 years. As of December 31, 2007, there were 22,188 restricted stock units outstanding to two consultants.

A summary of the status of the Company's nonvested stock options for the year ended December 31, 2007, is presented below:

	<b>Number of Shares</b>	<b>Weighted Average Grant Date Fair Value per Share</b>
Nonvested at January 1, 2007	3,462,549	\$ 12.96
Granted	1,639,845	5.86

Vested	(1,254,012)	9.83
Forfeited	(252,017)	8.95
Nonvested at December 31, 2007	3,596,365	8.02

As of December 31, 2007, there was \$24.1 million and \$14.7 million of unrecognized compensation cost related to options and restricted stock units, respectively, which is expected to be recognized over the weighted average vesting period of 2.4 years.

## 12. Warrants

During 1995 and 1996, the Company issued warrants to purchase shares of common stock. The warrants contain provisions for the adjustment of the exercise price and the number of shares issuable upon the exercise of the warrant in the event the Company declares any stock dividends or effects any stock split, reclassification or consolidation of its common stock. The warrants also contain a provision that provides for an adjustment to the

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exercise price and the number of shares issuable in the event that the Company issues securities for a per share price less than a specified price. As of December 31, 2004, warrants to purchase 131,628 shares of common stock were outstanding. During the second quarter ended June 30, 2005, warrants to purchase 110,888 shares of common stock were exchanged for 24,210 shares of common stock resulting in stock-based compensation expense of \$245,000 based on a fair market value of the common stock of \$10.12 per share. Warrants to purchase 8,304 shares of common stock expired during 2005. The remaining warrants to purchase 12,459 shares of common stock at a weighted average exercise price of \$12.64 per share all expired unexercised on December 1, 2007.

In connection with the sale of common stock in the private placement which closed on August 5, 2005, the Company concurrently issued warrants to purchase up to 3,426,000 shares of common stock at an exercise price of \$12.228 per share. See also Note 10 Common and Preferred Stock Private Placement. These warrants became exercisable on February 1, 2006 and expire in August 2010. During the year ended December 31, 2006, approximately 543,000 warrants were exercised and net settled for approximately 339,000 shares. As of December 31, 2007, warrants to purchase 2,882,873 shares of common stock remained outstanding. In connection with the sale of common stock in the public offering that closed on December 6, 2006, two holders of outstanding warrants to purchase a total of 1,710,091 shares of common stock agreed to amend the terms of their warrants to provide that such warrants would not be exercisable from December 6, 2006 until the date on which the Company has at least 100,000,000 shares of its common stock duly and validly authorized. In May 2007, the Company's stockholders approved an increase in the Company's authorized shares of common stock from 90,000,000 to 150,000,000. Accordingly, as of December 31, 2007, all warrants were exercisable.

**13. Commitments and contingencies**

*Operating Leases* The Company leases certain facilities and equipment under various operating leases, which expire at various dates through 2010. Future minimum rental payments required under operating leases are as follows at December 31, 2007 (in thousands):

**Year Ending December 31,**

2008	\$ 1,693
2009	1,883
2010	768
After 2010	
Total minimum lease payments	\$ 4,344

Rent expense under all operating leases for the years ended December 31, 2005, 2006 and 2007 was approximately, \$1.1 million, \$1.3 million, and \$1.5 million, respectively.

*Capital Leases* The Company's capital leases were not material for the years ended December 31, 2005, 2006 and 2007.



*Supply Agreement* In November 2007, the Company entered into a long-term supply agreement with Organon pursuant to which Organon will manufacture and supply specified quantities of recombinant human insulin. The initial term of this supply agreement will end on December 31, 2012 and can be automatically extended for consecutive two-year terms under specified circumstances. The Company has made annual purchase commitments through the initial term. If the Company terminates the supply agreement following failure to obtain or maintain regulatory approval of the Technosphere Insulin System or either party terminates the agreement following the parties' inability to agree after any regulatory authority mandated changes to product specifications that relate specifically to the use of insulin in Technosphere Insulin, the Company will be required to pay Organon a specified termination fee if Organon is unable to sell certain quantities of insulin to other parties.

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*Guarantees and Indemnifications* In the ordinary course of its business, the Company makes certain indemnities, commitments and guarantees under which it may be required to make payments in relation to certain transactions. The Company, as permitted under Delaware law and in accordance with its Bylaws, indemnifies its officers and directors for certain events or occurrences, subject to certain limits, while the officer or director is or was serving at the Company's request in such capacity. The term of the indemnification period is for the officer's or director's lifetime. The maximum amount of potential future indemnification is unlimited; however, the Company has a director and officer insurance policy that may enable it to recover a portion of any future amounts paid. The Company believes the fair value of these indemnification agreements is minimal. The Company has not recorded any liability for these indemnities in the accompanying consolidated balance sheets. However, the Company accrues for losses for any known contingent liability, including those that may arise from indemnification provisions, when future payment is probable. No such losses have been recorded to date.

*Litigation* The Company is involved in various legal proceedings and other matters. In accordance with SFAS No. 5, *Accounting for Contingencies*, the Company would record a provision for a liability when it is both probable that a liability has been incurred and the amount of the loss can be reasonably estimated.

In May 2005, the Company's former Chief Medical Officer filed a complaint against the Company in the California Superior Court, County of Los Angeles, alleging causes of action for wrongful termination in violation of public policy, breach of contract and retaliation. A trial on the claims remaining after pre-trial proceedings began on April 30, 2007 and concluded on June 5, 2007. On June 15, 2007, the Company announced the dismissal of the complaint.

In 2000, the Company issued 699,972 shares of common stock to three consultants in exchange for notes receivable aggregating approximately \$10.9 million. The fixed interest bearing notes were collateralized by the underlying common stock. The notes-for-stock transactions were accounted for as in-substance stock option grants to non-employees. In November 2004, the consultants informed the Company that they had entered into an agreement in October 2001 with Alfred E. Mann, the Company's chairman, chief executive officer and principal stockholder, under which Mr. Mann would purchase a portion of the consultants' common stock, and that the Company was to apply the proceeds to the amounts owed under the consultants' respective notes. The consultants informed the Company that they believed both the Company and Mr. Mann were in breach of the alleged agreement, and indicated their intent to seek alleged damages arising from the Company's failure to perform the alleged agreement. On October 19, 2005, the principal and interest on the notes aggregating \$14.6 million became due and payable and the Company pursued collection. On November 21, 2005, the consultants filed a complaint against the Company in the California Superior Court, County of Los Angeles, *Rollins et al. v. MannKind et al*, Case No. BC343381. The complaint alleges causes of action for breach of the above mentioned agreement, among other things. On January 19, 2006, the parties mediated and settled the case. Under the settlement, the Company repurchased 620,697 shares from the consultants in full satisfaction of the notes. These shares were tendered and cancelled on February 3, 2006. The Company also agreed to repurchase the remaining 79,275 shares held by the consultants for \$1.4 million in cash. The settlement was reflected as a \$1.4 million charge to general and administrative expense in the fourth quarter of the year ended December 31, 2005 with a corresponding amount payable included in accrued expenses and other current liabilities as of December 31, 2005. On February 21, 2006, the Company received and cancelled the 79,275 shares, and paid the purchase price of \$1.4 million to the consultants. The complaint has been dismissed in its entirety with prejudice.

In September and October 2005, the principal and interest totaling \$1.6 million on notes issued in exchange for approximately 78,000 shares of common stock to a former executive of the Company became due and payable to the Company. On December 31, 2005, the 78,000 shares of common stock issued in exchange for the notes receivable had a market value of approximately \$878,000.

The Company pursued collection. On January 31, 2006, former executive tendered 143,949 shares as full repayment of the notes in default and an additional note due in April 2006 issued in exchange for approximately

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32,000 shares of common stock. The 143,949 shares were valued at \$2.6 million on January 31, 2006 and represented principal and interest due through that date on all notes. The Company received and cancelled these shares on January 31, 2006.

*Licensing Arrangement* On October 12, 2006, the Company entered into an agreement with The Technion Research and Development Foundation Ltd. ( TRDF ), an Israeli corporation affiliated with the Technion-Israel Institute of Technology (the Technion ) to license certain technology from TRDF and to collaborate with TRDF in the further research in and the development and commercialization of such technology. In exchange for the rights that the Company obtained under this agreement, the Company agreed to pay to TRDF aggregate license fees of \$3.0 million and to issue to TRDF a total of 300,000 shares of the Company s common stock. The license fees will be paid and the shares issued in three equal installments. The first installment occurred on October 18, 2006. The second installment was paid on December 3, 2007. The third installment will occur, subject to the accomplishment of certain milestones, on October 12, 2008. The Company has also agreed to pay royalties to TRDF with respect to sales of certain products that contain or use the licensed technology or are covered by patents included in the licensed technology or are discovered through the use of the licensed technology. The Company agreed to pay up to \$6.0 million of the royalties in advance upon the receipt of specified regulatory approvals. The Company agreed to pay to TRDF specified percentages of any lump-sum sub-license payments that the Company receives if it decides to sub-license the technology. The Company has also agreed to pay a total of \$2.0 million to TRDF in three nearly equal installments to fund sponsored research to be conducted at TRDF by a team led by a faculty member at the Technion. The initial sponsored research payment was made upon signing of the agreement. The second sponsored research payment occurred on December 3, 2007 and the third sponsored research payment will occur, subject to the accomplishment of certain milestones, on October 12, 2008. The Company also agreed to retain the services of the Technion faculty member as a consultant, for which the Company agrees to pay the consultant \$60,000 per year and granted the individual an option to purchase 60,000 shares of the Company s common stock. Under the terms of the agreement, the Company issued 100,000 shares of common stock to TRDF on October 12, 2006 and November 29, 2007, respectively. Additionally, \$1.6 million in license fees were paid on October 18, 2006 and December 3, 2007, respectively.

**14. Employee benefit plans**

The Company administers a 401(k) Savings Retirement Plan (the MannKind Retirement Plan ) for its employees. For the years ended December 31, 2005, 2006 and 2007, the Company contributed \$372,000, \$567,000 and \$821,000 respectively, to the MannKind Retirement Plan.

**15. Income taxes**

Deferred income taxes reflect the tax effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting and income tax purposes. A valuation allowance is established when

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uncertainty exists as to whether all or a portion of the net deferred tax assets will be realized. Components of the net deferred tax asset as of December 31, 2006 and 2007 are approximately as follows (in thousands):

	<b>December 31,</b>	
	<b>2006</b>	<b>2007</b>
Deferred Tax Assets:		
Net operating loss carryforwards	\$ 220,643	\$ 317,939
Research and development credits	7,971	25,677
Accrued expenses	14,509	29,036
Non-qualified stock option expense	7,723	13,175
Depreciation	1,197	1,626
Total gross deferred tax assets	252,043	387,453
Valuation allowance	(252,043)	(387,453)
Net deferred tax assets	\$	\$

The Company's effective income tax rate differs from the statutory federal income tax rate as follows for the years ended December 31, 2005, 2006 and 2007:

	<b>December 31,</b>		
	<b>2005</b>	<b>2006</b>	<b>2007</b>
Federal tax benefit rate	35.0%	35.0%	35.0%
State tax benefit, net of federal benefit			
Permanent items			
Other			
Valuation allowance	(35.0)	(35.0)	(35.0)
Effective income tax rate	0.0%	0.0%	0.0%

As required by SFAS No. 109, management of the Company has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets. Management has concluded, in accordance with the applicable accounting standards, that it is more likely than not that the Company may not realize the benefit of its deferred tax assets. Accordingly, the net deferred tax assets have been fully reserved. Management reevaluates the positive and negative evidence on an annual basis. During the years ended December 31, 2005, 2006 and 2007, the change in the valuation allowance was \$47.8 million, \$96.2 million and \$135.4 million respectively, for income taxes.

At December 31, 2007, the Company had federal and state net operating loss carryforwards of approximately \$851.2 million and \$361.5 million available, respectively, to reduce future taxable income and which will expire at various dates beginning in 2008 and 2012, respectively. As a result of the Company's initial public offering, an ownership change within the meaning of Internal Revenue Code Section 382 occurred in August 2004. As a result, federal net operating loss and credit carry forwards of approximately \$216.0 million are subject to an annual use limitation of approximately \$13.0 million. The annual limitation is cumulative and therefore, if not fully utilized in a year can be utilized in future years in addition to the Section 382 limitation for those years. The federal net operating losses generated subsequent to the Company's initial public offering in August 2004 are currently not subject to any such limitation as there have been no ownership changes since August 2004 within the meaning of Internal Revenue Code Section 382. At December 31, 2007, the Company had research and development credits of \$30.4 million that expire at various dates through 2028.

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The Company has evaluated the impact of FIN 48 on its financial statements, which was effective beginning January 1, 2007. The evaluation of a tax position in accordance with FIN 48 is a two-step process. The first step is recognition: The enterprise determines whether it is more-likely-than-not that a tax position will be sustained upon examination, including resolution of any related appeals or litigation processes, based on the technical merits of the position. In evaluating whether a tax position has met the more-likely-than-not recognition threshold, the enterprise should presume that the position will be examined by the appropriate taxing authority that would have full knowledge of all relevant information. The second step is measurement: A tax position that meets the more-likely-than-not recognition threshold is measured to determine the amount of benefit to recognize in the financial statements. The tax position is measured at the largest amount of benefit that is greater than 50 percent likely of being realized upon ultimate settlement. Tax positions that previously failed to meet the more-likely-than-not recognition threshold should be recognized in the first subsequent financial reporting period in which that threshold is met. Previously recognized tax positions that no longer meet the more-likely-than-not recognition threshold should be derecognized in the first subsequent financial reporting period in which that threshold is no longer met. The Company believes that its income tax filing positions and deductions will be sustained on audit and does not anticipate any adjustments that will result in a material change to its financial position. Therefore, no reserves for uncertain income tax positions have been recorded pursuant to FIN 48. The cumulative effect, if any, of applying FIN 48 is to be reported as an adjustment to the opening balance of retained earnings in the year of adoption. The Company did not record a cumulative effect adjustment related to the adoption of FIN 48. Tax years since 1992 remain subject to examination by the major tax jurisdictions in which the Company is subject to tax.

**16. Related party transactions**

The Company issued 8,550,446 shares of its common stock to its principal stockholder during the year ended December 31, 2005 for proceeds of approximately \$87.3 million. In connection with this issuance, the board of directors approved the issuance of warrants to purchase 1,710,091 shares of the Company's common stock at \$12.228 per share, which expire on August 2, 2010. The issuance of shares and warrants to the principal stockholder was on terms identical to the other purchasers in the private placement, as approved by the Company's board of directors.

During the year ended December 31, 2006 the principal stockholder purchased 5,750,000 shares of common stock at \$17.42 per share in the Company's December 2006 equity offering on terms identical to other purchasers resulting in proceeds of approximately \$100.1 million to the Company. In connection with the equity offering the Company paid \$280,000 in filing fees related to the principal stockholder's filings made pursuant to the Hart-Scott-Rodino Antitrust Improvement Act of 1976. During the year ended December 31, 2006, the Company borrowed \$70.0 million from its principal stockholder under the loan arrangement described in Note 8. On December 12, 2006, in connection with the completion of their equity and convertible debt offerings, the Company paid principal and interest of \$70.0 million and \$1.6 million, respectively, under the loan arrangement.

On October 2, 2007, the Company sold 15.9 million shares of the Company's common stock to its principal stockholder at a price per share of \$9.41 and 11.1 million shares of common stock to other investors at a price per share of \$9.03. The sales of common stock resulted in aggregate net proceeds to the Company of approximately \$249.8 million after deducting offering expenses. Also, on October 2, 2007, the Company entered into a new loan arrangement with its principal stockholder to borrow up to a total of \$350.0 million before January 1, 2010. This new arrangement replaced the existing loan arrangement with its principal stockholder to borrow up to \$150.0 million through August 1, 2008. See Note 8 Related-Party Loan Arrangement.

Alfred E. Mann, our principal stockholder and chief executive officer, has established the Alfred Mann Institute for Biomedical Development at the Technion ( AMI-Technion ) to expedite the translation of intellectual property and technology of the Technion into commercial medical products for the public benefit. Over a period of several years, Mr. Mann will establish a \$100 million endowment for AMI-Technion. Mr. Mann does not directly or



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**NOTES TO FINANCIAL STATEMENTS (Continued)**

indirectly have any interest in TRDF (see Note 13 Commitments and Contingencies Licensing Arrangement).

On January 19, 2006, the Company settled a claim filed by three consultants related to certain notes-for-stock transactions (see Note 13 Commitments and Contingencies Litigation).

In connection with certain meetings of the Company's board of directors and on other occasions when the Company's business necessitated air travel for the Company's principal stockholder and other Company employees, the Company utilized the principal stockholder's private aircraft, and the Company paid the charter company that manages the aircraft on behalf of the Company's majority stockholder approximately \$62,000, \$212,000, and \$105,090, respectively, for the years ended December 31, 2005, 2006 and 2007 on the basis of the corresponding cost of commercial airfare. These payments were approved by the audit committee of the board of directors.

Heather Hay Murren, a member of our board of directors, is the Cofounder, Chair and Chief Executive Officer of Nevada Cancer Institute, a nonprofit organization. Nevada Cancer Institute is currently conducting a clinical trial for the Company through a clinical research organization and was paid approximately \$10,000 for the year ended December 31, 2007 by the clinical research organization.

The Company has entered into indemnification agreements with each of its directors and executive officers, in addition to the indemnification provided for in its amended and restated certificate of incorporation and amended and restated bylaws (see Note 13 Commitments and Contingencies Guarantees and Indemnifications).

**17. Subsequent events**

On January 30, 2008, the Company's board of directors approved an amendment to the 2004 Equity Incentive Plan to increase the number of shares of common stock available for issuance under the plan by 5,000,000 shares.

On February 6, 2008, the Compensation Committee approved a management proposal designed to encourage employee retention. The proposal involved the issuance of restricted stock units to the majority of employees and executive officers of the Company. A total of 1,678,674 restricted stock units were granted under the 2004 Equity Incentive Plan. These units will remain unvested until June 30, 2009, at which point they will fully vest. Stock compensation expense associated with this grant will be recorded on a straight line basis from February 6, 2008 through June 30, 2009 and is estimated to total approximately \$11.0 million.

On February 8, 2008, the Company closed a transaction to purchase seven patents and one patent application from Emisphere Technologies, Inc. for \$2.5 million. The patents relate to diketopiperazine delivery systems. The purchase price will be paid in three installments. The first payment of \$1.5 million towards the acquisition price was paid on February 11, 2008. An additional \$500,000 will be paid on the earlier of the filing of a new drug application, or NDA, with the United States Food and Drug Administration, or FDA for Technosphere Insulin or June 30, 2009. The remaining \$500,000 will be paid on the earlier of the final FDA approval of the NDA or September 30, 2010.

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**MANNKIND CORPORATION AND SUBSIDIARIES**  
**(A Development Stage Company)**

**NOTES TO FINANCIAL STATEMENTS (Continued)**

**18. Selected quarterly financial data (unaudited)**

	<b>March 31</b>	<b>June 30</b>	<b>September 30</b>	<b>December 31</b>
	<b>(In thousands, except per share data)</b>			
<b>2006</b>				
Net loss	\$ (43,559)	\$ (54,751)	\$ (60,970)	\$ (71,268)
Net loss applicable to common stockholders	\$ (43,559)	\$ (54,751)	\$ (60,970)	\$ (71,268)
Net loss per share applicable to common stockholders basic and diluted	\$ (0.87)	\$ (1.10)	\$ (1.23)	\$ (1.30)
Weighted average common shares used to compute basic and diluted net loss per share applicable to common stockholders	49,787	49,638	49,731	54,684

	<b>March 31</b>	<b>June 30</b>	<b>September 30</b>	<b>December 31</b>
	<b>(In thousands, except per share data)</b>			
<b>2007</b>				
Net loss	\$ (73,141)	\$ (71,989)	\$ (73,047)	\$ (75,013)
Net loss applicable to common stockholders	\$ (73,141)	\$ (71,989)	\$ (73,047)	\$ (75,013)
Net loss per share applicable to common stockholders basic and diluted	\$ (1.00)	\$ (0.98)	\$ (0.99)	\$ (0.75)
Weighted average common shares used to compute basic and diluted net loss per share applicable to common stockholders	73,388	73,421	73,520	99,605