**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, 2004

or

o **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** | **13-3607736** |
|---|---|
| (State or other jurisdiction of incorporation or organization) | (I.R.S. Employer Identification No.) |
| **28903 North Avenue Paine**<br>**Valencia, California** | **91355** |
| (Address of principal executive offices) | (Zip Code) |

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

Securities registered pursuant to Section 12(b) of the Act:
**None**

Securities registered pursuant to Section 12(g) of the Act:
**Common Stock, par value 0.01 per share**
(Title of class)

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 o

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. o

Indicate by check mark whether the registrant is an accelerated filer (as defined in Rule 12b-2 of the Act). Yes o No ☑

As of December 31, 2004, 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 National Market, was approximately $265,075,256. The registrant has elected to use December 31, 2004 as the calculation date because on June 30, 2004 (the last business date of the registrant's second fiscal quarter) the registrant was a privately held concern.

As of February 28, 2005, there were 32,768,753 shares of the registrant's Common Stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE:

Portions of the registrant's definitive Proxy Statement for the 2005 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 Form 10-K.

**MANNKIND CORPORATION**
**Annual Report on Form 10-K**
**For the Fiscal Year Ended December 31, 2004**

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**Forward-Looking Statements**

Statements in this annual report on Form 10-K 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; and our estimates regarding anticipated operating losses, future revenues, capital requirements and our needs for additional financing. In some cases, you can identify forward-looking statements by terms such as “anticipates,” “believes,” “could,” “estimates,” “expects,” “intends,” “may,” “plans,” “potential,” “predicts,” “projects,” “should,” “will,” “would,” “goal,” and similar expressions intended to identify forward-looking statements. These statements are only predictions 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 annual report on Form 10-K. 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.

## 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. Technospherc® and MedTone® are our registered trademark 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.

**OVERVIEW**

MannKind Corporation is a biopharmaceutical company focused on the discovery, development and commercialization of therapeutic products for diseases such as diabetes and cancer. We recently commenced Phase 3 clinical trials in Europe of our lead product, the Technosphere Insulin System, to study its potential for the treatment of diabetes. This therapy consists of a proprietary dry powder Technosphere formulation of insulin that is inhaled into the deep lung using our 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.

In our clinical trials to date, we have observed that our Technosphere Insulin System 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 all patients with diabetes. As a result, we believe that our Technosphere Insulin System will be beneficial not only for insulin-using diabetes patients but also for patients with type 2 diabetes who are currently using conventional therapies other than insulin. If further clinical trials support our initial observations, we believe the Technosphere Insulin System has the potential to be indicated for the treatment of type 2 diabetes after a patient has failed to respond adequately to diet and exercise. The use of insulin earlier in the progression of diabetes would represent a paradigm shift in the treatment of this disease.

To date, we have conducted multiple Phase 1 and Phase 2 clinical trials of our Technosphere Insulin System in Europe and the United States, which have involved more than 450 individuals and over 37,000 patient-days of home use. In a recently completed US Phase 2 clinical trial, the use of Technosphere Insulin at mealtimes significantly lowered blood glucose levels in patients with type 2 diabetes who previously were experiencing inadequate control of their disease. Even in patients with only mildly elevated blood glucose levels, we observed in this study that the typical risks of frequent or severe hypoglycemia generally associated with insulin therapy appear not to be associated with Technosphere Insulin, suggesting that our therapy may have a significant safety advantage over other currently available insulin therapies.

We are currently conducting a Phase 2 dosage-tolerance study and a Phase 3 efficacy study of the Technosphere Insulin System, which we anticipate will involve a total of approximately 500 individuals with type 2 diabetes. Both of these studies are taking place in Europe. We intend to initiate Phase 3 clinical trials in the United States by mid-2005, subject to our obtaining a satisfactory FDA review of our Phase 3 protocols. We anticipate that our entire clinical trial program will involve more than 3,000 patients using the Technosphere Insulin System alone or in combination with other therapies. In the United States, we have initiated one of several planned long-term safety trials involving individuals who participate in our Phase 2 and Phase 3 clinical trials. Based on our discussions with the FDA, we plan to accumulate two years of controlled safety data from patients with type 1 diabetes as well as type 2 diabetes before we file a new drug application for the Technosphere Insulin System.

Larger populations and longer durations of exposure may be necessary depending on the safety profile of our product.

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. We are in the process of developing additional Technosphere-based products for the delivery of other drugs.

We were incorporated in the State of Delaware on February 14, 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 filed with or furnished to the SEC.

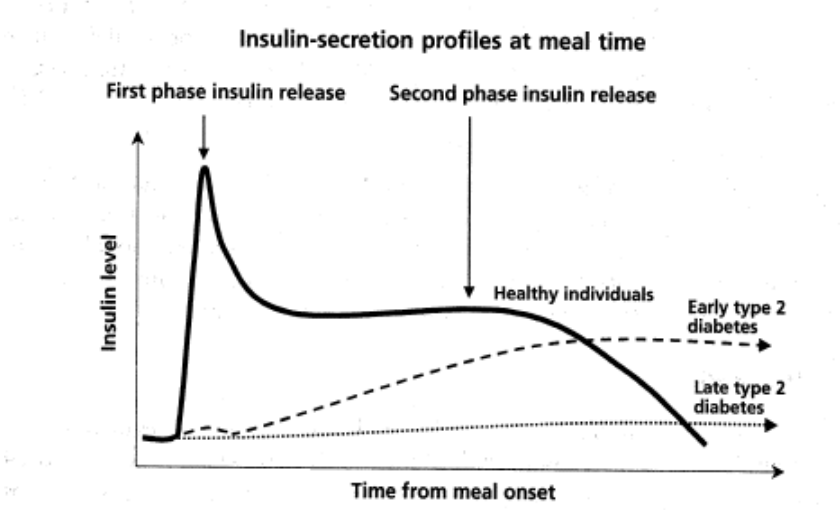
**OVERVIEW OF DIABETES**

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 utilize glucose as fuel, which is consumed 24 hours a 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 lowered resistance to infectious diseases, blindness, loss of circulation, kidney failure, impotence, heart attack, stroke and death.

According to the American Diabetes Association, or ADA, in the United States diabetes is estimated to cost society over $132 billion each year and is currently the fifth leading cause of death by disease. Data from the United States Centers for Disease Control, or CDC, and the National Institutes of Health indicate that the risk of death due to heart disease and the risk of stroke are up to four times higher in adults with diabetes than in those without the disease. Diabetes is the leading cause of new cases of blindness among adults, kidney disease and non-traumatic lower-limb amputations. The CDC estimated that, as of 2002, approximately 18.2 million people in the United States, or 6.3% of the population, suffered from diabetes. The CDC further estimated that 13 million cases were diagnosed and under treatment as of 2002 and that 1.3 million new cases would be diagnosed per year beyond that date. The ADA estimated that, in 2002, the direct costs for required drug treatment of diabetes in the United States were approximately $12 billion, of which approximately $7 billion were for insulin and delivery supplies and approximately $5 billion were for non-insulin oral medications.

There are two major forms of diabetes, type 1 and type 2. Type 1 diabetes is characterized by a complete lack 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, over time it becomes increasingly 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.

The illustration below summarizes reports published in the *New England Journal of Medicine* and the *American Journal of Medicine* of the insulin-secretion profiles at meal time of healthy individuals and of patients with type 2 diabetes. When a healthy person begins to eat a meal, the pancreas responds with the two phases of insulin release into the bloodstream that are depicted by the solid line in the illustration below. The first-phase of insulin release takes the form of a sharply-rising spike in insulin that acts as a signal to the liver to shut off its release of glucose into the bloodstream. In the second phase of insulin release, the pancreas secretes an extended wave of insulin that acts on cells throughout the body, enabling them to absorb the glucose ingested from the meal.




As depicted by the dashed line in the illustration, individuals with early type 2 diabetes cannot produce the first-phase insulin release spike and, as a result, their livers continue to release glucose while they absorb additional glucose from the meal. This can worsen high blood sugar levels. This state forces the pancreas to compensate by secreting excessive amounts of insulin during the second phase. Over time, this repeated cycle of inadequate early release followed by over-insulinization is correlated with subsequent exhaustion of the overall ability of the pancreas to secrete adequate amounts of insulin following a meal, which is depicted by the

dotted line in the illustration. This situation is further complicated by a decline in the ability of insulin-sensitive cells throughout the body to respond to insulin — a state known as insulin resistance. The inability to maintain control over blood glucose levels predisposes the patient with diabetes to serious, adverse health consequences.

**Challenges of treating type 2 diabetes**

Typically, the treatment of type 2 diabetes starts with management by diet and exercise and progresses to treatment with various non-insulin oral medications and then to treatment with insulin. Treatment through diet and exercise alone has not been an effective long-term solution for most patients with type 2 diabetes. Non-insulin oral medications, which act by increasing the amount of insulin produced by the pancreas or by increasing the sensitivity of insulin-sensitive cells, generally have significant adverse effects and are limited in their ability to manage the disease effectively.

Insulin therapy usually involves administering several subcutaneous needle injections of insulin each day. Although this treatment regimen is accepted as effective, it has many limitations, including:

- Patients dislike injecting themselves with insulin due to inconvenience and pain, and so tend not to comply adequately with prescribed treatment regimens. As a result, they do not properly medicate themselves.

- Even when properly administered, subcutaneous injections of insulin do not replicate the natural first-phase insulin spike. Instead, 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 “rapid-acting” insulin analogs. The consequence is for patients with diabetes to have inadequate levels of insulin present at the initiation of a meal and to be over-insulinized between meals. This results in high blood glucose levels early after meal onset, followed by a tendency for glucose to fall to abnormally low levels, a state known as hypoglycemia, during the period between meals. 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.

Because of the problems associated with the conventional administration of insulin by injection, patients and their physicians have sought alternative methods for the delivery of insulin. One such alternative being pursued by several pharmaceutical and biotechnology companies is the inhalation of an insulin formulation into the deep lung, where it can be absorbed directly into the bloodstream. Delivering insulin through the pulmonary route is less invasive than administering it by injection and, according to a 2001 study reported in *Diabetes Care*, is associated with greater patient satisfaction, which should increase patient compliance and lead to better glucose control.

We anticipate that the first pulmonary insulin product being developed by another pharmaceutical company may be approved for commercial sale as early as 2006. Although this and other competing pulmonary insulin products in development will address the inconvenience of conventional insulin therapy, we do not believe they will deliver insulin to the bloodstream any more rapidly than can be obtained from existing therapies. A 2004 review article in the *British Journal of Diabetes and Vascular Diseases* surveyed the data published on pulmonary insulin products in development and reported that these surveyed products are associated with an onset of action that is similar to “rapid-acting” insulin analogs, which are variations of insulin that gradually rise to reach peak blood levels within 30 to 90 minutes of injection. 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.

**THE MANNKIND SOLUTION**

Based on our clinical data, we believe our Technosphere Insulin System, if and when approved by the FDA, will be the first commercially available therapy that produces a profile of insulin levels in the bloodstream that approximates the natural first-phase insulin release spike normally seen in healthy individuals following the beginning of a meal. We believe that this is one of several significant, differentiating performance characteristics of our pulmonary insulin system, as described in more detail below.

**Approximates natural first-phase insulin release spike**

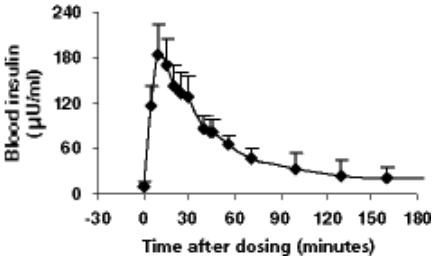
We believe a major advantage of our Technosphere Insulin System is the speed with which the insulin is delivered to the patient’s bloodstream. Our clinical trials have shown that the Technosphere Insulin System produces peak insulin levels in 10 to 14 minutes after inhalation. This timing approximates the onset and rise of the natural first-phase insulin release spike, which generally occurs within five to ten minutes after food first reaches the digestive system. Because our product produces an early insulin profile that

resembles the profile seen in healthy individuals, we anticipate that our insulin therapy may be able to achieve better control over the patient's glucose levels throughout the day, especially following a meal.

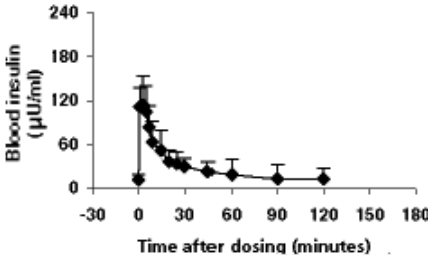
The clinical data below show the approximation of the first-phase insulin release spike in more detail. The chart on the left shows the mean changes in blood insulin levels of 12 patients with type 1 diabetes who inhaled a dose of our Technosphere Insulin prior to eating a standardized meal. For illustration purposes, we have shown data from a study of patients with type 1 diabetes, whom we studied in order to observe the response to administration of Technosphere Insulin without interference from the natural production of insulin. These results are typical of our observations recorded in the other clinical trials that we have completed, including trials involving patients with type 2 diabetes. Because different protocols are used for each clinical trial, it is not possible, nor would it be scientifically valid, for us to present blood insulin data aggregated across multiple trials. Moreover, not all of the clinical trials were designed to collect the kind of data presented in the chart below. However, the data presented below is consistent with the data obtained from each of our other clinical trials where comparable data was collected.

The key feature of the response shown on the left is the time taken for blood insulin levels to peak, which was approximately ten minutes in this study. The magnitude of the response is related to the dose of Technosphere Insulin administered; we have observed in our clinical trials that the timing of the response is consistent across a range of doses. For comparison purposes, these data are presented next to a chart that shows data published in 1981 in the *American Journal of Medicine* from nine healthy individuals who were rapidly administered a glucose solution intravenously — an experimental protocol that allowed investigators to evaluate the characteristics of the normal first-phase insulin release. These charts show that the rapid time-to-peak blood insulin levels produced by the Technosphere Insulin System in this study approximates the timing that has been demonstrated for first-phase insulin release in healthy individuals, which generally occurs within five to ten minutes after food first reaches the digestive system.

**Technosphere Insulin approximation of first-phase insulin release**




**First-phase insulin release in healthy individuals**




By approximating the first-phase insulin release spike, we expect that our Technosphere Insulin System will allow patients with some pancreatic function to achieve greater control over their glucose levels, which we expect may reduce exhaustion of insulin-secreting cells in the pancreas and possibly also reduce the degree of insulin resistance. We believe this effect would be beneficial in patients with type 2 diabetes who have advanced to the point of requiring conventional insulin therapy as well as in patients who are being treated with non-insulin oral medications and patients who are currently using diet and exercise therapy but who are having difficulty achieving proper glucose control. If further clinical trials confirm our observations to date, we believe our Technosphere Insulin System has the potential to be indicated for the treatment of type 2 diabetes after a patient has failed to respond adequately to diet and exercise. The use of insulin earlier in the progression of diabetes would represent a paradigm shift in the treatment of the disease.

**Convenience and ease of use**

Our Technosphere Insulin System is comprised of two components: our dry-powder Technosphere formulation technology and our MedTone inhaler through which the powder is delivered into the deep lung.

Our Technosphere formulation technology is centered on a class of pH-sensitive organic molecules that are designed to self-assemble into small carrier particles. Under mildly acidic conditions, these carrier particles assume a solid state, but at a more neutral pH they spontaneously dissociate into a liquid. Certain drugs, such as insulin, can be loaded onto these particles by combining mildly acidic solutions of the drug and the Technosphere material to form a mixture, which is then dried to form a powder. The structural characteristics of loaded Technosphere particles (i.e., particle size and surface topography) impart aerodynamic properties that enable them to fly deep into the lungs. Our pre-clinical studies suggest that Technosphere particles, unlike penetration enhancers, do not affect the tight junctions between cells, do not alter cell permeability and do not cause disruption of cell membranes. Instead, the Technosphere particles instantaneously change from a powder to a liquid upon contact with the neutral pH of the moist lung surface,allowing the drug to move rapidly down its concentration gradient into the bloodstream without any active assistance or enhancement.

We have observed that the carrier material also enters the bloodstream, but it is not metabolized and is rapidly excreted in the urine unchanged and with no accumulation.

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 powder deep into the lungs. The device incorporates an airflow regulator that is designed to ensure a consistent airflow from patient to patient and 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 multiple Phase 1 and Phase 2 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 the most convenient time for patients to take a dose of Technosphere Insulin is right at the start of a meal or shortly thereafter. In contrast, with subcutaneous injection, it is recommended that the user try to time a dose 15 to 45 minutes before the expected mealtime, raising issues such as miscalculation of time or unanticipated change in meal availability.

**More efficient delivery of pulmonary insulin**

Our Phase 1 and 2 clinical trials have indicated that the use of the Technosphere Insulin System is associated with high insulin bioavailability, which is a measure of the amount of insulin that is transferred to the bloodstream from the dosage form of the product. Bioavailability is typically expressed as a relative measure, compared to the amount of insulin that enters the bloodstream over the same period of time following the subcutaneous administration of the same quantity of regular human insulin. Based on the results of our clinical trials and on our analysis of published reports of the performance of other pulmonary insulin systems in development, we believe that the relative bioavailability associated with our Technosphere Insulin System is up to three times greater than that reported for the other inhaled insulin platforms.

**Safety**

To date, we have conducted Phase 1 and Phase 2 clinical trials in Europe and the United States, which have involved more than 450 individuals and over 37,000 patient-days of home use. We have seen a significantly reduced number of mild, moderate and severe hypoglycemic episodes associated with Technosphere Insulin compared with the incidence reported with use of other insulin products and oral agents to treat diabetes. In some patients, we have observed mild coughing, usually limited to the period when learning to use the inhalation technique. Other adverse events reported in our clinical trials—including backache, common cold, pneumonia, anemia and diarrhea—were either found to be unrelated to the administration of Technosphere Insulin or could not be conclusively linked to its usage.

We recently assessed pulmonary function in a patient group that received Technosphere Insulin over a 12-week period and found that there was no clinically or statistically significant difference between the baseline values and the final test results for this group. We have also found no evidence of treatment-induced insulin antibodies occurring in patients treated with Technosphere Insulin.

We have an ongoing program of safety surveillance and adverse event reporting for the purpose of evaluating the ongoing safety data concerning the use of our Technosphere Insulin System. Our safety data are necessarily preliminary until we have completed longer-term safety studies.

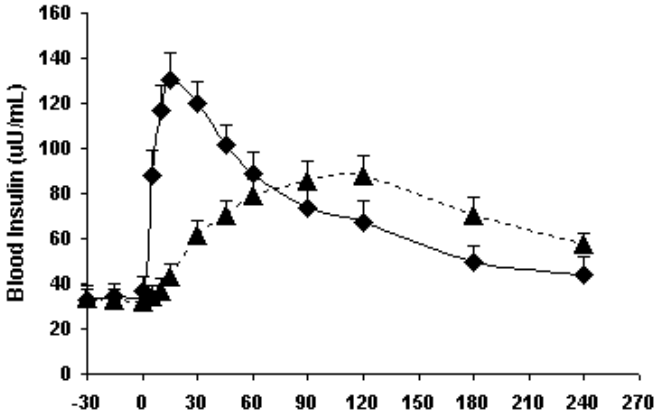
**OUR CLINICAL DEVELOPMENT PROGRAM**

This section describes the studies we plan to undertake and the results of our recently completed Phase 2 studies; later stage clinical trials might not confirm the findings from these earlier studies. We recently completed our Phase 2 clinical trials in the United States and held an "end of Phase 2" meeting with the FDA. We are currently conducting a Phase 2 clinical trial at 34 clinical research centers in Europe to study the tolerability of different doses of Technosphere Insulin in over 200 patients with type 2 diabetes. We also recently commenced a Phase 3 clinical trial in Europe. This trial will compare the effect, in patients with type 2 diabetes, of a mealtime dose of Technosphere Insulin to a mealtime dose of a rapid-acting insulin analog, in both cases in combination with basal insulin therapy.

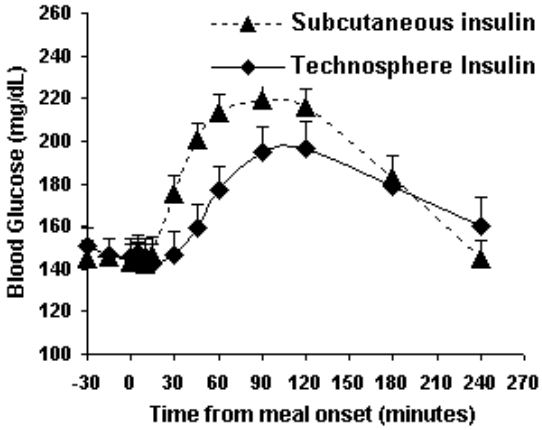
In recent clinical studies, we examined the ability of our Technosphere Insulin System to control blood glucose levels. In a Phase 2 study of 16 patients with type 2 diabetes, we compared the effect of mealtime doses of Technosphere Insulin on blood glucose levels to the effect of mealtime doses of subcutaneous 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 treated with 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 appearance of insulin in the bloodstream when Technosphere Insulin is inhaled as compared to the much slower increase 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 levels in patients in this clinical trial during the post-meal period to a greater extent than insulin administered subcutaneously.

**Post-meal insulin levels**

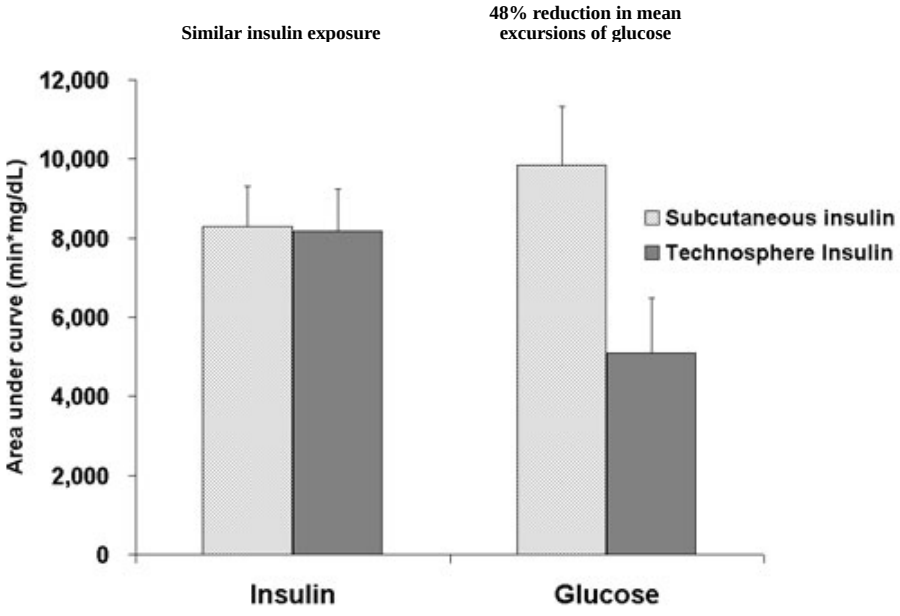



**Post-meal glucose levels**




We quantified the total exposure to insulin and the excursion of blood glucose levels by calculating the areas under the mean insulin and glucose curves, respectively. The results of this analysis are presented in the bar graph below. The bars on the left show that the areas under the insulin curves were virtually identical, indicating that patients in this trial received the same total exposure to insulin, whether from Technosphere Insulin or subcutaneous insulin. However, as shown by the bars on the right, when these patients inhaled Technosphere Insulin, there was a significantly decreased excursion in post-meal levels of blood glucose. Across all these patients, the mean excursion of post-meal glucose levels following administration of Technosphere Insulin was 48% less than the mean excursion observed following administration of subcutanous insulin.

**Post-meal insulin exposure and glucose excursion**



Based in part on this observation, we believe that approximating the first-phase insulin release spike allows patients with type 2 diabetes to achieve greater control over their glucose levels.

A recently completed study examined the longer-term effects of mealtime Technosphere Insulin on blood glucose levels. In this Phase 2 clinical trial, we studied 123 patients with type 2 diabetes whose pre-study treatment regimen consisted of either diet and exercise or one or more diabetes medications. This trial did not include patients whose diabetes had progressed to the point that they were already taking daily insulin. Patients were included in the study if their initial HbA1c levels were between 6.6% and 10.5%, which is an indication that they were not achieving optimal glucose control on their current therapy. HbAlc levels are a measure of the average blood glucose level over the previous three to four months and an indication of how well a patient is controlling glucose levels. Patients were evaluated in two groups: those with moderately severe elevations of HbA1c levels at baseline of 8.0% and above, values identified by the ADA as requiring definitive therapeutic intervention to minimize complications, and those with mild to moderate elevations of HbA1c levels at baseline ranging from 6.6% to 7.9%. By including patients with HbA1c values below 7.5%, we expanded the clinical evaluation of insulin treatment to patients who previously would have generally been regarded as inappropriate for insulin therapy because the modest expected improvement in glucose control would not justify the heightened risk that these patients will experience hypoglycemia. Patients were randomized, in a double-blind fashion, into either a group that inhaled Technosphere Insulin at mealtime or a control group that inhaled a placebo at mealtime. The use of a study agent at mealtime was the only variable in this study; all subjects continued their pre-study treatment regimen (diet and exercise or oral medications) and performed home blood glucose monitoring for the 12-week duration of the study.

All patients were started on active or control therapy at a dose of 6 units before each meal. The physicians adjusted the inhaled study drug doses in increments of 6 or 12 units as often as weekly in order to bring blood glucose to the desired level of control. The maximum dose of mealtime Technosphere Insulin allowed in the study was 48 units. In most cases, patients did not reach their final maximum dose level until they had already completed at least 8 out of 12 weeks of treatment.

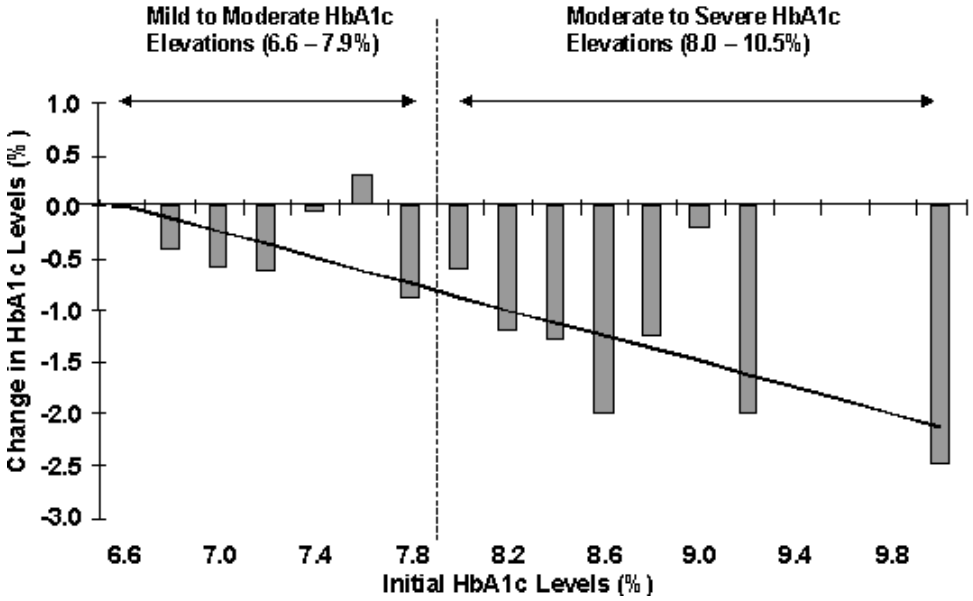
Patients in this trial with moderately severe elevations of HbA1c levels, treated with Technosphere Insulin, experienced a mean reduction in HbAlc levels of 1.37 percentage points over the limited duration of the study, compared to a mean reduction of 0.51 percentage points in the control-treated group. The difference in reduction of HbA1c levels between the Technosphere Insulin and the control groups was statistically ($p=0.0007$) and clinically significant in favor of Technosphere Insulin. Patients in this trial with mild to moderate elevations of HbA1c levels, treated with Technosphere Insulin, experienced a mean reduction in HbAlc levels of 0.43 percentage points, compared to a mean reduction of 0.18 percentage points in the control-treated group. This difference was also statistically ($p=0.0447$) and clinically significant in favor of Technosphere Insulin.

We believe that the results in this latter group are noteworthy. In this study, we saw significant reductions in HbA1c levels in patients with only mildly elevated baseline levels – a population for whom insulin therapy is not traditionally prescribed because the modest expected improvements in glucose control would not justify the heightened risk of hypoglycemia. However, in this study we were able to significantly reduce HbA1c levels without inducing any episodes of severe hypoglycemia or finding any difference in the occurrence of mild to moderate hypoglycemia between the active treatment and control groups.

One goal for this study was to determine the dose of Technosphere Insulin that was most commonly prescribed by physicians to bring patients' glucose control to desired levels. During the last four weeks of the study, after patients' glucose levels had stabilized, the mean dose was found to be approximately 30 units of Technosphere Insulin, regardless of whether patients had entered the study with

mild or with severe elevations of HbA1c. As illustrated in the graph below, the reduction of HbA1c levels across the study population seemed to be proportional to the degree to which HbA1c levels exceeded the normal upper limit at baseline. These observations suggest that the effect of the Technosphere Insulin therapy may be self-regulating within a certain dose range. Based on these observations, we believe that restoring the signaling function of the first-phase insulin release spike provides an important therapeutic benefit separate from the direct glucose-lowering effect of exogenous insulin.

**Glucose-lowering effect of Technosphere Insulin compared to initial HbA1c elevations**




Thus, we have seen in recent Phase 2 studies involving patients with type 2 diabetes that Technosphere Insulin can effectively reduce the excursion of glucose levels during the post-meal period and lower average glucose levels over a period of weeks. It is somewhat difficult to assess the full glucose lowering effect of Technosphere Insulin from our studies to date because HbA1c levels are a measure of average blood glucose levels over the preceding three to four months, and most patients were not dosed at their final maximum level until they had already completed several weeks of treatment. We plan to examine HbA1c data in the longer-term studies planned for Phase 3, which are expected to study efficacy over 26 weeks of treatment.

We plan to conduct multiple Phase 3 safety and efficacy clinical trials in different regions of the world, including Europe and the United States. We anticipate that the first US-based Phase 3 clinical trials will start by mid-2005, subject to our obtaining a satisfactory FDA review of our Phase 3 protocols. We anticipate that our entire clinical trial program will involve more than 3,000 patients using the Technosphere Insulin System alone or in combination with other therapies. In the United States, we have initiated one of several planned long-term safety trials involving individuals who participate in our Phase 2 and Phase 3 clinical trials. Based on our discussions with the FDA, our plan is to accumulate two years of controlled safety data from patients with type 1 diabetes as well as type-2 diabetes before we file a new drug application for the Technosphere Insulin System. Larger populations and longer durations of exposure may be necessary depending on the safety profile of our product.

**OUR RESEARCH PROGRAMS**

**Additional applications of our proprietary Technosphere formulation technology**

We believe that our proprietary Technosphere formulation technology is a platform that can provide a wide range of drug delivery alternatives, including the non-invasive pulmonary delivery of drugs that currently require injection. We believe this technology can also be extended to other forms of local administration, such as gastrointestinal delivery, because of its apparent ability to stabilize

drugs and facilitate transport across cellular membranes without damage, thereby enhancing the selectivity, ease of use and general effectiveness of existing drugs.

We are developing additional applications for our proprietary Technosphere formulation technology by formulating other drugs for pulmonary delivery, primarily for metabolic and immunological diseases.

**Immunology research programs**

Our Technosphere research activities are complemented by additional research efforts aimed primarily at the discovery and development of therapeutic cancer vaccines.

The immune system is a network of cells and organs that defends the body against infection and abnormal cells, such as cancer and transplanted 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 found on the surface of each cell as either normal or abnormal, and responding to them appropriately.

Any substance capable of triggering an immune response 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 sample antigens present in the body and present the epitopes associated with foreign antigens to other cells of the immune system whose function is to destroy any cell that expresses the same epitope; this is known as cell-mediated immunity. In this way, the immune system can launch a very specific response to infection or disease.

We are developing therapies for the treatment of solid-tumor cancers using our proprietary technologies for discovering critical tumor-related antigens, for designing DNA- and peptide-based compounds that evoke a cell-mediated immune response to those antigens and for delivering the compounds in vivo to the immune system in a manner that stimulates a potent response.

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

- *Specificity.* We target cancer epitopes to which the immune system has not developed a tolerance, instead of targeting the dominant epitopes expressed by cancerous cells, many of which are tolerated by the immune system. We have developed technology designed to identify the non-tolerated epitopes on the cancer cell surface, and we have developed a method of modifying these epitopes that is designed to activate an immune response. Through this process, we believe that the body's tolerance of the cancer cells can be broken, leading to the destruction of the cancer by the immune system.

- *Administration.* Our compounds are delivered directly into the patient's lymph nodes, where studies have shown they will have the greatest impact. In contrast to the conventional subcutaneous or intramuscular route of administration, we believe that the direct delivery of our compounds will bring local high concentrations of the active components of our compounds into contact with high concentrations of the cells needed to generate a potent cell-mediated immune response.

- *Selectivity, potency and duration of response.* We deliver our therapeutic compounds in a manner that we believe primes the immune system to respond to cancer cells expressing specific epitopes, in much the same way that a chronic infection evokes a progressively increased immune response to invading bacteria. Our administrative regimen is designed to boost the immune response over the course of a treatment cycle so that it becomes increasingly potent and long acting.

We have conducted initial studies of our cancer therapy in Europe and the United States, including Phase 1 and 2 clinical trials with 42 patients in the United States who had progressed to late stages of skin cancer. We observed that the delivery of a prototype formulation, targeting a single cancer epitope, was well tolerated by melanoma patients and produced a response by their immune system against that specific epitope. In late stages of such diseases, there are usually multiple generations of such cells, expressing multiple epitopes. Although we believe that our clinical data to date have been encouraging, we did not observe a strong correlation between the evoked immune response and clinical responses. As a result, we have continued to refine our cancer therapy program. We have developed several product candidates and expect to begin preclinical safety tests for one of these product candidates later this year, with the goal of commencing clinical trials in 2006. The results of these subsequent clinical trials may differ from the findings of our earlier trials.

## 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:

- *Commercialize our Technosphere Insulin System for the insulin-using diabetes market.* We intend to advance our Technosphere Insulin System through Phase 3 clinical trials and then into commercialization, with the goal of first establishing a significant presence for Technosphere Insulin in the insulin-using diabetes market. We believe that the market for insulin products will expand significantly among patients with type 2 diabetes as a result of the entry of other pulmonary insulin products, primarily due to the non-invasive nature of pulmonary insulin delivery. We believe the advantages of the Technosphere Insulin System, as compared to other pulmonary insulin products, will enable us to capture a significant portion of the existing and expanded insulin-using diabetes market.

- *Establish our Technosphere Insulin System as the preferred drug therapy within the broader population of people with type 2 diabetes.* 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;

  - patients for whom diet and exercise therapy has failed but who otherwise would have started non-insulin oral medications; and

  - patients currently using non-insulin oral medications.

  Based on our clinical data, we believe our Technosphere Insulin System, if and when approved by the FDA, will be the first commercially available therapy that produces a profile of insulin levels in the bloodstream that approximates the first-phase insulin release spike normally seen in healthy individuals following the beginning of a meal. We believe that no other conventional therapy has demonstrated that it can approximate the first-phase insulin release spike, and we are not aware of any other therapy in development that makes this claim. As a result, we believe that our Technosphere Insulin System has the potential to become the preferred drug therapy for the broader population of people with type 2 diabetes.

- *Evaluate strategic collaborations for the development, marketing and commercialization of our Technosphere Insulin System.* 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 and we believe this will enable us to obtain advantageous terms in potential collaborations. We intend to retain worldwide manufacturing rights for our Technosphere Insulin System.

- *Expand our proprietary Technosphere formulation technology for the delivery of other drugs.* We are developing additional applications for our proprietary Technosphere formulation technology by formulating other drugs for pulmonary delivery, primarily for metabolic and immunological diseases. We believe our proprietary Technosphere formulation technology can also be extended to other forms of local administration, such as gastrointestinal delivery, because of its apparent ability to stabilize drugs and facilitate transport across cellular membranes without damage.

- *Build upon our expertise in immune system diseases to develop new drugs.* We intend to build upon our expertise and intellectual property portfolio to develop new treatments for diseases other than diabetes. We are conducting research programs primarily focused on the development of therapeutic compounds for the active immunological treatment of cancer.

## SALES AND MARKETING

We currently have no sales, marketing or distribution capabilities and have no experience as a company in marketing or selling pharmaceutical products. Our efforts have primarily been directed at developing products for a number of different markets. Assuming that we receive regulatory approval for our product candidates, we anticipate that we will have to pursue different sales and marketing strategies tailored to each particular product and market segment. In order to commercially market any of our products, we will also need either to develop a sales and marketing infrastructure ourselves 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 will not be practical for some of our 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 the flexibility to enter into favorable 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. Our goal is to have our partners fund the clinical development and commercial launch of the Technosphere Insulin System in their respective territories.

**MANUFACTURING AND SUPPLY**

We purchase human recombinant insulin under a long-term contract with Diosynth B.V., a global producer of insulin and a subsidiary of Akzo Nobel. This agreement has no specified termination date, but generally may be terminated upon two-years' advance notice by either party. In addition, Diosynth has agreed to support our regulatory filings relating to the Technosphere Insulin System in the United States and abroad. We believe Diosynth 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 cGMP.

We have a long-term supply agreement with Vaupell, Inc., an independent third party, for the manufacture and supply of our MedTone inhaler and the cartridges that are inserted into it. We rely on this manufacturer to comply with relevant regulatory requirements, including compliance with Quality System Regulations, or QSRs. We believe our manufacturer has the capacity to meet our Phase 3 clinical and initial commercial requirements.

Currently, we manufacture the raw Technosphere material, but we are in the process of qualifying a secondary manufacturer to supply us with commercial quantities of this raw material. 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. We believe that our Danbury facility has adequate capacity to meet our currently anticipated clinical trial needs. We are continuing to increase our filling and packaging capacity through the acquisition of new equipment and the expansion of our clean rooms and other manufacturing facilities. We believe that our building improvements have been adequately validated to date and that the facility continues to substantially conform with cGMP. We have initiated the design and construction of a modular filling and packaging system that will increase our filling and packaging capacity. The new system is designed to operate at high speeds in a very small space, and can be expanded by using multiple units.

**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.

With respect to our Technosphere Insulin System, our core patents claim the composition of matter of the Technosphere material as well as methods for manufacturing unloaded Technosphere particles and Technosphere particles that incorporate drugs. The first of these patents expires in 2012, but subsequent patents provide additional coverage of the composition of matter of the current product until 2020. We also hold patents that claim methods of using Technosphere particles for the pulmonary delivery of drugs. These patents relating to Technosphere Insulin do not expire until 2015. In addition, we are prosecuting patent applications related to the MedTone inhaler device and the capsules that contain the dry powder. We have filed and intend to continue to file additional patent applications on improvements to the Technosphere technology and its manufacture, as well as on specific compositions of matter formed using this technology in combination with drugs. To date, we have been issued 11 US and foreign Technosphere-related patents and have 34 pending applications in different jurisdictions claiming inventions related to the Technosphere technology and the dry powder inhaler.

Our cancer immunotherapy program is built on proprietary methods for the selection, design and administration of epitopes. We have 59 pending patent applications relating to this technology, both as methods of use and compositions of matter. We are pursuing patents on the use of our administration method to induce and maintain a cell-mediated immune response. The prosecution is ongoing in many jurisdictions; however, we have been granted patents for this method in Australia and New Zealand, which do not expire until 2018. We also have patent applications related to differential antigen processing and product designs. Two patents from this group have issued in the United States, which provides us with protection until at least 2020. In addition to applications of these broad technologies, we have filed and will continue to file patent applications on specific compounds and the protocols for administering them.

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 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 creator of inventions 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 Insulin System and cancer vaccine products under development, we have identified certain third-party patents that a court may interpret to restrict our freedom to operate (that is, to cover our products) in the areas of Technosphere formulations, pulmonary insulin delivery and the treatment of cancer. Specifically, 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 and compositions of matter related to DNA-based vaccines that also may trigger an allegation of infringement upon the commercial manufacture and sale of cancer therapy. We believe, based in part on advice of counsel, 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 products or cancer therapies 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, 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. In either event, our business would be harmed and our profitability could be materially adversely 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 US 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 developed independently by them or others to our projects, 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 intensely 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, ease of use and cost.

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.

**Other pulmonary and oral insulin delivery systems**

Several pharmaceutical and biotechnology companies are developing systems for the pulmonary delivery of insulin. Pfizer, Inc. and Sanofi-Aventis, in collaboration with Nektar Therapeutics, have been conducting Phase 3 clinical trials for the Exubera product. In March 2004, these collaborators filed a submission seeking regulatory approval in Europe, and in March 2005, they received notice of acceptance of filing for an NDA filed with the FDA. Novo Nordisk A/S, in collaboration with Aradigm Corporation, has been developing a pulmonary insulin product, and Eli Lilly and Company, in collaboration with Alkermes, Inc., is also developing a pulmonary insulin product, which is currently in Phase 2 clinical trials. Kos Pharmaceuticals, Inc. is also developing a pulmonary insulin product. On the basis of published reports, we believe that the performance characteristics of our Technosphere Insulin System will have an advantage over these other pulmonary insulin products, particularly with respect to time-to-peak blood insulin levels and relative bioavailability.

There are also several companies, including Nobex Corporation, Generex Biotechnology Corporation and Emisphere Technologies, Inc., that are pursuing development of products for the oral delivery of insulin. We believe these products are currently in relatively early clinical trials.

**Non-insulin oral medications**

We expect that our Technosphere Insulin System will compete with currently available non-insulin oral medications for type 2 diabetes. These products include sulfonylureas, metformin and various insulin sensitizers. The sulfonylureas, which are mostly generic, act by directly stimulating insulin secretion and have been the principal non-insulin oral medication used to treat type 2 diabetes for several decades. Metformin, which is now available as a generic drug and is also marketed by Bristol-Meyers Squibb Company as Glucophage, has also been widely used for the treatment of type 2 diabetes. Insulin sensitizers, including Avandia, which is being marketed by GlaxoSmithKline PLC, and Actos, which is being marketed by Takeda Pharmaceuticals North America, Inc. and Eli Lilly & Company, are increasingly being used to treat type 2 diabetes.

**Injected insulin**

In the subcutaneous insulin market, our competitors have made considerable efforts to develop faster acting injectable insulin formulations. Humalog, which was developed by Eli Lilly and Company, and Insulin Aspart, or NovoLog, which was developed by Novo Nordisk A/S, are the two principal injectable insulin formulations with which we expect to compete.

**Other injected diabetes medications**

There is considerable interest in a new class of injectible diabetes drugs known as incretin mimetic agents. These drugs simulate or alter the activity of naturally occurring hormones that are released from the digestive system, such as GLP-1, GIP and others. These hormones modulate the metabolism of energy-containing compounds in the body, such as glucose, fat and protein. The most advanced of these drugs are SYMLIN and Exenatide, being developed by Amylin Pharmaceuticals, Inc. in collaboration with Eli Lilly & Company. Several other pharmaceutical companies are working on additional incretin mimetic agents or on incretin modifiers, such as DPP-IV inhibitors, which act to extend the potency of GLP-1.

**Immunotherapy**

Over the last decade or so, a variety of companies have sought to develop therapeutic compounds that provide a selective immune response against cancer. Some of these companies, including Dendreon Corporation, Antigenics Inc., CancerVax Corporation and Corixa Corporation, have focused on products derived from the patients' own cancer, which can take the form of whole cells or cell fragments, or on tumor antigens extracted from cancerous cells. Other companies, including CancerVax Corporation, Progenics Pharmaceuticals, Inc., Therion Biologics Corporation and Vical Incorporated, are pursuing therapies designed to work across a broad spectrum of patients and tumor types.

**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 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 replicated. 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 investigational 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. Companies also must generally determine the details of properly treating pediatric patients with a drug and this can sometimes mean that specific pediatric studies must be performed. 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 I clinical trials are often conducted in healthy human volunteers and such cases do not provide evidence of efficacy. In 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 traditionally 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.

- 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 begin once Phase 2 evaluations demonstrate 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 a new drug application, or NDA, for non-biological drugs such as insulin, 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.

- The FDA reviews all NDAs submitted before it accepts them for filing. It may request additional information rather than accepting an application for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA. The FDA has substantial discretion in the approval process and may disagree with an applicant's interpretation of the data submitted in its NDA. Also, as part of this review, the FDA may refer the application to an appropriate advisory committee, typically a panel of clinicians, for review, evaluation and a recommendation. The FDA is not bound by the recommendation of an advisory committee. Manufacturing establishments often also are subject to inspections prior to NDA approval to assure compliance with cGMP and with manufacturing commitments made in the relevant marketing application. Under the Prescription Drug User Fee Act, or PDUFA, certain pharmaceutical establishment, product and application fees were established. Submission of an NDA with clinical data requires payment of a fee. For fiscal year 2005, the required fee is $672,000. Under PDUFA, the FDA assigns a review goal for standard applications of 10 months from acceptance of the application, at which time the FDA may approve the product or request additional information. It is not unusual for the FDA to ask for more information upon completion of this first

review cycle. There can be no assurance that an application will be approved during the first review cycle or any subsequent review cycles or that the FDA may not extend the PDUFA deadlines.

- FDA approval of the NDA must be granted prior to any commercial sale or shipment of the drug product. The FDA may deny an NDA approval if safety, efficacy or other regulatory requirements are not satisfied. The FDA may also require additional testing or information before approving the NDA. If regulatory approval of the product is granted, such approval may require post-marketing testing and surveillance to monitor the safety of the product or may entail limitations on the indicated uses for which the product may be marketed or advertised. The FDA may require additional testing or information before approving the NDA. In addition, product approval may be withdrawn if compliance with regulatory standards is not maintained or if problems occur following the commencement of marketing.

Clinical trials are designed and conducted in a variety of ways. A “placebo-controlled” trial is one in which the trial tests the results of a group of patients, referred to as an “arm” of the trial, receiving the drug being tested against those of an arm that receives a placebo, which is a substance of identical appearance that is not therapeutic in a medical or chemical sense. In a “double-blind” study, neither the researcher nor the patient knows into which arm of the trial the patient has been placed, or whether the patient is receiving the drug or the placebo. “Randomized” means that upon enrollment, patients are placed into one arm or the other at random by computer. “Parallel control” trials generally involve a study arm with a patient population that is not exposed to the study medication (i.e., is either on placebo or standard treatment protocols) for comparison to the drug being tested and groups are assigned upon patient admission to the study and remain in those groups for the duration of the study. An “open label” study is one where the researcher and the patient know that the patient is receiving the drug. A trial is said to be “pivotal” if it is designed to meet statistical criteria with respect to pre-determined “endpoints,” or clinical objectives, that the sponsor believes, based usually on its interactions with the relevant regulatory authority, will be sufficient for regulatory approval. In most cases, at least two “pivotal” Phase 3 clinical trials are necessary for approval. Claims regarding the superiority of one drug product over another generally must be supported by so-called head-to-head clinical trials involving comparison of one drug to another to which superiority is claimed. Under the PREA of 2003, an NDA also must include an assessment, generally based on clinical study data, on the safety and efficacy of a drug 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 may be 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 premarket review of combination products, the FDA designates one of its centers to have primary jurisdiction for the premarket review and regulation of both components. 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 a future drug marketing application for our Technosphere Insulin System will involve three separate review groups of the FDA: (1) the Metabolism 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. Although the FDA has not made an official final decision in this regard, we currently understand that the Metabolic and Endocrine Drug Products Division will be the lead group and obtain consulting reviews from the other two FDA groups.

The testing and approval process requires substantial time, effort and financial resources. 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 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 and the supplier of our MedTone inhaler and cartridges are subject to federal registration and listing requirements and, if applicable, to state licensing requirements. Facilities are subject to inspection by the FDA and similar national agencies, as well as state and local authorities at any time. Failure, including those of our insulin and MedTone inhaler 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 premarket 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. Failure to comply with these regulatory requirements could result in civil fines, product seizures, injunctions, and/or criminal prosecution of responsible individuals and us. Further, the company we have contracted to manufacture our MedTone inhaler and cartridges will be subject to the QSRs, which require 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 other 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 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 assure you 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 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 clinical studies demonstrating safety and efficacy for that product. Instead of providing completely new safety and efficacy data, therefore, a competitor could make a copy of any of our drugs and only need to submit manufacturing information and clinical data demonstrating that the copy is bioequivalent to our product in order to gain marketing approval from the FDA.

Another type of application allowed by the Hatch-Waxman Act, 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.

Hatch-Waxman requires a competitor that submits an ANDA or a Section 505(b)(2) application with respect to one of our drugs to notify us of their application and potential infringement of our patent rights. Hatch-Waxman places certain timing requirements on us with respect to filing an infringement action against such an applicant, if we choose to do so. The timing of competitive FDA approvals of ANDAs or Section 505(b)(2) applications is related to the patent status of our approved products, if any.

While the Hatch-Waxman Act provides competitors the ability to market copies of approved innovator drug products with the submission of significantly less clinical data, depending on the patent status of the innovator, the Act also provides under certain circumstances for the restoration of a portion of a product's patent term that is lost during a drug's clinical development and NDA review by the FDA. Hatch-Waxman also provides for a statutory protection, known as market exclusivity, which prohibits the FDA's approval or acceptance of certain competitor new drug applications. Patent term restoration can return up to five years of patent term for a patent that covers a new drug product or its use to compensate for time lost during the regulatory review process. This period is

generally one-half the time between the effective date of an IND and the submission date of an NDA, plus the time between the submission date of an NDA and the approval of that application, subject to a maximum extension of five years. No extension can extend the total patent life beyond 14 years after the drug approval date. The application for patent term extension is subject to approval by the USPTO, in conjunction with the FDA. It takes at least six months to obtain approval of the application for patent term extension, and there can be no guarantee that the application will be granted.

The Hatch-Waxman Act also provides for differing periods of marketing exclusivity for new drugs approved under NDAs. Among the types of exclusivity are those for "new chemical entities" and those for innovative changes to previously approved drugs, where new clinical trials (other than bioavailability studies) are essential to the approval of the NDAs. Our lead product, the Technosphere Insulin System, is an innovative change to a previously approved drug with the same active ingredient, insulin. Marketing exclusivity for the Technosphere Insulin System, if available and granted by the FDA, would prohibit the agency for a period of three years from approving and ANDA or Section 505(b)(2) application for competitive versions of our new formulation. This three-year exclusivity, however, only covers the innovation associated with the NDA to which it attaches. Thus, the three-year exclusivity would not prohibit the FDA from approving ANDAs or Section 505(b)(2) applications for drugs containing the same active ingredient but without our new dosage formulation. Hatch-Waxman also does not prevent the approval of a full NDA containing all the safety and efficacy data and information required for approval, even where approval of the same drug would have been blocked under an ANDA or Section 505(b)(2) application.

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. 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, 2007, and there can be no assurances that it will be reauthorized.

**EMPLOYEES**

As of December 31, 2004, we had 273 full-time employees, all of whom are employed at-will. Seventy-six of these employees were engaged in research and development, 88 in manufacturing, 62 in clinical, regulatory affairs and quality assurance and 47 in administration, finance, management, information systems, corporate development and human resources. Thirty-three of these employees have a Ph.D. degree and/or M.D. degree and are engaged in activities relating 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.

The following are some of our scientific advisors and their primary affiliations:

| Name | Primary affiliation |
|---|---|
| James J. Collins, D. Phil | Professor at Boston University |
| Alexander Fleming, M.D. | Chief Executive Officer of the Kinexum Corporation |
| Edward S. Horton, M.D. | Chief of Clinical Research at the Joslin Diabetes Center |
| Thomas Kundig, M.D. | Professor at the University of Zurich |
| Harold E. Lebovitz, M.D. | Professor of Medicine and the Chief of Endocrinology Emeritus at the State University of New York — Brooklyn |
| Frederick Levy, Ph.D. | Associate Member of the Ludwig Institute for Cancer Research |
| Greg Petsko, Ph.D. | Professor at Brandeis University |
| Jesse Roth, M.D. | Chief Geriatrician of the Long Island Jewish Medical Center |
| Jay S. Skyler, M.D. | Chief of Diabetes & Endocrinology at the University of Miami School of Medicine |
| Rolf Zinkernagel, M.D., Ph.D. | Nobel Laureate in Medicine and Institute Director at the University of Zurich |

**EXECUTIVE OFFICERS**

The following table sets forth our current executive officers and their ages as of December 31, 2004:

| Name | Age | Position(s) |
|---|---|---|
| Alfred E. Mann | 79 | Chairman of the Board of Directors and Chief Executive Officer |
| Hakan S. Edstrom | 54 | President, Chief Operating Officer and Director |
| Richard L. Anderson | 65 | Corporate Vice President and Chief Financial Officer |
| Dan R. Burns | 53 | Corporate Vice President and Chief Commercial Officer |
| Wayman Wendell Cheatham, M.D., FACE | 56 | Corporate Vice President and Chief Medical Officer |
| David Thomson, Ph.D., J.D | 38 | Corporate Vice President, General Counsel and Corporate Secretary |
| Diane M. Palumbo | 51 | Corporate Vice President, Human Resources |

***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. Since 1993, Mr. Mann has served as Chairman and Co-Chief Executive Officer of Advanced Bionics Corporation, a medical device manufacturer that was acquired by Boston Scientific Corporation in June 2004. 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 and Western University 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, 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 Opthalmics Inc. Mr. Edstrom is currently a director of Q-Med AB, a biotechnology and medical device company, and Ixion Biotechnology, Inc., a biotechnology 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. He was previously Senior Vice President, Chief Financial Officer and Secretary at NeoRx Corporation, a Seattle-based publicly traded biotechnology company. From January 1997 to September 2002, Mr. Anderson held various executive positions at NeoRx, including President, Chief Operating 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.

***Dan R. Burns*** has been our Corporate Vice President and President, MannKind Biopharmaceuticals since September 2002. Prior to joining us, he served as Chief Executive Officer of HealthTalk Interactive a pharmaceutical services firm from 2000 to 2002. From 1998 to 1999 Mr. Burns served as Chief Executive Officer of ProScript, a biopharmaceutical company. He served as President and Chief Operating Officer of Trophix Pharmaceuticals, Inc. from 1997 to 1998. Prior to joining Trophix Pharmaceuticals, for 18 years, Mr. Burns held a number of senior executive positions both internationally and domestically with Bristol Myers Squibb. Mr. Burns holds degrees in Psychology and Business Administration from McMaster University and Mohawk College.

***Wayman Wendell Cheatham, M.D., FACE*** has been our Corporate Vice President since August 2002 and our Chief Medical Officer since November 2004. From April 1999 to August 2002, he was Vice President of Medical & Regulatory Affairs for Takeda Pharmaceuticals North America, Inc., a manufacturer of ethical pharmaceuticals. From August 1996 to April 1999, Dr. Cheatham served as Director of Medical Affairs for Novo Nordisk Pharmaceuticals North America, Inc., a manufacturer of ethical pharmaceuticals and therapeutic biologic preparations. Dr. Cheatham received his M.D. degree from the Pennsylvania State University College of Medicine in 1975 and is board certified in Internal Medicine and in Endocrinology & Metabolism. Dr. Cheatham is also a member of the board of directors of the American Diabetes Association.

***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 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.

***Diane M. Palumbo.*** has been our Corporate Vice President of Human Resources since November 2004. Prior to joining us, she was President of her own Human Resources Consulting Company from July 2003 to November 2004. 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.

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

**Item 2. Properties**

In early 2001, we acquired a facility in Danbury, Connecticut to house our Technosphere-related activities, including development and manufacturing of Technosphere Insulin. This facility includes two buildings comprising approximately 187,000 square feet and currently house our research and development, administrative and manufacturing functions, primarily for Technosphere Insulin formulation, filling and packaging. We lease approximately 20,000 square feet of laboratory space in Elmsford, New York for approximately $36,000 per month, pursuant to a lease that ends in June 2005, and we lease approximately 22,700 square feet of office space in Paramus, New Jersey for approximately $38,400 per month, pursuant to a lease that ends in January 2009. We believe that our facility in Danbury has sufficient space to contain additional Technosphere Insulin manufacturing capacity necessary to satisfy potential commercial demand for our products for several years after we launch our Technosphere Insulin System and other Technosphere-related products.

We own and occupy approximately 120,000 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 immunology programs. We also use this facility to provide support for the development of our Technosphere programs.

**Item 3. Legal Proceedings**

We are not currently a party to any material legal proceedings. We may from time to time become a party to legal proceedings arising in the ordinary course of business. During the year ended December 31, 2000, we issued an aggregate 699,972 shares of common

stock to three consultants in exchange for notes receivable aggregating approximately $10,891,000. The notes are collateralized by the underlying common stock, bear interest at fixed rates, and are payable in October 2005. On November 10, 2004, the borrowers notified us that they believed that they had entered into an agreement in October 2001 with the Alfred E. Mann, our Chairman, Chief Executive Officer and principal stockholder under which Mr. Mann would purchase from the borrowers some of the common stock, with the proceeds to be paid to us to pay down the notes. The borrowers have informed us that they believe both we and Mr. Mann are in breach of certain agreements related to the transaction and indicated they intend to seek alleged damages arising from any failure of the agreement to be performed. We believe that the ultimate resolution of this matter will not have a material impact on our financial position or results of operations.

**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, 2004.

**PART II**

**Item 5. Market for the Registrant's Common Equity, Related Stockholder Matters and Issuer Purchase of Equity Securities**

**Common Stock Market Price**

Our common stock has been traded on 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 bid prices for our common stock as reported by Nasdaq. These quotations reflect inter-dealer prices, without retail mark-up, markdown or commission, and may not represent actual transactions.

| | High | Low |
|---|---|---|
| Year ended December 31, 2004 | | |
| Third quarter (from July 28, 2004) | $ 24.31 | $ 10.71 |
| Fourth quarter | $ 20.40 | $ 14.32 |

The closing sales price of our common stock on the Nasdaq National Market was $13.51 on February 28, 2005 and there were 289 registered holders of record as of that date. `

**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.

**Securities Authorized for Issuance Under Equity Compensation Plans**

The information required to be disclosed by Item 201(d) of Regulation S-K is incorporated herein by reference to our Proxy Statement.

**Recent Sales of Unregistered Securities**

The following list sets forth information regarding all securities sold by us during the fiscal year ended December 31, 2004 without registration under the Securities Act of 1933, as amended. All share amounts give effect to the one-for-three reverse stock split of our common stock effected on July 22, 2004 in connection with our initial public offering.

(1) In January to March 2004, we issued an aggregate of 980,392 shares of our Series C preferred stock to 38 accredited investors for aggregate consideration of $50 million. Upon the closing of our initial public offering, these shares were converted into 4,464,266 shares of our common stock.

(2) On July 22, 2004, we issued an aggregate of 22,309 shares of our common stock upon the conversion of warrants originally issued in 1996 and held by six warrantholders.

(3) From January 1, 2004 through July 29, 2004, we granted options under our equity incentive plans to purchase 74,333 shares of common stock to employees, directors and consultants, having exercise prices ranging from $7.95 to $9.18 per share. During such time, 526 shares of common stock were purchased pursuant to exercises of stock options and 46,397 shares were cancelled and returned to the equity plan pools.

The offers, sales, and issuances of the securities described in paragraphs (1) and (2) were deemed to be exempt from registration under the Securities Act in reliance on Section 4(2) of the Securities Act and/or Rule 506 of Regulation D in that the issuance of securities to the accredited investors did not involve a public offering. The recipients of securities in each of these transactions acquired the securities for investment only and not with a view to or for sale in connection with any distribution thereof and appropriate legends were affixed to the securities issued in these transactions. Each of the recipients of securities in these transactions was an accredited investor under Rule 501 of Regulation D.

The offers, sales and issuances of the securities described in paragraph (3) were deemed to be exempt from registration under the Securities Act in reliance on Rule 701 in that the transactions were under compensatory benefit plans and contracts relating to compensation as provided under Rule 701. The recipients of such securities were our employees, directors or bona fide consultants and received the securities under our equity incentive plans. Appropriate legends were affixed to the securities issued in these transactions. Each of the recipients of securities in these transactions had adequate access, through employment, business or other relationships, to information about us.

**Use of Proceeds**

The initial public offering of our common stock, par value $0.01 per share, was effected through a Registration Statement on Form S-1 (File No. 333-115020) that was declared effective by the SEC on July 27, 2004, and a Registration Statement on Form S-1 (File No. 333-117702) that became effective upon filing with the SEC on July 28, 2004. The Registration Statements covered the offer and sale of up to 7,187,500 shares of our common stock, including an over-allotment option we granted to the underwriters to purchase up to 937,500 shares of our common stock from us, for an aggregate offering price of $100.6 million. Our initial public offering commenced on July 28, 2004. On August 2, 2004, 6,250,000 shares of our common stock were sold for an aggregate offering price of $87.5 million. The managing underwriters in the offering were UBS Investment Bank, Piper Jaffray, Wachovia Securities, Jefferies & Company, Inc. and Harris Nesbitt. The underwriters exercised 307,100 shares of the over-allotment option on August 28, 2004 and the closing occurred on September 1, 2004.

Our initial public offering resulted in aggregate net proceeds to us of approximately $83.2 million, including approximately $4.0 million in proceeds from the exercise of the underwriter’s over-allotment option. In connection with the offering, we paid $6.4 million in underwriting discounts and commissions and offering expenses of approximately $2.2 million.

No offering expenses were paid directly or indirectly to any of our directors or officers (or their associates) or person owning ten percent or more of any class of our equity securities or to any other affiliates. All offering expenses were paid directly to others. The foregoing payments were direct payments made to third parties who were not our directors or officers (or their associates), persons owning ten percent or more of any class of our equity securities or any other affiliate, except that the proceeds used for working capital included regular compensation for officers and directors.

As of December 31, 2004, we estimate that we had used approximately $27.6 million for operating activities and approximately $3.5 million for the purchase of manufacturing equipment. The remainder of the proceeds has been invested into short-term securities and cash equivalents. The use of proceeds does not represent a material change from the use of proceeds described in the prospectus we filed pursuant to Rule 424(b) of the Securities Act with the SEC on July 28, 2004.

We expect to use a majority of the balance of the net proceeds of the offering and our existing cash, cash equivalents and marketable securities, primarily for late stage clinical trials of Technosphere Insulin, production and supply activities for Technosphere Insulin, the expansion of our commercial manufacturing plant and equipment for Technosphere Insulin, and for general corporate purposes, which may include in-licensing or acquiring additional technologies. We have no current plans, agreements or commitments with respect to any future acquisitions or in-licensing, and we are not currently engaged in any negotiations with respect to any transactions of that nature.

The amount and timing of our actual expenditures may vary significantly depending on numerous factors, such as the progress of our

product development and commercialization efforts and the amount of cash used by our operations. Accordingly, our management will have broad discretion in the application of the net proceeds, and investors will be relying on the judgment of our management regarding the application of the net proceeds. Pending these uses, we plan to invest the net proceeds in short-term, interest-bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the United States. The goal with respect to the investment of these net proceeds is capital preservation and liquidity so that funds are readily available to fund our research and development operations.

**Item 6. Selected Financial Data**

The following selected consolidated financial data should be read in conjunction with MannKind 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 report.

| Statement of operations data: | Year ended December 31, | | | | |
|---|---|---|---|---|---|
| | 2000 | 2001 | 2002 | 2003 | 2004 |
| | (in thousands, except per share amounts) | | | | |
| Revenue | $ 154 | $ 326 | $ — | $ — | $ — |
| Operating expenses: | | | | | |
| Research and development | 20,542 | 19,763 | 42,724 | 45,613 | 59,266 |
| General and administrative | 4,854 | 10,629 | 13,215 | 20,699 | 17,883 |
| In-process research and development costs | — | 19,726 | — | — | — |
| Goodwill impairment | — | — | 151,428 | — | — |
| Total operating expenses | 25,396 | 50,118 | 207,367 | 66,312 | 77,149 |
| Loss from operations | (25,242) | (49,792) | (207,367) | (66,312) | (77,149) |
| Other income (expense) | 204 | 288 | 487 | 36 | 226 |
| Interest income | 379 | 1,261 | 617 | 398 | 932 |
| Loss before provision for income taxes | (24,659) | (48,243) | (206,263) | (65,878) | (75,991) |
| Income tax provision | (2) | (2) | (2) | (1) | (1) |
| Net loss | (24,661) | (48,245) | (206,265) | (65,879) | (75,992) |
| Deemed dividends related to beneficial conversion feature of convertible preferred stock | — | — | (1,421) | (1,017) | (19,822) |
| Accretion on redeemable preferred stock | (149) | (239) | (251) | (253) | (60) |
| Net loss applicable to common stockholders | $ (24,810) | $ (48,484) | $ (207,937) | $ (67,149) | $ (95,874) |
| Basic and diluted net loss per share | $ (3.95) | $ (4.60) | $ (15.43) | $ (3.63) | $ (3.80) |
| Shares used to compute basic and diluted net loss per share | 6,278 | 10,534 | 13,472 | 18,488 | 25,221 |

| Balance sheet data: | As of December 31, | | | | |
|---|---|---|---|---|---|
| | 2000 | 2001 | 2002 | 2003 | 2004 |
| | (in thousands) | | | | |
| Cash, cash equivalents and marketable securities | $ 35,053 | $ 53,730 | $ 31,052 | $ 55,945 | $ 90,533 |
| Working capital | 29,081 | 47,477 | 24,171 | 49,097 | 82,837 |
| Total assets | 42,645 | 251,487 | 104,773 | 125,876 | 163,483 |
| Deferred compensation and other liabilities | 132 | 231 | 207 | 404 | 76 |
| Redeemable convertible preferred stock | 4,445 | 4,684 | 4,935 | 5,188 | — |
| Deficit accumulated during the development stage | (46,582) | (94,827) | (301,092) | (366,971) | (442,963) |
| Total stockholders' equity | 31,890 | 235,017 | 90,773 | 111,577 | 150,363 |

**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. We recently commenced Phase 3 clinical trials in Europe of our lead product, the Technosphere Insulin System, to study its potential for the treatment of diabetes. This therapy consists of a proprietary dry powder Technosphere formulation of insulin that is inhaled into the deep lung using our 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.

We were incorporated in February 1991 under the laws of the State of Delaware as Pharmaceutical Discovery Corporation, or PDC. On December 12, 2001, AlleCure and CTL merged with wholly-owned subsidiaries of PDC. Pursuant to the merger, all of the outstanding shares of capital stock of AlleCure and CTL were exchanged for shares of capital stock of PDC, and AlleCure and CTL became wholly-owned subsidiaries of PDC. In connection with the merger, PDC changed its name to MannKind Corporation. On December 31, 2002, AlleCure and CTL merged with and into MannKind and ceased to be separate entities.

To date, we have not generated any revenues, and except for our recently completed initial public offering, we have funded our operations primarily through private placements of equity securities. We are a development stage enterprise and have incurred significant losses since our inception in 1991. As of December 31, 2004, we have incurred a cumulative net loss of $443.0 million which includes a goodwill impairment charge of $151.4 million. We do not anticipate receiving revenues from the sales of any product prior to regulatory approval and commercialization of our Technosphere Insulin System. 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 and commercialization of our Technosphere Insulin System for the treatment of diabetes;
- expand our manufacturing operations and quality systems to meet our currently anticipated commercial production needs as we advance the Technosphere Insulin System through Phase 3 clinical trials and into commercialization;
- expand our other research, discovery and development programs focused primarily on the development of therapies for cancer;
- expand our proprietary Technosphere formulation technology and develop additional applications for the 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.

We have a limited history of operations with our current management team and, to date, we have not generated any revenues from sales of any product. We currently do not 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.

Since 1991, we have been successful in completing several rounds of private equity financing. In 2003, we raised $100.0 million through private placements of our equity securities, comprised of 3,493,194 shares of common stock sold at a weighted average price of $14.31 per share and 980,392 shares of Series C convertible preferred stock that were subscribed for in 2003 at a price of $51.00 per share. Of the $50.0 million of Series C convertible preferred stock subscribed for in 2003, $31.8 million, representing the purchase price for 624,449 shares of Series C convertible preferred stock, was received in 2003 and $18.2 million, representing the purchase price of the remaining 355,943 shares of Series C convertible preferred stock, was received in the first quarter of 2004. On August 2, 2004, we sold 6,250,000 shares of common stock in an initial public offering for aggregate gross proceeds of $87.5 million. The underwriters exercised 307,100 shares of the over-allotment option on August 28, 2004, and the closing occurred on September 1, 2004 for aggregate gross proceeds of $4.3 million. After deducting the underwriters' commission and offering expenses, we received aggregate net proceeds of $83.2 million.

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, 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 and manufacturing and related activities. This staff is divided between our facilities in Valencia, California, Elmsford, New York, Paramus, New Jersey and Danbury, Connecticut. We expense research and development costs as we incur them.

Clinical development timelines, likelihood of success and total costs vary widely. We are currently focused primarily on advancing the Technosphere Insulin System through Phase 3 clinical trials. We plan to commercialize our lead product as a treatment for type 2 diabetes. 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 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. We anticipate that our research and development expenses, particularly for the Technosphere Insulin System, will increase significantly with the continuation of existing and the initiation of new clinical trials, the resulting manufacturing costs associated with producing materials for these clinical trials, and the expansion, qualification and validation of our commercial manufacturing processes.

**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 business insurance and professional services costs.

We expect general and administrative expenses to increase significantly, in part due to increased (non-cash) stock compensation expense resulting in part from the anticipated adoption of Statement of Financial Accounting Standards (SFAS) No. 123R, *Share-based Payment: an Amendment of FASB Statement 123 and 95*. See "—Recent accounting pronouncements." Also, we became a public company in July 2004. As a public company, we expect our general and administrative expenses to increase significantly in such areas as audit and legal fees, internal control compliance and insurance. A significant portion of these increases will be paid directly to third parties; most of the remainder will be related to increased staffing in these areas.

**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.

**Goodwill, intangibles and other long-lived assets**

Assessing goodwill, intangibles and other long-lived assets for impairment requires us to make assumptions and judgments regarding the carrying value of these assets. Goodwill and intangible assets with indefinite lives are tested for impairment annually, or on an

interim basis if events or circumstances indicate that the fair value of the asset has decreased below its carrying value. Other long-lived assets are tested 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 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 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 uneven payment flows. 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 enrollment 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**

We have recorded compensation expense related to options to purchase our common stock issued to employees and consultants. We have elected to follow Accounting Principles Board (APB) Opinion No. 25, *Accounting for Stock Issued to Employees*, and related interpretations, in accounting for our stock-options issued to employees, and we have adopted the disclosure-only alternative of SFAS No. 123, *Accounting for Stock-Based Compensation*. Accordingly, we have recorded stock-based compensation expense in connection with the grant of common stock options to employees based on the intrinsic-value method provided for under APB No. 25 rather than the alternative fair-value method provided for under SFAS No. 123. The intrinsic value of an employee stock option under APB No. 25 is equal to the difference between the exercise price of the option and the estimated fair value, on the measurement date, of the common stock purchasable with the option. In the notes to our financial statements, we provide pro forma disclosures that indicate the effect on our net income as if we had applied the fair-value method.

The measurement date for stock-based compensation, if any, in connection with an employee stock option is generally the option grant date. However, modifying option terms subsequent to the grant date can result in a remeasurement of stock option compensation on the modification date and subsequently under certain circumstances. 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. Under the repricing program, each holder of outstanding options granted under the stock plans who was an employee of ours on November 5, 2003 could elect to exchange up to all of his or her outstanding options that had an exercise price greater than $7.95 for repriced stock

options with an exercise price of $7.95 per share and a term of four years. The option repricing became effective on November 5, 2003. Each replacement option vested 50% in November 2004 and then monthly thereafter until fully vested in November 2005. Employees who voluntarily resigned in the 12-month period beginning November 5, 2003 forfeited their repriced options. Employees who were involuntarily terminated in the 12-month period beginning November 5, 2003 vested 50% upon termination and forfeited the remaining portions of their options. Compensation cost for all options repriced under the repricing program will be remeasured on a quarterly basis until the options expire or are exercised or canceled. Stock options issued to consultants are accounted for in accordance with the provisions of SFAS No. 123 and Emerging Issues Task Force (EITF) Issue No. 96-18, *Accounting for Equity Instruments That Are Issued to Other Than Employees for Acquiring, or in Conjunction with Selling, Goods or Services.* Under SFAS No. 123, stock-based compensation for stock options granted to non-employees is equal to the fair value of the stock options rather than the intrinsic value under APB No. 25. We determine the fair value of options granted to non-employees using the Black-Scholes option valuation model, which was developed for use in estimating the fair value of traded options that have no vesting restrictions and are fully transferable. The Black-Scholes option valuation model requires the input of highly subjective assumptions, including the expected volatility of our stock price. Stock-based compensation related to options granted to consultants is generally remeasured periodically as the underlying options vest.

Stock-based compensation expense includes amounts attributable to certain issuances of common stock for notes receivable that we have accounted for as in-substance stock options and are further described in the notes to our annual financial statements appearing in this Report. Stock-based compensation expense is assigned to operating expense categories in our statements of operations according to nature of the services rendered by the employee or consultant to whom the expense applies. We recognized stock-based compensation expense of $352,000 in 2002, $4.5 million in 2003 and $6.8 million in 2004.

In future periods, we are required to remeasure stock-based compensation cost for all employee options repriced under the repricing program that remain outstanding and to periodically remeasure the stock-based compensation cost of options we have granted to consultants. Since the amount of compensation cost attributable to the repriced options and consultant options is dependent on the fair value of our common stock underlying the options on the future remeasurement dates, the amount of stock-based compensation recognized in any given future period cannot be predicted and may have a material impact on our results of operations.

In December 2004, the Financial Accounting Standard Board (“FASB”) issued SFAS No. 123R. The statement requires companies to expense share-based payments to employees, including stock options, based on the fair value of the award at the grant date. The statement also eliminates the intrinsic value method of accounting for stock options permitted by APB No. 25, which we currently follow. We are required to adopt the standard for the quarter that begins July 1, 2005. While the fair value method under SFAS No. 123R is very similar to the fair value method under SFAS No. 123 with regards to measurement and recognition of stock-based compensation, management is currently evaluating the impact of several of the key differences between the two standards on our financial statements. For example, SFAS No. 123 permits recognizing forfeitures as they occur while SFAS No. 123R will require estimating future forfeitures and adjusting estimates on a quarterly basis. SFAS No. 123R will also require a classification change in the statement of cash flows, whereby a portion of any tax benefits from stock options will move from operating cash flows to financing cash flows (total cash flows will remain unchanged). While we continue to evaluate the impact of SFAS No. 123R on our financial statements, we believe that the expensing of stock-based compensation will have an impact on our Statements of Operations similar to our pro forma disclosure under SFAS No. 123.

**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, 2004, we have established a valuation allowance of $114.2 million against all of our gross 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.

## RESULTS OF OPERATIONS

### Years ended December 31, 2004 and 2003

#### Revenues

No revenues were recorded for the years ended December 31, 2004 or 2003. We do not anticipate receiving revenues from the sales of any product prior to regulatory approval and commercialization of our Technosphere Insulin System.

#### Research and development expenses

Research and development expenses increased by $13.7 million to $59.3 million for the year ended December 31, 2004 compared to $45.6 million for the year ended December 31, 2003, an increase of 30.0%. The increase was primarily due to ongoing expenditures in 2004 related to our Technosphere Insulin System. Continuation of preclinical and clinical studies in 2004 increased research expenditures by $15.0 million, which also resulted in increased manufacturing costs of $8.9 million to supply clinical trial materials and to continue the validation of our manufacturing system. The increased costs were offset by a decrease of $6.2 million in research and development costs resulting from the termination of AlleCure product development programs and the redesign of CTL product development programs initiated in the first quarter of 2003. Additionally, offsetting the total increase in research and development expenses is an estimated $4.0 million benefit recognized pursuant to a program under which we can exchange qualified research and development income tax credits for cash in the State of Connecticut. Approximately $1.5 million of the $4.0 million recognized under this program consisted of cash received during the third quarter of 2004, with the remaining $2.5 million receivable as of December 31, 2004. We anticipate that our research and development expenses will increase significantly with the continuation of existing and initiation of new clinical trials and the resulting manufacturing costs associated with producing materials for these clinical trials.

#### General and administrative expenses

General and administrative expenses decreased by $2.8 million to $17.9 million for the year ended December 31, 2004 compared to $20.7 million for the year ended December 31, 2003, a decrease of 13.6%. The decrease was primarily due to $3.3 million in transition and severance expenses resulting from the consolidation in 2003 of our California operations into our Valencia, California facility and reduction of our California workforce, offset by increases in 2004 in non-cash stock-based compensation expense of $0.4 million.

#### Other income (expense)

Other income of $226,000 for the year ended December 31, 2004 relates primarily to investment income of $96,000 and the recovery of $136,000 of rental income that was fully reserved in prior years. Other income of $36,000 for 2003 consists primarily of investment income of $46,000, offset by a $20,000 reserve against rental income due to non-payment by the lessee.

#### Interest income

Interest income increased by $534,000 to $932,000 for the year ended December 31, 2004 compared to $398,000 for the year ended December 31, 2003, an increase of 134.2%. The increase was primarily due to higher levels of cash and marketable securities available for investment during 2004 compared to 2003, resulting from the receipt of $83.2 million in net proceeds from our initial public offering and $18.2 million from the collection of stock subscriptions for Series C convertible preferred stock.

#### Deemed dividends

Deemed dividends of $19.8 million and $1.0 million for the years ended December 31, 2004 and 2003, respectively, represent the beneficial conversion charge to common stockholders related to the downward adjustment of the Series B and C preferred stock conversion price. No further deemed dividends will be recognized for these securities as all outstanding preferred stock automatically converted into common stock at the close of our initial public offering in the third quarter of 2004.

### Years ended December 31, 2003 and 2002

#### Revenues

No revenues were recorded for the years ended December 31, 2003 or 2002. We do not anticipate receiving revenues from the sales of any product prior to regulatory approval and commercialization of our Technosphere Insulin System.

**Research and development expenses**

Research and development expenses increased by $2.9 million to $45.6 million for the year ended December 31, 2003 compared to $42.7 million for the year ended December 31, 2002, an increase of 6.8%. The increase was primarily due to increased clinical and manufacturing expenses for our Technosphere Insulin System. Our clinical expenses increased in 2003 due to an increase in the number of individuals participating in our Phase 2 clinical trials. The expansion of our manufacturing production capacity to support the anticipated Technosphere Insulin clinical trial material requirements increased manufacturing costs, which included depreciation, repair and maintenance of equipment, validation costs and development costs for new machinery. We anticipate that our research and development expenses will increase significantly with the continuation of existing and initiation of new clinical trials and the resulting manufacturing costs associated with producing materials for these clinical trials.

**General and administrative expenses**

General and administrative expenses increased by $7.5 million to $20.7 million for the year ended December 31, 2003 compared to $13.2 million for the year ended December 31, 2002, an increase of 56.6%. The increase was primarily due to stock-based compensation expense of $3.8 million and transition and severance expenses of $3.3 million, which resulted from the consolidation of our California facilities into our Valencia, California facility and the reduction of the California workforce from 198 employees as of December 31, 2002 to 80 employees as of December 31, 2003.

**Goodwill Impairment**

In 2001, we recorded goodwill of approximately $151.4 million as part of our acquisition of AlleCure and CTL on December 12, 2001. We reevaluate goodwill each year in connection with SFAS No. 142, Goodwill and Other Intangible Assets, and any related impairment losses are recognized in earnings when identified. Toward the end of the third quarter of 2002, we initiated an internal study to assess whether the product development programs acquired in the merger with AlleCure and CTL were meeting their objectives. As a result of this study, our management concluded in December 2002 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, during the first quarter of 2003, we closed the CTL facility and reduced headcount for AlleCure and CTL by approximately 50%. In connection with our annual test for impairment of goodwill as of December 31, 2002, we determined that on the basis of the internal study, the goodwill recorded for the AlleCure and CTL units was potentially impaired. We performed the second step of our annual impairment test as of December 31, 2002 for each of the potentially impaired reporting units and estimated the fair value of the AlleCure and CTL programs, as acquired in the merger, using the expected present value of future cash flows which are now expected to be negligible. Accordingly, the goodwill balance of $151,428,000 was determined to be fully impaired and an impairment loss was recorded in fourth quarter of 2002.

**Other income (expense)**

Other income of $36,000 for the year ended December 31, 2003 consists primarily of investment income of $46,000, offset by a $20,000 reserve against rental income due to non-payment by the lessee. For 2002, other income of $487,000 is comprised primarily of rental income related to leasing a portion of our facility to a third party.

**Interest income**

Interest income decreased by $219,000 to $398,000 for the year ended December 31, 2003 compared to $617,000 for the year ended December 31, 2002, a decrease of 35.5%. The decrease was primarily due to lower average fund balances available for investment.

**Deemed dividends**

Deemed dividends of $1.0 million and $1.4 million for the years ended December 31, 2003 and 2002, respectively, represent the beneficial conversion charge to common stockholders related to the downward adjustment of the Series B and C preferred stock conversion price. No further deemed dividends will be recognized for these securities as all outstanding preferred stock automatically converted into common stock at the close of our initial public offering in the third quarter of 2004.

**LIQUIDITY AND CAPITAL RESOURCES**

Prior to our initial public offering, we have historically funded our operations primarily through the private placement of equity securities with our majority stockholder and his affiliated entities, who have invested approximately $228.5 million of the approximately $328.5 million that we have raised prior to the closing of our initial public offering on August 2, 2004. In 2003, we raised $100.0 million through private placements of our equity securities, comprising 3,493,194 shares of common stock sold at a weighted average price of $14.31 per share, and 980,392 shares of Series C convertible preferred stock that were subscribed for in 2003. Of the $50.0 million of Series C convertible preferred stock subscribed for in 2003, $31.8 million, representing the purchase price of 624,449 shares of Series C convertible preferred stock, was received in 2003 and $18.2 million, representing the purchase price of the remaining 355,943 shares of Series C convertible preferred stock, was received in the first quarter of 2004. All of the shares of our Series C convertible preferred stock were issued in the first quarter of 2004.

On August 2, 2004, we closed our initial public offering at a price to the public of $14.00 per share. We sold 6,250,000 shares of our common stock in the offering for a gross offering price of $87.5 million. We granted the underwriters a 30-day option to purchase up to an additional 937,500 shares of common stock to cover over-allotments, if any. This option was exercised for 307,100 shares on August 28, 2004 and closing occurred on September 1, 2004 with gross proceeds to us of approximately $4.3 million. In connection with the initial public offering, we paid $6.4 million in underwriting discounts and commissions to underwriters and incurred $2.2 million in other offering expenses. After deducting the underwriting discounts and commissions and other offering expenses, we received net proceeds from the initial public offering, including the over-allotment, of approximately $83.2 million. These proceeds and the conversion of our preferred stock to common stock are reflected in the accompanying consolidated financial statements as of and for the year ended December 31, 2004.

Our operating activities used net cash of $59.9 million in 2004, $52.8 million in 2003 and $48.7 million in 2002. During these periods, we recorded increasing expenses due principally to increases in research and development, expanded clinical trials, and recruitment of management and technical staff, which resulted in increasing operating cash outflows. We expect our negative operating cash flow to continue for several years.

Our investing activities used $9.6 million in 2004, $6.9 million for the purchase of property and equipment and $2.7 million in net purchases and sales of marketable securities. In 2003, our investing activities generated $2.2 million, principally from the proceeds from the net sales and purchases of marketable securities of $7.3 million, offset by $5.1 million for the purchase of property and equipment. Our investing activities used $50.5 million in 2002 for the purchase of property and equipment of $34.1 million and net purchases and sales of marketable securities of $16.4 million.

Our financing activities provided cash of $101.5 million in 2004 generated primarily from the receipt of $83.2 million in net proceeds from our initial public offering in the third quarter of 2004 and $18.2 million from the collection of stock subscriptions for 355,943 shares of Series C convertible preferred stock in the first quarter of 2004. In 2003, our financing activities provided $82.8 million primarily from the collection of $31.8 million of stock subscriptions for 624,449 shares of Series C convertible preferred stock and $50.0 million from the sale of 3,493,194 shares of common stock in 2003. In 2002, financing activities generated $60.2 million primarily from the sale of 4,155,757 shares of common stock, which provided $58.9 million in proceeds.

As of December 31, 2004, we had $90.5 million in cash, cash equivalents and marketable securities. We expect our existing capital resources and interest income will be sufficient to fund currently planned operations into the third quarter of 2005. We intend to seek additional funding through public or private equity financing, arrangements with corporate partners or other sources. There can be no assurance that we will be able to obtain such additional capital or enter into such relationships with corporate partners on a timely basis, on favorable terms, or at all. If adequate funds are not available, we may be required to delay, reduce or eliminate expenditures for certain of our programs, including our Technosphere Insulin development activities. Because the majority of our expenses in 2005 can be reduced or eliminated in a relatively short period, we believe that if we are unable to obtain additional capital we can continue activities, on a reduced basis, into 2006.

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 formulation technology. In addition, portions of our capital resources will be devoted to expanding our other product development programs for the treatment of solid-tumor cancers. We anticipate that we will expend a portion of our capital to scale up our manufacturing capabilities in our Danbury facilities. We also intend to use our capital resources for general corporate purposes, which may include in-licensing or acquiring additional technologies.

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 and share a portion of the costs associated with the development, manufacture and

commercialization of our Technosphere Insulin product candidate. 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, 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, 2004, we did not have any off-balance sheet arrangements as defined under Item 303(a)(4)(ii) of SEC Regulation S-K.

**COMMITMENTS AND CONTINGENCIES**

Our contractual obligations consist of operating leases, purchase obligations, capital lease commitments and deferred compensation. Some of our current and former employees elected to defer part or all of their compensation from 1991 through 1998, resulting in total deferred compensation of $1.4 million at December 31, 2004. The amounts due for deferred compensation are non-interest-bearing with no repayment terms. Our other obligations are included in the table below.

Future payments under our operating lease obligations, including a facility lease executed in March 2005, and open purchase commitments consisted of the following at December 31, 2004 (in thousands):

| | Payments due in | | | | |
|---|---|---|---|---|---|
| **Contractual obligations** | **Less than one year** | **1-3 years** | **3-5 years** | **5 years** | **Total** |
| Open purchase order commitments(1) | 12,940 | 1,428 | – | – | 14,368 |
| Operating lease obligations | 753 | 963 | 499 | – | 2,215 |
| Total contractual obligations | 13,693 | 2,391 | 499 | – | 16,583 |

(1) *The amounts included in open purchase order commitments are subject to performance under the purchase order by the supplier of the goods or services and do not become our obligation until such performance is rendered. The amount shown is principally for the purchase of materials for our clinical trials and the acquisition of manufacturing equipment.*

**RELATED PARTY TRANSACTIONS**

For a description of our related party transactions see “Certain relationships and related party transactions.”

**RECENT ACCOUNTING PRONOUNCEMENTS**

In December 2004, the FASB issued SFAS No. 123R, *Share-based Payment: an Amendment of FASB Statement 123 and 95*. The statement requires companies to expense share-based payments to employees, including stock options, based on the fair value of the award at the grant date. The statement also eliminates the intrinsic value method of accounting for stock options permitted by APB No. 25, *Accounting for Stock Issued to Employees*, which we currently follow. We are required to adopt the standard for the quarter that begins July 1, 2005. While the fair value method under SFAS No. 123R is very similar to the fair value method under SFAS No. 123 with regards to measurement and recognition of stock-based compensation, management is currently evaluating the impact of several of the key differences between the two standards on our financial statements. For example, SFAS No. 123 permits

recognizing forfeitures as they occur while SFAS No. 123R will require estimating future forfeitures and adjusting estimates on a quarterly basis. SFAS No. 123R will also require a classification change in the statement of cash flows, whereby a portion of any tax benefits from stock options will move from operating cash flows to financing cash flows (total cash flows will remain unchanged). While we continue to evaluate the impact of SFAS No. 123R on our financial statements, we believe that the expensing of stock-based compensation will have an impact on our Statements of Operations similar to our pro forma disclosure under SFAS No. 123.

In March 2004, the FASB ratified the measurement and recognition guidance and certain disclosure requirements for impaired securities as described in EITF Issue No. 03-1, *The Meaning of Other-Than-Temporary Impairment and Its Application to Certain Investments*. In September 2004, the FASB issued a proposed Staff Position ("FSP") EITF Issue No. 03-1a, "Implementation Guidance for the Application of Paragraph 16 of EITF 03-1". The proposed FSP will provide measurement and recognition guidance with respect to debt securities that are impaired solely due to interest rates and/or sector spreads. The FSP delays the effective date of EITF Issue No. 03-1 until such time that the FASB issues the final standard. Management has not determined what impact the adoption of the measurement and recognition guidance in EITF Issue No. 03-1 will have on our financial statements.

**RISKS AND UNCERTAINTIES THAT MAY AFFECT RESULTS**

The risks described below may not be the only risks we face. Additional risks that we do not currently think are material may also impair our business operations. If any of the events or circumstances described in the following risks actually occur, our business, financial condition or results of operations could suffer, and the trading price of our common stock could decline.

**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 several years, if at all.

We have never been profitable and had a net loss of $76.0 million for the year ended December 31, 2004. As of December 31, 2004, we had an accumulated deficit of $443.0 million. 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 additional 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 will suffer.***

It is costly to develop therapeutic products and conduct clinical trials for these products. Although we currently are focusing on our Technosphere Insulin System as our lead product candidate, we may in the future conduct clinical trials and perform preclinical research for a number of additional product candidates. Our future revenues may not be sufficient to support the expense of these activities.

Based upon our current expectations, we believe that our existing capital resources will enable us to continue planned operations into the third quarter of 2005 even if we do not enter into a collaborative agreement. 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 expect that we will need 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;
- actions taken by the FDA and other regulatory authorities with respect to our products and competitive products;
- our success in establishing strategic business collaborations;
- the timing and amount of milestone or other payments we might receive from potential third parties;
- the timing and amount of payments we might receive from potential licenses;
- the costs of discontinuing projects and technologies or decommissioning existing facilities, if we undertake those activities;
- 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; and
- the costs of preparing, filing, prosecuting, maintaining and enforcing patent claims and other intellectual property rights or defending against claims of infringement by others.

We have raised capital in the past primarily through the sale of equity securities. We may in the future pursue the sale of equity and/or debt securities, or the establishment of other funding facilities. Issuances of debt or additional equity could impact your rights as a holder of our common stock, may dilute your ownership percentage 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. We cannot assure you, however, that any strategic collaborations, sales of securities or sale or license 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, licensing arrangements, sales of securities 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.

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

To date, we have not completed the development of any products through to commercialization. Only our Technosphere Insulin System is currently undergoing clinical trials, while our other product candidates are in research 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 advance our Technosphere Insulin System through Phase 3 clinical trials and demonstrate in these trials that our Technosphere Insulin System is safe and effective. We currently anticipate conducting several pivotal Phase 3 clinical trials as well as several special population studies involving, in total, more than 3,000 patients, which will require the expenditure of additional time and resources. We must also receive the necessary approvals from the FDA and similar foreign regulatory agencies before this product 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 immunology. 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 many 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 formulation 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 drugs or therapeutics. 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 fail to enter into a strategic collaboration with respect to our Technosphere Insulin System, our most clinically advanced program, we may not be able to execute on our business model.***

Our current strategy for developing, manufacturing and commercializing our 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.

If we are not able to enter into a collaboration on terms that are favorable to us for our products, we could be required to undertake and fund product development, clinical trials, manufacturing and marketing activities solely at our own expense. For example, we are currently evaluating potential collaborations with respect to our Technosphere Insulin System. We currently estimate that the cost of a self-funded Phase 3 program over the next 12 months would be in the range of $110 to $140 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 following initial Phase 3 clinical trials or with respect to any other product candidate could substantially increase our requirements for capital, which might not be available on favorable terms, or at all. Alternatively, we would have to substantially reduce our development efforts, which would delay or otherwise impede the commercialization of our product candidates.

***Testing of a particular product candidate may not yield successful results, or even if it does, we still may be unable to commercialize that product candidate.***

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

- safety and efficacy results obtained from our preclinical and initial clinical studies may be inconclusive or may not be predictive of results obtained in later-stage clinical trials or following long-term use and we may 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 have initiated one of several long-term safety studies of our Technosphere Insulin system designed to evaluate a number of safety issues, including pulmonary function. Our Technosphere Insulin System is intended for multiple uses per day. Due to the size and time frame over which the clinical trials are conducted, the results of clinical trials may not be indicative of the effects of long-term use. If long-term use of our product 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, our collaborators 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 third-party payors do not reimburse customers for our products, they might not be used or purchased, which would adversely affect our revenues.***

Our revenues and profitability may be affected by the continuing efforts of governments and third-party payors to contain or reduce the costs of healthcare through various means. For example, in certain foreign markets the pricing or profitability 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 payors 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 product candidates, and therefore may limit our ability to generate 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 payors, such as governmental and private insurance plans. Third-party payors are increasingly challenging the prices charged for medical products and services. In addition, because each third-party payor individually approves reimbursement, obtaining these approvals is a time-consuming and costly process that will require us to provide scientific and clinical support for the use of each of our products to each third-party payor separately with no assurance that approval will be obtained. This process could delay the market acceptance of new products and could have a negative effect on our revenues and operating results. Even if we succeed in bringing one or more products to market, we cannot be certain that these products will be considered cost-effective or that reimbursement to the consumer will be available, in which case our business and results of operations will be harmed and the market price of our common stock may decline.

***If we do not achieve our projected development goals in the timeframes we announce and expect, the commercialization of our product candidates may be delayed and our business will be harmed.***

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 may 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;
- the receipt of approvals by our competitors and by us from the FDA and other regulatory agencies;
- other actions by regulators;
- 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;
- the costs of expanding and maintaining manufacturing operations, as necessary;
- the extent of scheduling conflicts with participating clinicians and clinical institutions; and
- our ability to identify and enroll patients who meet clinical trial eligibility criteria.

In addition, if we do not obtain sufficient additional funds through strategic collaborations, sales of securities or the sale or license 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 may 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.

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

We currently rely on hospitals and clinical research organizations to conduct, supervise or monitor some or all aspects of clinical trials involving our product candidates, including our Technosphere Insulin System. Further, we may also enter into license agreements, partnerships or other collaborative arrangements to support 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 product candidates. We cannot assure you 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.

***If we are unable to manage growth in connection with our transition from an early-stage development company to a company that commercializes therapeutics, our operations will suffer.***

We will need to add a significant number of new personnel, broaden our areas of expertise, and expand our manufacturing capabilities in order to successfully implement our commercialization strategy for our Technosphere Insulin System. Over the next two years, we estimate that we will need to recruit a significant number of new employees, principally in the clinical development and manufacturing production areas. Organizational growth and expansion of operations could strain our existing managerial, operational, financial and other resources.

***We have never manufactured any of our product candidates 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 use our Danbury, Connecticut facility to manufacture raw Technosphere material, 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 price, our facilities expansion could be delayed or its costs increased.

We have never manufactured any of our product candidates 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 assure you 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 will 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 its raw material, the transition could also require significant start-up time to qualify 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.

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 our potential third-party manufacturers fail to deliver the required commercial quantities of our products on a timely basis and at commercially reasonable prices, 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 on a timely basis, we would likely be unable to meet demand for our products and we would lose potential revenues.

***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 will be harmed and the market price of our common stock may 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. We currently have a long-term supply agreement with Diosynth B.V., an independent supplier of insulin and a subsidiary of Akzo Nobel, which is currently our sole supplier for insulin. We are aware of at least five other suppliers of bulk insulin. Currently, we manufacture the raw Technosphere material, but we are in the process of qualifying a secondary manufacturer to supply us with commercial quantities of this raw material. We recently entered into a long-term supply agreement with Vaupell, Inc., the supplier of our MedTone inhaler and cartridges. We must rely on our suppliers to comply with relevant regulatory and other legal requirements, including the production of insulin in accordance with current drug Good Manufacturing Practices, or 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, our development or manufacturing may be delayed. Any such events would delay the submission of our product candidates 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.

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

A broad base of physicians and specialists treat patients with diabetes. A large sales force will be required in order to educate and support these physicians and specialists. Therefore, we plan to enter into collaborations with one or more pharmaceutical companies to sell, market and distribute our Technosphere Insulin System. If we fail to enter into collaborations, we will be required to establish our own direct sales, marketing and distribution capabilities. Establishing these capabilities can be time-consuming and expensive and we estimate that establishing a specialty sales force would cost more than $20 million. Because of our size, we would be at a disadvantage to our potential competitors, all of which have collaborated with large pharmaceutical companies that have substantially more resources than we do. As a result, we 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.

***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 initially are focusing on the development of the Technosphere Insulin System for the treatment of diabetes, and we face intense competition in this area. Pfizer, Inc. and Sanofi-Aventis, in collaboration with Nektar Therapeutics, have been conducting Phase 3 clinical trials for the Exubera product. In March 2004, these collaborators filed a submission seeking regulatory approval in Europe, and in March 2005, they filed a new drug application, or NDA, with the FDA and an FDA decision could be made by early 2006. Novo Nordisk A.S., in collaboration with Aradigm Corporation, has a pulmonary insulin product in development. Eli Lilly and Company, in collaboration with Alkermes, Inc., is conducting clinical trials for a pulmonary insulin product. In addition, a number of established pharmaceutical companies have or are developing proprietary technologies or have entered into arrangements with, or acquired, companies with technologies for the treatment of diabetes. We also face substantial competition for the development of our other product candidates. See “Business—Competition.”

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.

The rapid rate of scientific discoveries and technological changes could result in one or more of our products becoming obsolete or noncompetitive. Our competitors may develop or introduce new products that would render our technology and our Technosphere Insulin System less competitive, uneconomical or obsolete. The fact that another company will likely be the first to commercialize a pulmonary insulin system may give that company an advantage in terms of being able to gain reputation and market share as well as set parameters for the pulmonary insulin market such as pricing. Our future success will depend not only on our ability to develop our products 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, cancer and inflammatory and autoimmune diseases. 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.

***If our products do not become widely accepted by physicians, patients, third-party payors and the healthcare community, we may be unable to generate significant revenue, if any.***

Our product candidates are new and unproven. Even if our product candidates obtain regulatory approvals, they may not gain market acceptance among physicians, patients, third-party payors 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 product candidates will depend on many factors, including:

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

Physicians will not recommend our products until clinical data or other factors demonstrate the safety and efficacy of our products 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 payors and the effectiveness of our competitors in marketing their therapies. Because of these and other factors, our products may not gain market acceptance, which would materially harm our business, financial condition and results of operations.

***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 various product candidates, including the Technosphere Insulin System, 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 may not be able to obtain insurance coverage that will be adequate to satisfy any liability that may arise. 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 will be harmed and the market price of our common stock may decline.

We currently carry worldwide liability insurance in the amount of $5 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 requires us to carry local coverage. We intend to obtain

product liability coverage for commercial sales in the future. However, insurance coverage in our industry can be very expensive and difficult to obtain and we cannot assure you that we will be able to obtain sufficient coverage at an acceptable cost, if at all. If we are sued for any injury caused by our technology or products, or by third-party products that we manufacture, our liability could exceed our insurance coverage and total assets.

***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, 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 estimate that the cost to complete the soil cleanup plan for industrial use is $1.5 to $3.0 million over the next 18 to 24 months. 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 latter 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 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, including Messrs. Mann, Edstrom, Burns and Anderson, Ms. Palumbo, and Drs. Cheatham and Thomson, 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.

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 and Co-Chief Executive Officer of Advanced Bionics Corporation, which was acquired by Boston Scientific Corporation, and 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 be able to expend the same time or focus on our activities as other, similarly situated chief executive officers. Mr. Mann typically devotes anywhere between 25 and 50 hours a week to our business. 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.

***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.***

Our amended and restated certificate of incorporation and bylaws include anti-takeover 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, because we are incorporated in Delaware, 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 from merging or combining with us. 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.

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

Our headquarters and some of our research and development activities are located in Southern California, where they are subject to an enhanced risk of natural and other disasters such as power and telecommunications failures, mudslides, fires and earthquakes. A 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.

***Failure to achieve and maintain effective internal controls in accordance with Section 404 of the Sarbanes-Oxley Act could have a material adverse effect on our business and stock price.***

We are in the process of documenting and testing our internal control procedures in order to satisfy the requirements of Section 404 of the Sarbanes-Oxley Act, which, beginning with our fiscal year ending December 31, 2005, will require annual management assessments of the effectiveness of our internal controls over financial reporting and a report by our independent auditors that both addresses management's assessments and provides for the independent auditor's assessment of the effectiveness of our internal controls. During the course of our testing, we may identify deficiencies which we may not be able to remediate in time to meet the deadline for compliance with Section 404. Testing and maintaining internal controls also involves significant costs and can divert our management's attention from other matters that are important to our business. We may not be able to conclude on an ongoing basis that we have effective internal controls over financial reporting in accordance with Section 404, and our independent auditors may not be able or willing to issue a favorable assessment of our conclusions. Failure to achieve and maintain an effective internal control environment could harm our operating results and could cause us to fail to meet our reporting obligations. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our stock.

**Risks Related to Regulatory Approvals**

***Our product candidates must undergo rigorous preclinical 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 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. We expect, based on our discussions with the FDA and on our understanding of the interactions between the FDA and other pharmaceutical companies developing pulmonary insulin delivery systems, that we will need safety data covering at least two years from patients treated with our Technosphere Insulin System and that we must conduct a two-year carcinogenicity study of Technosphere Insulin in rodents to obtain approval, among other requirements. We cannot be certain when or under what conditions we will undertake further clinical trials, including a US Phase 3 program for our Technosphere Insulin System. 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. 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. 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.

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. To our knowledge, no pulmonary insulin product has yet been approved for marketing and we are not aware of any precedent for the successful commercialization of products based on our technology or technologies similar to ours. However, an application for approval for another pulmonary insulin product candidate was recently filed in the United States and a decision could be made by the FDA in early 2006. 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 the Technosphere Insulin System will be reviewed and approved.

***Also, recent events regarding questions about the safety of marketed drugs, 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 the Company's 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. The FDA advised us that the Technosphere Insulin System must be tested 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 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.

***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 and other product candidates until we have obtained regulatory approval, and any delay in obtaining, or inability to obtain, regulatory approval could harm our business. In addition, regulatory authorities may also 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.

***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. For example, based on currently available clinical studies, we believe that our Technosphere Insulin System may have certain advantages over currently approved insulin products or pulmonary insulin products in development, including its approximation of the natural first-phase insulin release spike. Nonetheless, there are no assurances that these and other advantages, if any, of the 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 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 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. Quality System Regulations, or 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 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.***

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.

Any regulatory approvals that we receive for our product candidates may also be subject to limitations on the indicated uses for which the product candidate may be marketed or contain requirements for potentially costly post-marketing follow-up clinical trials.

***Reports of side effects or safety concerns in our 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 product 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 products 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 product.

For example, in August 2004, an analyst reported that the United Kingdom Committee on the Safety of Medicines had expressed concern that a European application for approval of a drug for the treatment of diabetes was not licensable at the time. Earlier in 2004, Sanofi-Aventis, on behalf of Pfizer and Nektar, filed for regulatory approval in Europe of Exubera. Although the identity of the drug was not disclosed in the analyst's report, the news nonetheless triggered temporary but sharp declines in the market prices of Nektar's common stock as well as our common stock.

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, know-how 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 technologies.

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 if we attempt to enforce them and they are challenged in court or in other proceedings, such as oppositions, which may be brought in US or foreign jurisdictions to challenge the validity of a patent. A third party may challenge the validity or enforceability of a patent after its issuance by the US Patent and Trademark Office, or USPTO.

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 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. 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 a patent and the courts do not always arrive at uniform conclusions.

A third party may claim that we are using inventions covered by such third party's patents and may go to court to stop us from engaging in our normal operations and activities. These 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 that a court may interpret to restrict our freedom to operate (that is, to cover our products) in the areas of Technosphere formulations, pulmonary insulin delivery and the treatment of cancer. Specifically, 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.

Patent litigation is costly and time-consuming. Among other things, such 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. Although patent and intellectual property disputes in the pharmaceutical area have often been settled for licensing or similar arrangements, associated costs may be substantial and could include ongoing royalties. 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. See "Business—Intellectual Property and Proprietary Technology."

***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 those products in any jurisdiction, including the United States. 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.

## RISKS RELATED TO OUR COMMON STOCK

**We expect that our stock price will fluctuate significantly.**

We completed our initial public offering on August 2, 2004. Prior to that, our stockholders could not buy or sell our common stock publicly. An active public market for our common stock may not continue to develop or be sustained. The stock market, particularly in recent years, has experienced significant volatility particularly with respect to pharmaceutical and biotechnology stocks. 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 their clinical trial results, acquisitions, strategic alliances, technological innovations and newly approved commercial products;
- the availability of critical materials used in developing and manufacturing our Technosphere Insulin System or other product candidates;
- developments concerning our patents, proprietary rights and potential infringement claims;
- the expense and time associated with, and the extent of our ultimate success in, securing regulatory approvals;
- changes in securities analysts' estimates of our financial and operating performance;
- sales of large blocks of our common stock, including sales by our executive officers, directors and significant stockholders; and
- 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.

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 National 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.

**Alfred E. Mann, our Chairman, 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.**

Mr. Mann has been our primary source of financing to date. As of December 31, 2004, Mr. Mann beneficially owned approximately 48.7% of our outstanding shares of capital stock. As of the same date, members of Mr. Mann's family beneficially owned at least a further 3.1% 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. In the event we sell additional equity in future financings, Mr. Mann may participate in those financings, which may increase his beneficial ownership percentage of our common stock.

Subject to compliance with 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, 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, four of his children and Dr. Joseph Schulman, the director of AMF. The AEMFBE is a membership foundation consisting of five members, including Mr. Mann and the same four 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 could negatively affect our stock price.**

As of December 31, 2004, we had approximately 32.8 million shares of common stock outstanding, all of which are available for public sale, subject in some cases to volume and other limitations. 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. The holders of 916,715 shares of our common stock and the holders of warrants to purchase 131,628 shares of our common stock have rights, subject to some conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. Furthermore, if we were to include in a company-initiated registration statement shares held by those holders 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, 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.**

Our amended and restated certificate of incorporation and bylaws include anti-takeover 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, because we are incorporated in Delaware, 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 from merging or combining with us. 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. See "Description of capital stock—Amended and restated certificate of incorporation and bylaw provisions."

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

We have not used derivative financial instruments for speculation or trading purposes. However, we are exposed to market risk related to changes in interest rates. Our current policy is to maintain a highly liquid short-term investment portfolio consisting mainly of US money market funds and government and investment-grade corporate debt. Our cash is deposited in and invested through highly rated financial institutions in North America. Our short-term investments are subject to interest rate risk and will fall in value if market interest rates increase. If market interest rates were to increase immediately and uniformly by ten percent from levels at December 31, 2004, we estimate that the fair value of our investment portfolio would decline by an immaterial amount.

**Effects of Inflation**

Our assets are primarily monetary, consisting of cash, and cash equivalents, which are not directly affected by inflation. We also believe that we have intangible assets in the value of our technology. In accordance with generally accepted accounting principles, we have not capitalized the value of this intellectual property on our consolidated balance sheet. Due to the nature of this intellectual property, we believe that these intangible assets are not affected by inflation. Because we intend to retain and continue to use our equipment, furniture and fixtures and leasehold improvements, we believe that the incremental inflation related to replacement costs of such items will not materially affect our operations. However, the rate of inflation affects our expenses, such as those for employee compensation and contract services, which could increase our level of expenses and the rate at which we use our resources.

**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**

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in our reports filed under the Securities Exchange Act of 1934, as amended, is recorded, processed, summarized and reported within the time periods specified in the Securities and Exchange Commission’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.

As required by Securities and Exchange Commission Rule 13a-15(b), we carried out an evaluation under the supervision and with the participation of our management, including our chief executive officer and chief financial officer, of the effectiveness of the design and operation of our disclosure controls and procedures as of the end of the period covered by this report. Based on the foregoing, our chief executive officer and chief financial officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level.

There has been no change in our internal control over financial reporting during the fiscal quarter ended December 31, 2004 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

## PART III

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

The information regarding the identification and business experience of MannKind's directors under the caption "Proposal 1 – Election of Directors" in MannKind's Proxy Statement for the annual meeting of stockholders to be held in May 2004 to be filed with the Securities and Exchange Commission within 120 days after the end of MannKind's fiscal year ended December 31, 2004, is incorporated herein by reference. For information regarding the identification and business experience of MannKind's executive officers, see "Executive Officers" at the end of Item 1 in Part I of this Annual Report on Form 10-K. Information concerning filing requirements applicable to MannKind's executive officers and directors under the caption "Section 16(a) Beneficial Ownership Reporting Compliance" in MannKind's Proxy Statement is incorporated herein by reference.

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) in connection with "Investor" materials. In addition, we intend to promptly disclose (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 MannKind's 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 caption "Security Ownership of Certain Beneficial Owners and Management" in MannKind's Proxy Statement is incorporated herein by this reference. The remaining information called for by this item relating to "Securities Authorized for Issuance under Equity Compensation Plans" is incorporated herein by reference to MannKind's Proxy Statement.

### Item 13. Certain Relationships and Related Transactions

The information under the caption "Certain Transactions" in MannKind's Proxy Statement is incorporated herein by reference.

With the exception of the information specifically incorporated by reference from MannKind's Proxy Statement in this annual report on Form 10-K, MannKind's 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," "Report of the Compensation Committee of the Board of Directors" and "Performance Measurement Comparison" in MannKind's Proxy Statement is not incorporated by reference in this annual report on Form 10-K.

### Item 14. Principle Accounting Fees and Services

The information under the caption "Principal Accounting Fees and Services" in MannKind's 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 annual report on Form 10-K beginning on page F-2:



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. (b) Reports on Form 8-K. On November 3, 2004, MannKind filed a Form 8-K announcing its third quarter 2004 financial results. On November 3, 2004, MannKind filed a Form 8-K in connection with a press release announcing results from its US-based late phase 2 clinical study of Technosphere Insulin.

(c) Exhibits. The following exhibits are filed as part of, or incorporated by reference into, this annual report on Form10-K:

### Exhibit Index

| Exhibit number | Description of document |
|---|---|
| 3.1# | Registrant's Restated Certificate of Incorporation. |
| 3.2# | Registrant's Amended and Restated Bylaws. |
| 4.1# | Form of Common Stock Certificate. |
| 4.2# | Registration Rights Agreement made and entered into as of 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#* | Form of Indemnity Agreement entered into between the Registrant and its directors and officers. |
| 10.2#* | 2004 Equity Incentive Plan and Form of Stock Option Agreement thereunder. |
| 10.3# | 2004 Non-Employee Directors' Stock Option Plan and Form of Stock Option Agreement thereunder. |
| 10.4#* | 2004 Employee Stock Purchase Plan and Form of Offering Document thereunder. |
| 10.5#* | Executive Severance Agreement, dated August 1, 2003, between the Registrant and Wendell Cheatham. |
| 10.6#* | Executive Severance Agreement, dated August 1, 2003, between the Registrant and Hakan Edstrom. |
| 10.7#* | Executive Severance Agreement, dated August 1, 2003, between the Registrant and David Thomson. |
| 10.8#* | Executive Severance Agreement, dated August 1, 2003, between the Registrant and Dick Anderson. |
| 10.9#* | Executive Severance Agreement, dated August 1, 2003, between the Registrant and Dan Burns. |
| 10.10#* | Change of Control Agreement, dated August 1, 2003, between the Registrant and Wendell Cheatham. |
| 10.11#* | Change of Control Agreement, dated August 1, 2003, between the Registrant and Hakan Edstrom. |
| 10.12#* | Change of Control Agreement, dated August 1, 2003, between the Registrant and David Thomson. |
| 10.13#* | Change of Control Agreement, dated August 1, 2003, between the Registrant and Dick Anderson. |
| 10.14#* | Change of Control Agreement, dated August 1, 2003, between the Registrant and Dan Burns |
| 10.15#† | Supply Agreement made on January 1, 2000 by and between Diosynth B.V. and Pharmaceutical Discovery Corporation. |
| 10.16# | Pharmaceutical Discovery Corporation 1991 Stock Option Plan. |

| Exhibit number | Description of document |
|---|---|
| 10.17# | Pharmaceutical Discovery Corporation 1999 Stock Plan and Form of Stock Option Plan thereunder. |
| 10.18# | AlleCure Corp. 2000 Stock Option and Stock Plan. |
| 10.19# | CTL Immunotherapies Corp. 2000 Stock Option and Stock Plan. |
| 10.20# | 2001 Stock Awards Plan. |
| 10.21†† | Supply Agreement made as of December 31, 2004 by and between the Registrant and Vaupell, Inc. (incorporated by reference to Exhibit 99.1 to the Registrant's current report on Form 8-K (File No. 333-115020), filed with the Securities and Exchange Commission on February 23, 2005). |
| 21.1 | Subsidiary of the Registrant. |
| 23.1 | Consent of Deloitte & Touche LLP, Independent Registered Accounting Firm. |
| 31.1 | Certification of Chief Executive Officer pursuant to Rules 13a-14 and 15d-14 promulgated under the Securities Exchange Act of 1934. |
| 31.2 | Certification of Chief Financial Officer pursuant to Rules 13a-14 and 15d-14 promulgated under the Securities Exchange Act of 1934. |
| 32.1 | Certifications of Chief Executive Officer and Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes Oxley Act of 2002. |

# Incorporated by reference to the Registrant's Registration Statement on Form S-1 (File No. 333-115020), filed with the Securities and Exchange Commission on April 30, 2004, as amended.

* Indicates management contract or compensatory plan.

† Confidential treatment has been granted with respect to certain portions of this exhibit. Omitted portions have been filed separately with the Securities and Exchange Commission.

†† Confidential treatment has been requested with respect to certain portions of this exhibit. Omitted portions have been filed separately with the Securities and Exchange Commission

## 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 15, 2005

## 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.

| Signature | Title | Date |
|---|---|---|
| /s/ Alfred E. Mann<br>Alfred E. Mann | Chief Executive Officer and Chairman of the Board of Directors (*Principal Executive Officer*) | March 15, 2005 |
| /s/ Hakan S. Edstrom<br>Hakan S. Edstrom | President, Chief Operating Officer and Director | March 15, 2005 |
| /s/ Richard L. Anderson<br>Richard L. Anderson | Corporate Vice President and Chief Financial Officer (*Principal Financial and Accounting Officer*) | March 15, 2005 |
| /s/ Kathleen Connell, Ph.D.<br>Kathleen Connell, Ph.D. | Director | March 15, 2005 |
| /s/ Ronald Consiglio<br>Ronald Consiglio | Director | March 15, 2005 |
| /s/ Llew Keltner M.D., Ph.D.<br>Llew Keltner M.D., Ph.D. | Director | March 15, 2005 |
| /s/ Michael Friedman, M.D.<br>Michael Friedman, M.D. | Director | March 15, 2005 |
| /s/ Kent Kressa<br>Kent Kressa | Director | March 15, 2005 |
| /s/ David H. MacCallum<br>David H. MacCallum | Director | March 15, 2005 |

**MannKind Corporation and Subsidiaries (A Development Stage Company)**

**INDEX TO FINANCIAL STATEMENTS**

Report of Independent Registered Public Accounting Firm

Board of Directors
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, 2003 and 2004 and the related statements of operations, stockholders' equity (deficit) and cash flows for each of the three years in the period ended December 31, 2004 and for the period from February 14, 1991 (date of inception) to December 31, 2004. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with 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. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. Our audit includes consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, 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 financial statements present fairly, in all material respects, the financial position of MannKind Corporation and subsidiaries at December 31, 2003 and 2004 and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2004 and for the period from February 14, 1991 (date of inception) to December 31, 2004 in conformity with accounting principles generally accepted in the United States of America.

/s/ DELOITTE & TOUCHE LLP
Los Angeles, California
March 11, 2005

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

**CONSOLIDATED BALANCE SHEETS**
**(in thousands, except share and per share data)**

| | December 31, 2003 | December 31, 2004 |
|---|---|---|
| **Assets** | | |
| Current assets: | | |
| Cash and cash equivalents | $ 47,020 | $ 78,987 |
| Marketable securities | 8,925 | 11,546 |
| Restricted cash | — | 583 |
| State R&D credit exchange receivable—current | — | 1,500 |
| Prepaid expenses and other current assets | 1,859 | 3,265 |
| Total current assets | 57,804 | 95,881 |
| Property and equipment—net | 67,323 | 66,511 |
| Restricted cash | 559 | — |
| State R&D credit exchange receivable—net of current portion | — | 1,030 |
| Other assets | 190 | 61 |
| Total | $ 125,876 | $ 163,483 |
| **Liabilities and stockholders' equity** | | |
| Current liabilities: | | |
| Accounts payable | $ 1,926 | $ 3,477 |
| Accrued expenses and other current liabilities | 4,015 | 8,194 |
| Payable to stockholder | 1,406 | — |
| Deferred compensation—current | 1,360 | 1,373 |
| Total current liabilities | 8,707 | 13,044 |
| Deferred compensation—net of current portion | 284 | — |
| Other liabilities | 120 | 76 |
| Total liabilities | 9,111 | 13,120 |
| Commitments and contingencies | | |
| Series A redeemable convertible preferred stock, $0.01 par value—267,213 shares authorized, 267,212, issued and outstanding at December 31, 2003 and no shares authorized, issued and outstanding at December 31, 2004; aggregate liquidation value, $5,188 as of December 31, 2003 | 5,188 | — |
| Stockholders' equity: | | |
| Undesignated preferred stock, $0.01 par value—10,000,000 shares authorized; no shares issued or outstanding at December 31, 2003 and 2004 | — | — |
| Series B convertible preferred stock, $0.01 par value—192,618 shares authorized, issued and outstanding at December 31, 2003 and no shares authorized, issued and outstanding at December 31, 2004; aggregate liquidation value, $15,000 at December 31, 2003 | 15,000 | — |
| Series C convertible preferred stock issuable | 50,000 | — |
| Series C convertible preferred stock subscriptions receivable | (18,153) | — |
| Common stock, $0.01 par value—90,000,000 shares authorized; 19,974,727 and 32,756,237 shares issued and outstanding at December 31, 2003 and 2004, respectively | 200 | 327 |
| Additional paid-in capital | 433,141 | 592,999 |
| Notes receivable from stockholders | (1,412) | — |
| Notes receivable from officers | (228) | — |
| Deficit accumulated during the development stage | (366,971) | (442,963) |
| Total stockholders' equity | 111,577 | 150,363 |
| Total | $ 125,876 | $ 163,483 |

See notes to financial statements.

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

**STATEMENTS OF OPERATIONS**
**(in thousands, except per share data)**

| | Year ended December 31, | | | Cumulative period from February 14, 1991 (date of inception) to December 31, 2004 |
|---|---|---|---|---|
| | 2002 | 2003 | 2004 | |
| Revenue | $ — | $ — | $ — | $ 2,858 |
| Operating expenses: | | | | |
| Research and development | 42,724 | 45,613 | 59,266 | 202,913 |
| General and administrative | 13,215 | 20,699 | 17,883 | 75,340 |
| In-process research and development costs | — | — | — | 19,726 |
| Goodwill impairment | 151,428 | — | — | 151,428 |
| Total operating expenses | 207,367 | 66,312 | 77,149 | 449,407 |
| Loss from operations | (207,367) | (66,312) | (77,149) | (446,549) |
| Other income (expense) | 487 | 36 | 226 | (1,970) |
| Interest income | 617 | 398 | 932 | 5,571 |
| Loss before provision for income taxes | (206,263) | (65,878) | (75,991) | (442,948) |
| Income taxes | (2) | (1) | (1) | (15) |
| Net loss | (206,265) | (65,879) | (75,992) | (442,963) |
| Deemed dividends related to beneficial conversion feature of convertible preferred stock | (1,421) | (1,017) | (19,822) | (22,260) |
| Accretion on redeemable preferred stock | (251) | (253) | (60) | (952) |
| Net loss applicable to common stockholders | $ (207,937) | $ (67,149) | $ (95,874) | $ (466,175) |
| Basic and diluted net loss per share | $ (15.43) | $ (3.63) | $ (3.80) | |
| Shares used to compute basic and diluted net loss per share | 13,472 | 18,488 | 25,221 | |

See notes to financial statements.

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

**STATEMENTS OF STOCKHOLDERS' EQUITY (DEFICIT)**
**(in thousands)**

| | Series B convertible preferred stock | | Series C convertible preferred stock | | Series C convertible preferred stock issuable | Series C convertible preferred stock subscriptions receivable | Common stock | | Additional paid-in capital | Notes receivable from stockholders | Notes receivable from officers | Deficit accumulated during the development stage | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Shares | Amount | Shares | Amount | | | Shares | Amount | | | | | |
| BALANCE, FEBRUARY 14, 1991 | | | | | | | | | | | | | |
| Issuance of common stock for cash | — | $ — | — | $ — | $ — | $ — | 998 | $ 10 | $ 890 | $ — | $ — | $ — | $ 900 |
| Net loss | — | — | — | — | — | — | — | — | — | — | — | (911) | (911) |
| BALANCE, FEBRUARY 29, 1992 | — | — | — | — | — | — | 998 | 10 | 890 | — | — | (911) | (11) |
| Issuance of common stock for cash and services | — | — | — | — | — | — | 73 | 1 | 887 | — | — | — | 888 |
| Capital contribution | — | — | — | — | — | — | — | — | 20 | — | — | — | 20 |
| Net loss | — | — | — | — | — | — | — | — | — | — | — | (1,175) | (1,175) |
| BALANCE, FEBRUARY 28, 1993 | — | — | — | — | — | — | 1,071 | 11 | 1,797 | — | — | (2,086) | (278) |
| Issuance of common stock for cash | — | — | — | — | — | — | 11 | — | 526 | — | — | — | 526 |
| Issuance of stock for notes receivable | — | — | — | — | — | — | 8 | — | 400 | (400) | — | — | — |
| Net loss | — | — | — | — | — | — | — | — | — | — | — | (1,156) | (1,156) |
| BALANCE, FEBRUARY 28, 1994 | — | — | — | — | — | — | 1,090 | 11 | 2,723 | (400) | — | (3,242) | (908) |
| 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) |
| BALANCE, DECEMBER 31, 1994 | — | — | — | — | — | — | 1,126 | 11 | 4,528 | — | — | (5,246) | (707) |
| 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) |
| BALANCE, DECEMBER 31, 1995 | — | — | — | — | — | — | 1,127 | 11 | 4,942 | — | — | (8,061) | (3,108) |
| 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) |
| BALANCE, DECEMBER 31, 1996 | — | — | — | — | — | — | 1,131 | 11 | 5,139 | — | — | (10,631) | (5,481) |
| 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) |
| BALANCE, DECEMBER 31, 1997 | — | — | — | — | — | — | 1,718 | 17 | 5,526 | — | — | (12,911) | (7,368) |
| Issuance of common stock for cash and services | — | — | — | — | — | — | 2,253 | 23 | 12,703 | — | — | — | 12,726 |
| 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) |

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

**STATEMENTS OF STOCKHOLDERS' EQUITY (DEFICIT) — (continued)**
**(in thousands)**

| | Series B convertible preferred stock | | Series C convertible preferred stock | | Series C convertible preferred stock issuable | Series C convertible preferred stock subscriptions receivable | Common stock | | Additional paid-in Capital | Notes receivable from stockholders | Notes receivable from officers | Deficit accumulated during the development stage | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Shares | Amount | Shares | Amount | | | Shares | Amount | | | | | |
| BALANCE, DECEMBER 31, 1998 | — | $ — | — | $ — | $ — | $ — | 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) |
| BALANCE, DECEMBER 31, 1999 | — | — | — | — | — | — | 4,496 | 46 | 21,129 | — | — | (21,921) | (746) |
| Conversion of notes payable | — | — | — | — | — | — | 63 | 1 | 1,073 | — | — | — | 1,074 |
| Issuance of Series B preferred stock for cash | 193 | 15,000 | — | — | — | — | — | — | — | — | — | — | 15,000 |
| Issuance of common stock for cash, services and notes | — | — | — | — | — | — | 4,690 | 46 | 33,945 | (2,358) | — | — | 31,633 |
| Discount on notes below market rate | — | — | — | — | — | — | — | — | — | 241 | — | — | 241 |
| Accrued interest on notes | — | — | — | — | — | — | — | — | — | (117) | — | — | (117) |
| Purchase of Series A redeemable convertible preferred stock | — | — | — | — | — | — | — | — | (993) | — | — | — | (993) |
| Amount in excess of redemption obligation | — | — | — | — | — | — | — | — | 999 | — | — | — | 999 |
| Accretion to redemption value on Series A redeemable convertible preferred stock | — | — | — | — | — | — | — | — | (149) | — | — | — | (149) |
| Stock-based compensation | — | — | — | — | — | — | — | — | 9,609 | — | — | — | 9,609 |
| Net loss | — | — | — | — | — | — | — | — | — | — | — | (24,661) | (24,661) |
| BALANCE, DECEMBER 31, 2000 | 193 | 15,000 | — | — | — | — | 9,249 | 93 | 65,613 | (2,234) | — | (46,582) | 31,890 |
| Issuance of common stock for cash | — | — | — | — | — | — | 3,052 | 30 | 78,000 | — | — | — | 78,030 |
| Cash received for common stock to be issued | — | — | — | — | — | — | — | — | 3,900 | — | — | — | 3,900 |
| Issuance of common stock for services | — | — | — | — | — | — | 3 | — | 60 | — | — | — | 60 |
| Exercise of stock options | — | — | — | — | — | — | 1 | — | 13 | — | — | — | 13 |
| Accrued interest on notes | — | — | — | — | — | — | — | — | — | (189) | — | — | (189) |
| Payments on notes receivable | — | — | — | — | — | — | — | — | — | 28 | — | — | 28 |
| Accretion to redemption value on Series A redeemable convertible preferred stock | — | — | — | — | — | — | — | — | (239) | — | — | — | (239) |
| Stock-based compensation | — | — | — | — | — | — | — | — | 1,565 | — | — | — | 1,565 |
| Issuance of put option by stockholder | — | — | — | — | — | — | — | — | (2,949) | — | — | — | (2,949) |
| Record merger of entities | — | — | — | — | — | — | — | — | 171,154 | — | — | — | 171,154 |
| Net loss | — | — | — | — | — | — | — | — | — | — | — | (48,245) | (48,245) |
| BALANCE, DECEMBER 31, 2001 | 193 | 15,000 | — | — | — | — | 12,305 | 123 | 317,117 | (2,395) | — | (94,827) | 235,018 |
| Issuance of common stock for cash | — | — | — | — | — | — | 3,922 | 40 | 58,775 | — | — | — | 58,815 |
| Issuance of common stock for cash already received | — | — | — | — | — | — | 234 | 2 | (2) | — | — | — | — |
| Issuance of stock award to employee | — | — | — | — | — | — | 3 | — | 84 | — | — | — | 84 |
| Cash received for common stock issuable | — | — | — | — | — | — | — | — | 98 | — | — | — | 98 |
| Accrued interest on notes | — | — | — | — | — | — | — | — | — | (229) | — | — | (229) |
| Payments on notes receivable | — | — | — | — | — | — | — | — | — | 1,314 | — | — | 1,314 |
| Beneficial conversion feature of Series B convertible preferred stock | — | — | — | — | — | — | — | — | 1,421 | — | — | — | 1,421 |
| Deemed dividend | — | — | — | — | — | — | — | — | (1,421) | — | — | — | (1,421) |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| related to beneficial conversion feature of Series B convertible preferred stock | | | | | | | | | | | | | |
| Accretion to redemption value on Series A redeemable convertible preferred stock | — | — | — | — | — | — | — | — | (251) | — | — | — | (251) |
| Stock-based compensation | — | — | — | — | — | — | — | — | 268 | — | — | — | 268 |
| Put option redemption by stockholder | — | — | — | — | — | — | — | — | 1,921 | — | — | — | 1,921 |

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

**STATEMENTS OF STOCKHOLDERS' EQUITY (DEFICIT)— (continued)**
**(in thousands)**

| | Series B convertible preferred stock | | Series C convertible preferred stock | | Series C convertible preferred stock issuable | Series C convertible preferred stock subscriptions receivable | Common stock | | Additional paid-in capital | Notes receivable from stockholders | Notes receivable from officers | Deficit accumulated during the development stage | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Shares | Amount | Shares | Amount | | | Shares | Amount | | | | | |
| Net loss | — | $ — | — | $ — | $ — | $ — | — | $ — | $ — | $ — | $ — | $ (206,265) | $ (206,265) |
| BALANCE, DECEMBER 31, 2002 | 193 | 15,000 | — | — | — | — | 16,464 | 165 | 378,010 | (1,310) | — | (301,092) | 90,773 |
| Issuance of Series C convertible preferred stock subscriptions. | — | — | — | — | 50,000 | (50,000) | — | — | — | — | — | — | — |
| Cash collected on Series C convertible preferred stock subscriptions | — | — | — | — | — | 31,847 | — | — | — | — | — | — | 31,847 |
| Issuance of common stock for cash | — | — | — | — | — | — | 3,494 | 35 | 49,965 | — | — | — | 50,000 |
| Non-cash compensation expense of officer resulting from stockholder contribution | — | — | — | — | — | — | — | — | 70 | — | — | — | 70 |
| Issuance of common stock for cash already received | — | — | — | — | — | — | 17 | — | — | — | — | — | — |
| Notes receivable by stockholder issued to officers | — | — | — | — | — | — | — | — | 225 | — | (225) | | |
| Accrued interest on notes | — | — | — | — | — | — | — | — | — | (102) | (3) | — | (105) |
| Beneficial conversion feature of Series B convertible preferred stock | — | — | — | — | — | — | — | — | 1,017 | — | — | — | 1,017 |
| Deemed dividend related to beneficial conversion feature of Series B convertible preferred stock | — | — | — | — | — | — | — | — | (1,017) | — | — | — | (1,017) |
| Accretion to redemption value on Series A redeemable convertible preferred stock | — | — | — | — | — | — | — | — | (253) | — | — | — | (253) |
| Stock-based compensation | — | — | — | — | — | — | — | — | 4,501 | — | — | — | 4,501 |
| Put shares sold to majority stockholder | — | — | — | — | — | — | — | — | 623 | — | — | — | 623 |
| Net loss | — | — | — | — | — | — | — | — | — | — | — | (65,879) | (65,879) |
| BALANCE, DECEMBER 31, 2003 | 193 | 15,000 | — | — | 50,000 | (18,153) | 19,975 | 200 | 433,141 | (1,412) | (228) | (366,971) | 111,577 |
| Issuance of Series C convertible preferred stock for cash | — | — | 356 | 18,153 | (18,153) | 18,153 | — | — | — | — | — | — | 18,153 |
| Issuance of Series C convertible preferred stock for cash already received | — | — | 624 | 31,847 | (31,847) | — | — | — | — | — | — | — | — |
| Exercise of stock options | — | — | — | — | — | — | 86 | — | 1,079 | — | — | — | 1,079 |
| Exercise of warrants | — | — | — | — | — | — | 4 | — | 46 | — | — | — | 46 |
| Accrued interest on notes | — | — | — | — | — | — | — | — | — | (107) | — | — | (107) |
| Repayment of notes receivable by stockholder issued to officers | — | — | — | — | — | — | — | — | (225) | — | 228 | — | 3 |
| Repayment of stock note receivable | — | — | — | — | — | — | (90) | (1) | (1,518) | 1,519 | — | — | — |
| Conversion of Series A | — | — | — | — | — | — | 891 | 9 | 5,239 | — | — | — | 5,248 |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| convertible preferred stock to common stock | | | | | | | | | | | | | |
| Conversion of Series B convertible preferred stock to common stock | (193) | (15,000) | — | — | — | — | 811 | 8 | 14,992 | — | — | — | — |
| Conversion of Series C convertible preferred stock to common stock | — | — | (980) | (50,000) | — | — | 4,464 | 45 | 49,955 | — | — | — | — |
| Issuance of common shares in exchange for warrants | — | — | — | — | — | — | 22 | — | — | — | — | — | — |
| Issuance of common shares under Employee Stock Purchase Plan | — | — | — | — | — | — | 36 | — | 430 | — | — | — | 430 |
| Net proceeds from initial public offering | — | — | — | — | — | — | 6,557 | 66 | 83,110 | — | — | — | 83,176 |
| Beneficial conversion feature of Series B convertible preferred stock | — | — | — | — | — | — | — | — | 19,822 | — | — | — | 19,822 |
| Deemed dividends related to beneficial conversion feature of Series B and Series C convertible preferred stock | — | — | — | — | — | — | — | — | (19,822) | — | — | — | (19,822) |
| Accretion to redemption value on Series A redeemable convertible preferred stock | — | — | — | — | — | — | — | — | (60) | — | — | — | (60) |
| Stock-based compensation | — | — | — | — | — | — | — | — | 6,810 | — | — | — | 6,810 |
| Net loss | — | — | — | — | — | — | — | — | — | — | — | (75,992) | (75,992) |
| BALANCE, DECEMBER 31, 2004 | — | $ — | — | $ — | $ — | $ — | 32,756 | $ 327 | $ 592,999 | $ — | $ — | $ (442,963) | $ 150,363 |

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

**STATEMENTS OF CASH FLOWS**
**(in thousands)**

| | Years ended December 31, | | | Cumulative period from February 14, 1991 (date of inception) to December 31, 2004 |
|---|---|---|---|---|
| | 2002 | 2003 | 2004 | |
| CASH FLOWS FROM OPERATING ACTIVITIES: | | | | |
| Net loss | $(206,265) | $(65,879) | $ (75,992) | $ (442,963) |
| Adjustments to reconcile net loss to net cash used in operating activities: | | | | |
| Depreciation and amortization | 5,072 | 7,657 | 7,179 | 23,246 |
| In-process research and development | — | — | — | 19,726 |
| Stock-based compensation expense | 352 | 4,501 | 6,810 | 24,246 |
| Discount on stockholder notes below market rate | — | — | — | 241 |
| Non-cash compensation expense of officer resulting from stockholder contribution | — | 70 | — | 70 |
| Loss on sale and abandonment/disposal of property and equipment | 27 | 2,803 | 528 | 3,351 |
| Accrued interest expense on notes payable to stockholders | — | — | — | 1,538 |
| Non-cash interest expense | — | — | 3 | 3 |
| Accrued interest on notes | (229) | (105) | (107) | (747) |
| Goodwill impairment | 151,428 | — | — | 151,428 |
| Loss on available-for-sale securities | 67 | 76 | 86 | 229 |
| Changes in assets and liabilities: | | | | |
| State R&D credit exchange receivable | — | — | (2,530) | (2,530) |
| Prepaid expenses and other current assets | 1,402 | (910) | (1,406) | (3,265) |
| Restricted cash | — | (559) | (24) | (583) |
| Other assets | 254 | (93) | 129 | (61) |
| Accounts payable | (1,157) | (2,283) | 1,551 | 3,477 |
| Accrued expenses and other current liabilities | 387 | 2,258 | 4,179 | 8,194 |
| Other liabilities | — | (87) | (46) | 74 |
| Payment of deferred compensation | (5) | (220) | (271) | 1,373 |
| Net cash used in operating activities | (48,667) | (52,771) | (59,911) | (212,953) |
| CASH FLOWS FROM INVESTING ACTIVITIES: | | | | |
| Purchase of marketable securities | (76,255) | (51,960) | (16,353) | (144,568) |
| Sales of marketable securities | 59,853 | 59,294 | 13,648 | 132,795 |
| Purchase of property and equipment | (34,147) | (5,183) | (6,895) | (93,200) |
| Proceeds from sale of property and equipment | — | 75 | — | 92 |
| Net cash (used in) provided by investing activities | (50,549) | 2,226 | (9,600) | (104,881) |
| CASH FLOWS FROM FINANCING ACTIVITIES: | | | | |
| Cash received for common stock to be issued | — | — | — | 3,900 |
| Repurchase of common stock | — | (1,028) | — | (1,028) |
| Issuance of common stock for cash | 58,913 | 50,000 | 84,731 | 320,571 |
| Put shares sold to majority stockholder | — | 623 | — | 623 |
| Borrowings under lines of credit | — | — | — | 4,220 |
| Proceeds from notes receivables | 1,314 | — | — | 1,742 |
| Principal payments on notes payable | (24) | — | — | (1,667) |
| Payable to stockholder | — | 1,406 | (1,406) | — |
| Issuance of Series B convertible preferred stock for cash | — | — | — | 15,000 |
| Collection of Series C convertible preferred stock subscriptions receivable | — | 31,847 | 18,153 | 50,000 |
| Borrowings on notes payable | — | — | — | 3,460 |
| Net cash provided by financing activities | 60,203 | 82,848 | 101,478 | 396,821 |

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

**STATEMENTS OF CASH FLOWS — (continued)**
**(in thousands)**

| | Years ended December 31, | | | Cumulative period from February 14, 1991 (date of inception) to December 31, 2004 |
|---|---|---|---|---|
| | 2002 | 2003 | 2004 | |
| NET INCREASE (DECREASE) IN CASH AND CASH EQUIVALENTS | $ (39,013) | $ 32,303 | $ 31,967 | $ 78,987 |
| CASH AND CASH EQUIVALENTS, BEGINNING OF PERIOD | 53,730 | 14,717 | 47,020 | — |
| CASH AND CASH EQUIVALENTS, END OF PERIOD | $ 14,717 | $ 47,020 | $ 78,987 | $ 78,987 |
| SUPPLEMENTAL CASH FLOWS DISCLOSURES: | | | | |
| Cash paid for income taxes | $ 2 | $ 1 | $ 1 | $ 15 |
| Interest paid in cash | 16 | 4 | 5 | 80 |
| Accretion on redeemable convertible preferred stock | (251) | (253) | (60) | (952) |
| Issuance of common stock upon conversion of notes payable | — | — | — | 3,331 |
| Increase in additional paid-in capital resulting from merger | — | — | — | 171,154 |
| Issuance of common stock for notes receivable | — | — | — | 2,758 |
| Issuance of put option by stockholder | — | — | — | (2,949) |
| Put option redemption by stockholder | 1,921 | — | — | 1,921 |
| Notes receivable by stockholder issued to officers | — | 225 | — | 225 |
| Issuance of Series C convertible preferred stock subscriptions | — | 50,000 | — | 50,000 |
| Issuance of Series A redeemable convertible preferred stock | — | — | — | 4,296 |
| Conversion of Series A redeemable convertible preferred stock | — | — | (5,248) | (5,248) |

In connection with the Company's initial public offering, all shares of Series B and Series C convertible preferred stock, in the amount of $15,000,000 and $50,000,000, respectively, automatically converted into common stock in August 2004.

See notes to financial statements.

**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 development and commercialization of therapeutic products for diseases such as diabetes and cancer. The Company recently commenced Phase 3 clinical trials in Europe for its lead product, the Technosphere Insulin System, to study its potential for the treatment of diabetes. The therapy consists of the Company's proprietary dry-powder Technosphere formulation of insulin that is 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, 2004 the Company has reported accumulated net losses of $442,963,000, which include a goodwill impairment charge of $151,428,000 (see Note 2), and negative cash flow from operations of $212,953,000. 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 into the third quarter of 2005. 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. If planned operating results are not achieved or the Company is not successful in raising additional equity financing, management believes that planned expenditures could be reduced substantially, extending the time period over which the Company's currently available capital resources will be adequate to fund the Company's operations into 2006.

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 $19,726,000 and goodwill of $151,428,000 were recorded at the entity level. The historical basis of PDC and the historical basis relating to the ownership interests of Alfred 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.

***Reverse Stock Split —*** On May 27, 2004, the Company's board of directors approved a one-for-three reverse stock split, which was effected on July 22, 2004. All common share and per common share amounts in the consolidated financial statements and notes to financial statements have been adjusted for all periods presented to give effect to the reverse stock split, including reclassifying an amount equal to the reduction in par value to additional paid-in capital.

***Initial Public Offering*** - On August 2, 2004, the Company completed an initial public offering of its common stock at a price to the public of $14.00 per share. The Company sold 6,250,000 shares of common stock in the offering resulting in gross proceeds of $87.5 million. In connection with the offering, the Company paid $6.1 million in underwriting discounts and commissions to underwriters and incurred $2.2 million in other offering expenses. After deducting the underwriting discounts and commissions and other offering expenses, the Company received net proceeds from the offering of approximately $79.2 million. The Company had granted the underwriters a 30-day option to purchase up to an additional 937,500 shares of common stock from the Company to cover over-allotments, if any. This option was exercised for 307,100 shares on August 28, 2004 and closing occurred on September 1, 2004 with net proceeds to the Company of $4.0 million. Additionally, in connection with the initial public offering, all of the outstanding shares of the Company's preferred stock were converted into shares of its common stock. Accordingly, the automatic conversion of preferred stock on August 2, 2004 into common stock is reflected in the accompanying audited consolidated financial statements.

**2. Summary of significant accounting policies**

***Reclassifications***-Certain reclassifications have been made to the prior years' financial statements to conform to the 2004 presentation. Auction rate securities in the amount of $5.2 million and $7.1 million were reclassified from cash equivalents to marketable securities as of December 31, 2002 and 2003. The reclassification had the effect of increasing purchases of marketable securities and reducing both cash flows from investing activities and the net increase in cash and cash equivalents by $5.2 million in the previously reported statements of cash flows during the year ended December 31, 2002 and by $1.9 million in the previously reported statements of cash flows during the year ended December 31, 2003.

***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***-The Company accounts for marketable securities as available for sale, in accordance with Statement of Financial Accounting Standards ("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.

***Deferred Offering Costs***-In connection with its initial public offering, the Company has $464,216 of deferred offering costs included in prepaid expenses and other current assets in the accompanying balance sheet at December 31, 2003. These costs were offset against the proceeds from the initial public offering in August 2004. There are no deferred offering costs as of December 31, 2004.

***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 income 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. The Company has recorded an offset to R&D expenses of $4.0 million through the year ended December 31, 2004 related to this research and development credit exchange program. Of this amount, approximately $1.5 million consisted of cash received during the third quarter of 2004.

***Fair Value of Financial Instruments***-The carrying amounts of financial instruments, which include cash equivalents, marketable securities, accounts payable, accrued expenses and other current liabilities and payable to stockholder, approximate their fair values due to their relatively short maturities. The carrying amounts of the notes receivable from stockholders and officers reflect market rates of interest for similar loans of similar amounts and terms available from a third party (see Notes 6 and 7).

***Goodwill and Identifiable Intangibles***-As of December 31, 2001, the Company's balance sheet included goodwill of $151,428,000, which resulted from the merger with AlleCure and CTL on December 12, 2001, as described in Note 1. Upon adoption of SFAS No. 142, *Goodwill and Other Intangible Assets*, on January 1, 2002, the Company, under the initial transitional test, determined there was no impairment of goodwill, principally because as of the date of the transitional impairment test, management believed the basis to initially record the goodwill remained appropriate and did not indicate the goodwill was impaired. In connection with the implementation of SFAS No. 142, 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. Toward the end of the third quarter of 2002, the Company initiated an internal study to assess whether the product development programs acquired in the merger with AlleCure and CTL were meeting their objectives. As a result of the internal study, the Company's management concluded in December 2002 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, during the first quarter of 2003, 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 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 $151,428,000 was determined to be fully impaired and an impairment loss was recorded in the fourth quarter of 2002. As of December 31, 2003 and 2004 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. If the estimated future cash flows from the use of an asset are less than the carrying value, a write-down would be recorded to reduce the related asset to its estimated fair value. The Company recorded a write-down of long-lived assets of approximately $2,154,000, and $428,000, for the years ended December 31, 2003 and 2004, respectively.

***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.

***Stock-Based Compensation***-At December 31, 2004, the Company has four stock-based compensation plans, which are described more fully in Note 10. The Company accounts 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, *Accounting for Stock Issued to Employees*, and its interpretations, and has adopted the disclosure-only alternative of SFAS No. 123, *Accounting for Stock-Based Compensation*. Stock options issued to consultants are accounted for in accordance with the provisions of Emerging Issues Task Force Issue ("EITF") No. 96-18, *Accounting for Equity Instruments That Are Issued to Other Than Employees for Acquiring, or in Conjunction with Selling, Goods or Services*, and FASB Interpretation No. 28 ("FIN 28"), *Accounting for Stock Appreciation Rights and Other Variable Stock Option or Award Plans*.

Under SFAS No. 123, the Company estimates the fair value of each stock option at the grant date or modification date, if any, using the Black-Scholes option-pricing model with the following weighted-average assumptions:

| | Year ended December 31, | | |
|---|---|---|---|
| | 2002 | 2003 | 2004 |
| Risk-free interest rate | 3.53% | 2.90% | 3.40% |
| Expected lives | 8 years | 4 years | 4 years |
| Volatility | 100% | 100% | 100% |

The weighted-average expected lives for the years ended December 31, 2003 and 2004 decreased to approximately 4 years from 8 years for year ended December 31, 2002 primarily because options granted during 2003 under the re-pricing program described in Note 10 have a 4-year term.

Had compensation cost been determined under the accounting provisions of SFAS No. 123, the Company's net loss would have been adjusted to the pro forma amounts indicated below (in thousands):

| | | Year ended December 31, | |
|---|---|---|---|
| | 2002 | 2003 | 2004 |
| Net loss-as reported | $ (206,265) | $ (65,879) | $ (75,992) |
| Add: Stock-based employee compensation expense included in reported net loss | 366 | 4,224 | 5,694 |
| Deduct: Total stock-based employee compensation expense determined under the fair value based method for all awards | (5,738) | (6,586) | (10,302) |
| Net loss-pro forma | (211,637) | (68,241) | (80,600) |

| | Year ended December 31, | | |
|---|---|---|---|
| | 2002 | 2003 | 2004 |
| Deemed dividends related to beneficial conversion features of convertible preferred stock | (1,421) | (1,017) | (19,822) |
| Accretion on redeemable preferred stock | (251) | (253) | (60) |
| Net loss applicable to common stockholders — pro forma | $(213,309) | $ (69,511) | $(100,482) |
| Basic and diluted loss applicable to common stockholders per share, as reported | $ (15.43) | $ (3.63) | $ (3.80) |
| Basic and diluted loss applicable to common stockholders per share, pro forma | $ (15.83) | $ (3.76) | $ (3.98) |

***Research and Development***sResearch 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, depreciation and are net of any tax credit exchange recognized for the state research and development credit exchange program. Expenditures relating to research and development are expensed as incurred.

***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. Common shares outstanding during the period include shares of common stock issued in exchange for notes receivable, including those that are being accounted for as in-substance stock options (see Note 6). 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:

| | December 31, | | |
|---|---|---|---|
| | 2002 | 2003 | 2004 |
| Series A redeemable convertible preferred stock on an as converted to common stock basis | 890,706 | 890,706 | — |
| Series B convertible preferred stock on an as converted to common stock basis | 702,867 | 746,408 | — |
| Series C convertible preferred stock on an as converted to common stock basis | — | — | — |
| Stock warrants to purchase common stock | 289,401 | 174,917 | 131,628 |
| Common stock options | 1,904,603 | 2,099,824 | 4,067,979 |

***Segment 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, or decision-making group, 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.

***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.

Included in general and administrative expense for the year ended December 31, 2003 are approximately $2,163,000 of costs related to the consolidation of the Company's separate California facilities into the Company's Valencia facility. The $2,163,000 consists of

$1,077,000 in severance costs, $438,000 in office closure costs and $648,000 related to the abandonment of fixed assets. Payments of $1,406,000 have been made as of December 31, 2003. The remaining liability of $109,000 is included in accrued expenses and other current liabilities at December 31, 2003. Payments of $44,000 were made during the year ended December 31, 2004, and the remaining liability of $65,000, which the Company expects to pay in February 2005, is included in accrued expenses and other current liabilities.

***Recently Issued Accounting Standards***- In December 2004, the Financial Accounting Standard Board (FASB) issued SFAS No. 123R, *Share-based Payment: an Amendment of FASB Statements No. 123 and 95*. The statement requires companies to expense share-based payments to employees, including stock options, based on the fair value of the award at the grant date. The statement also eliminates the intrinsic value method of accounting for stock options permitted by APB No. 25, which the Company currently follows. The Company is required to adopt the standard for the quarter that begins July 1, 2005. While the fair value method under SFAS No. 123R is very similar to the fair value method under SFAS No. 123 with regards to measurement and recognition of stock-based compensation, management is currently evaluating the impact of several of the key differences between the two standards on the Company's financial statements. For example, SFAS No. 123 permits recognition of forfeitures as they occur while SFAS No. 123R will require estimating future forfeitures and adjusting estimates on a quarterly basis. SFAS No. 123R will also require a classification change in the statement of cash flows, whereby a portion of any tax benefit from stock options will move from operating cash flows to financing cash flows (total cash flows will remain unchanged). While the Company continues to evaluate the impact of SFAS No. 123R on its financial statements, management believes that the expensing of stock-based compensation will have an impact on the Company's Statements of Operations similar to the pro forma disclosure under SFAS No. 123.

In March 2004, the FASB ratified the measurement and recognition guidance and certain disclosure requirements for impaired securities as described in EITF Issue No. 03-1, *The Meaning of Other-Than-Temporary Impairment and Its Application to Certain Investments*. In September 2004, the FASB issued a proposed Staff Position (FSP) EITF Issue No. 03-1a, *Implementation Guidance for the Application of Paragraph 16 of EITF 03-1*. The proposed FSP will provide measurement and recognition guidance with respect to debt securities that are impaired solely due to interest rates and/or sector spreads. The FSP delays the effective date of EITF Issue No. 03-1 until such time that the FASB issues the final standard. The Company has not determined what impact the adoption of the measurement and recognition guidance in EITF Issue No. 03-1 will have on its financial statements.

**3. Investment in securities**

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

| | December 31, 2003 | | December 31, 2004 | |
|---|---|---|---|---|
| | Cost basis | Fair value | Cost basis | Fair value |
| US government securities | $ 518 | $ 518 | $ 1,443 | $ 1,443 |
| Corporate debt instruments | 1,307 | 1,307 | 2,353 | 2,353 |
| Auction rate preferred stock | 7,100 | 7,100 | — | — |
| Auction rate municipal bonds | — | — | 7,750 | 7,750 |
| | $ 8,925 | $ 8,925 | $ 11,546 | $ 11,546 |

The Company's policy is to maintain a highly liquid short-term investment portfolio. The contractual maturities for US government securities and corporate debt instruments at December 31, 2004 are less than one year. The contractual maturities for auction rate municipal bonds at December 31, 2004 are between 21 and 40 years. Despite the long-term nature of their stated contractual maturities, the Company has the ability to quickly liquidate these securities. Proceeds from the sale and maturities of available-for-sale securities amounted to approximately $59,853,000, $59,294,000 and $13,648,000 for the years ended December 31, 2003 and 2004, respectively. Gross realized gains and losses for available-for-sale securities were insignificant for the years ended December 31, 2002, 2003 and 2004. 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. Property and equipment**

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

| | Estimated useful life (years) | December 31, 2003 | December 31, 2004 |
|---|---|---|---|
| Land | — | $ 5,273 | $ 5,273 |
| Buildings | 39 | 9,566 | 9,566 |
| Building improvements | 5-39 | 36,296 | 37,397 |
| Machinery and equipment | 3-10 | 16,530 | 18,080 |
| Furniture, fixtures and office equipment | 7-10 | 2,234 | 2,391 |
| Computer equipment and software | 3-5 | 3,048 | 3,308 |
| Leasehold improvements | | 627 | 627 |
| Construction in progress | | 789 | 3,326 |
| Deposits on equipment | | 5,656 | 5,911 |
| | | 80,019 | 85,879 |
| Less accumulated depreciation and amortization | | (12,696) | (19,368) |
| Property and equipment — net | | $ 67,323 | $ 66,511 |

Depreciation and amortization expense for the years ended December 31, 2002, 2003 and 2004, and the cumulative period from February 14, 1991 (date of inception) to December 31, 2004 was $5,072,000, $7,657,000, $7,179,000 and $23,246,000, respectively.

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

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

| | December 31, 2003 | December 31, 2004 |
|---|---|---|
| Salary and related expenses | $ 2,004 | $ 2,325 |
| Research and clinical trial costs | 1,224 | 4,116 |
| Other | 787 | 1,753 |
| Accrued expenses and other current liabilities | $ 4,015 | $ 8,194 |

**6. Notes receivable from stockholders**

During the year ended December 31, 2000, the Company issued an aggregate of 238,000 shares of common stock to an executive of CTL and a consultant of CTL in exchange for full recourse notes receivable of $1,179,000 each, for an aggregate amount of $2,358,000. The notes bear interest at fixed rates and are payable in five years. The notes were prepayable at the option of the note holder. The notes were collateralized by the underlying common stock. The note holders had no obligation to provide services to the Company under the terms of the stock purchases. The notes bore fixed rates of interest that were less than market rates of interest available for similar loans of similar amounts and terms from a third party; consequently, the Company recognized compensation expense equal to the discount on the notes based on market rates of interest and the terms of the notes. The total discount on the notes of $241,000 was expensed to general and administrative expense during the year ended December 31, 2000 as the note holders had no further obligation to the Company. During the year ended December 31, 2002, the executive of CTL paid his $1,179,000 note in full along with $135,000 of accrued interest. As of December 31, 2003, notes receivable reflected in stockholders' equity consisted of $1,179,000 in principal and $233,000 in accrued interest. During the year ended December 31, 2004, the consultant of CTL tendered to the Company 90,025 shares of the Company's common stock held by the consultant to satisfy in full his $1,179,000 note plus $340,000 of accrued interest.

In December 2001, the Company's majority stockholder entered into an agreement (the "Put" agreement) with the executive of CTL that permits the executive to require the majority stockholder to purchase approximately 119,145 shares from the executive with the note receivable for a fixed price of approximately $2,949,000, or $24.75 per share. In accordance with SEC Staff Accounting Bulletin Topic 5.T, *Accounting for Expenses or Liabilities Paid by Principal Stockholder*, the Company recorded the Put obligation of the majority stockholder as common stock subject to repurchase and as a decrease in additional paid-in capital. In February 2002, the executive exercised a portion of the Put for approximately $1,921,000 (77,611 shares), which was paid in cash by the majority

stockholder. The Company reflected the partial redemption of the Put by the majority stockholder as a decrease in common stock subject to repurchase and an increase in additional paid-in capital. The executive resigned in September 2002 and, pursuant to a post-employment agreement that was formalized and executed in January 2003, the Company modified the terms of options to purchase 30,317 shares of common stock held by the former executive (see Note 12-Severance agreements) and assumed the majority stockholder's remaining Put obligation of approximately $1,028,000. The remaining $1,028,000 of the Put (41,534 shares) was exercised in December 2002 and paid in cash by the Company in January 2003. During the year ended December 31, 2002, the estimated fair value per share of the Company's common stock declined below the exercise price of the Put. As a result, during the year ended December 31, 2002 the Company recorded $405,000 of stock-based compensation expense, which was the difference between the amount paid to the former executive and the amount received from the majority stockholder and represented the intrinsic value of the 41,534 shares subject to the Put. In December 2003, the majority stockholder purchased the 41,534 shares for an aggregate price of approximately $623,000.

The Company issued 110,000 shares of common stock to an executive of AlleCure in exchange for notes receivable, in the amounts of $1,214,000 during the year ended December 31, 2000 and $750,000 during the year ended December 31, 2001. The notes bear interest at fixed rates and are payable in five years. The notes are pre-payable at the option of the note holder. The notes are collateralized by the underlying common stock. The note holder has 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 12-Severance agreements). The note-for-stock transactions are being 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 results in the exercise price of the in-substance stock option being unknown until the notes are paid in full. Accordingly, the Company is 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 is 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 represents the intrinsic value of the in-substance options at December 31, 2004.

During the year ended December 31, 2000 and during the year ended December 31, 2001, the Company issued an aggregate 701,333 shares of common stock to various consultants in exchange for notes receivable aggregating approximately $10,923,000. The notes bear interest at fixed rates and are payable in five years. The notes are pre-payable at the option of the note holders. The notes are collateralized by the underlying common stock. The note holders have no further obligation to the Company under the terms of the stock purchases. The note-for-stock transactions are being 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 is 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 $8,372,000 in 2000 and $15,000 in 2001. These amounts, which are included in research and development expense in the accompanying statements of operations, were estimated using the Black-Scholes option-pricing model and the following weighted-average assumptions: volatility of 100%, term of five years, interest rate of 5.06%.

**7. Notes receivable from officers**

In March 2003, a limited liability company controlled by the Company's majority stockholder loaned the aggregate principal sum of $225,000 to two officers pursuant to promissory notes and purchased the principal residence owned by one officer as part of his relocation to California. In accordance with SEC Staff Accounting Bulletin Topic 5.T, *Accounting for Expenses or Liabilities Paid by Principal Stockholder*, the Company recorded the loans from the majority stockholder as an increase in additional paid-in capital and as a note receivable, which is classified within stockholders' equity. In addition, $70,000 was recorded as compensation expense with a corresponding credit to additional paid-in capital representing the amount of the residential purchase price paid to one officer that exceeded the appraised value. This $70,000 is included in general and administrative expenses on the Company's statement of operations for the year ended December 31, 2003. The notes bore fixed rates of interest that were less than market rates of interest available for similar loans of similar amounts and terms from a third party. Consequently, the Company also recognized a non-cash compensation expense equal to the discount on the notes. The total discount on the notes of approximately $14,000 was amortized to compensation expense over the term of the note. The notes were secured by the officers' title and interest in future bonus payments, if any, from the Company. As of April 15, 2004, both notes had been fully repaid.

**8. Deferred compensation**

Certain stockholders and officers elected to defer part or all of their compensation from 1991 through 1998 due to cash flow difficulties in those years. The amounts due for deferred compensation are non interest-bearing with no repayment terms.

Deferred compensation consists of the following (in thousands):

| | December 31, 2003 | 2004 |
|---|---|---|
| Deferred compensation to stockholders and officers | $ 1,644 | $ 1,373 |
| Less non-current portion | (284) | — |
| Deferred compensation-current | $ 1,360 | $ 1,373 |

In February 2003, pursuant to a settlement agreement with one of the officers, the Company agreed to pay the deferred compensation amount outstanding to the former officer in the amount of approximately $775,000 in three payments. The Company paid approximately $220,000 and $271,000 of this amount during the years ended 2003 and 2004, respectively. The remaining $284,000 is due in April 2005. The settlement also obligated the Company to make certain severance related payments which are more fully described in Note 12-Severance agreements.

**9. Common and preferred stock**

***Initial Public Offering of Common Stock*** - Upon closing of the initial public offering of the Company's common stock on August 2, 2004, 6,250,000 shares of common stock were sold. The underwriters exercised a 30-day option related to the initial public offering and purchased 307,100 shares of common stock on August 28, 2004. Additionally, in connection with the initial public offering, all 267,212 shares of the Company's Series A redeemable convertible preferred stock, all 192,618 shares of the Company's Series B convertible preferred stock and all 980,392 shares of the Company's Series C convertible preferred stock, each outstanding as of December 31, 2003, converted into 6,166,372 shares of common stock on August 2, 2004.

***Common Stock***-The Company is authorized to issue 90,000,000 shares of common stock. As of December 31, 2004, 32,756,237 shares of common stock are issued and outstanding.

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

| | December 31, 2003 | December 31, 2004 |
|---|---|---|
| Common stock options | 2,099,825 | 4,067,979 |
| Conversion of Series A preferred stock | 890,706 | — |
| Conversion of Series B preferred stock | 746,408 | — |
| Conversion of Series C preferred stock | — | — |
| Exercise of warrants | 174,917 | 131,628 |
| | 3,911,856 | 4,199,607 |

***Preferred Stock***-The Company is authorized to issue 10,000,000 shares of preferred stock. As of December 31, 2004, no shares of preferred stock are authorized, issued and outstanding.

***Series A Redeemable Convertible Preferred Stock***-As of December 31, 2003, the Company had outstanding 267,212 shares of 5.12% cumulative dividend Series A redeemable convertible preferred stock. These shares were automatically converted to 890,706 shares of common stock on August 2, 2004 upon the closing of the initial public offering. Each share of Series A redeemable convertible preferred stock was convertible into approximately 3.3 shares of common stock (subject to adjustment in the event of the issuance of common stock below a price per share of $4.86 and subject to proportionate adjustment for stock dividends, stock subdivisions, stock redivisions, reverse stock splits and stock consolidations). The Series A convertible preferred stock offering was determined not to contain a beneficial conversion feature on the offering commitment date nor any subsequent date. The Series A convertible preferred stock was also redeemable at the option of its holders at any time following September 30, 2002 for a cash sum equal to the redemption value of $16.22 per share, together with all unpaid cumulative dividends. The cumulative dividends for Series A redeemable convertible preferred stock were accrued annually so that the carrying value would equal the redemption amount on September 30, 2002 and thereafter. In addition, differences between the redemption amount and the net proceeds received (i.e., the

costs of financing) were accreted through September 30, 2002.

***Series B Convertible Preferred Stock***-As of December 31, 2003, the Company had outstanding 192,618 shares of Series B convertible preferred stock. These shares were automatically converted to 811,400 shares of common stock on August 2, 2004 upon the closing of the initial public offering. Each share of Series B convertible preferred stock was initially convertible into approximately 3.3 shares of common stock, adjusted for dilution as defined. The holders of the Series B convertible preferred stock were entitled to a weighted-average antidilution adjustment to the conversion price in the event that the Company issues equity securities for an effective purchase price of less than $23.37 per share (on an as-if-converted-to-common stock basis) in an equity financing. The conversion price was also subject to proportionate adjustment for stock subdivisions, stock combinations and stock dividends. The Series B convertible preferred stock offering was determined not to contain a beneficial conversion feature on the offering commitment date. During the year ended December 31, 2003, the conversion price was adjusted downward to $20.10 per share resulting in a beneficial conversion charge to common stockholders of $1,017,000. During 2004, through the effective date of the Company's initial public offering, the conversion price was adjusted downward to $18.49 per share resulting in a beneficial conversion charge to common stockholders of approximately $1,518,000. These charges have been reflected by the Company as both a reduction and increase in additional paid-in capital during the respective periods. Although the charges have no net effect on stockholders' equity, they increase the net loss applicable to the common stockholders and net loss per share.

***Series C Convertible Preferred Stock***-In December 2003, the Company issued stock subscriptions receivable in the aggregate amount of $50,000,000 for 980,392 shares of Series C convertible preferred stock. All of the 980,392 shares of Series C convertible preferred stock were issued in the first quarter of 2004 and automatically converted to 4,464,266 shares of common stock upon the closing of the initial public offering. Approximately $31,847,000 of the $50,000,000 in stock subscriptions was collected in December 2003. The remaining stock subscription receivable of approximately $18,153,000 as of December 31, 2003 was collected during the first quarter of 2004. Each share of Series C was convertible into approximately 3.3 shares of common stock, adjusted for dilution as defined. The holders of the Series C convertible preferred stock were entitled to a weighted-average antidilution adjustment to the conversion price in the event that the Company issued equity securities for an effective purchase price of less than $15.30 per share (on an as-if-converted-to-common stock basis) in an equity financing. The Series C convertible preferred stock was determined not to have any beneficial conversion value upon issuance since the initial effective conversion price of $15.30 per share on an as-if-converted-to-common stock basis was greater than the estimated fair value per share of the common stock into which the Series C convertible preferred stock was convertible on the offering commitment date. As of the close of the initial public offering on August 2, 2004, the conversion price was adjusted downward to $11.20 resulting in a beneficial conversion charge to common stockholders of approximately $18,304,000.

***Registration rights*** – As of December 31, 2004 the holders of 916,715 shares of the Company's common stock and the holders of warrants to purchase 131,628 shares of the Company's common stock have rights, subject to some conditions, to require the Company to file registration statements covering their shares or to include their shares in registration statements that the Company may file for itself or other stockholders.

**10. Stock option plans**

During 2004, the Company's board of directors and stockholders approved the amendment and restatement of the 2001 Stock Awards Plan, now known as the 2004 Equity Incentive Plan (the "Plan"). The Plan provides for the granting of stock options to employees, directors and consultants. As of December 31, 2004, 3,097,138 of options were outstanding under the Plan and an additional 1,819,204 shares of common stock were available for issuance under the Plan. During 2004, the Company's board of directors and stockholders also approved the 2004 Non-Employee Directors' Stock Option Plan. The plan provides for the automatic, non-discretionary grant of options to the Company's non-employee directors. As of December 31, 2004, 180,000 options were outstanding under the plan and an additional 620,000 shares of common stock were available for issuance under the plan. The Company has two other stock award plans: the 1991 Stock Option Plan (the "1991 Plan") and the 1999 Stock Plan (the "1999 Plan"). Both of these plans provide for the granting of stock options to directors, employees and consultants. As of December 31, 2004, 125,698 of options were outstanding under the 1991 Plan and 303,824 of options were outstanding under the 1999 Plan. There were no additional shares available for issuance under the 1991 Plan and the 1999 Plan at December 31, 2003 or 2004.

Prior to the merger of CTL and AlleCure into the Company, CTL had granted options to purchase shares of its common stock under its 2000 Stock Option and Stock Plan (the "CTL Plan"). Similarly, AlleCure had granted options to purchase shares of its common stock under its 2000 Stock Option and Stock Plan (the "AlleCure Plan"). Pursuant to the plans of reorganization and agreements of merger between the Company and each of CTL and AlleCure, the Company has assumed the obligation to issue shares of the

Company's common stock, at the exchange ratio agreed to in the merger agreement, upon the exercise of options granted under the CTL Plan and the AlleCure Plan. After the merger date, no further options were granted under either the CTL Plan or AlleCure Plan. As of December 31, 2004 there were an aggregate of 120,347 options outstanding under these plans. The assumption of options issued by CTL and AlleCure by the Company in connection with the merger on December 12, 2001 resulted in a new measurement date. On this date, the outstanding options had an intrinsic value of approximately $2,528,000. Approximately $632,000 of the $2,528,000 related to vested options and was therefore recorded immediately as compensation expense. The remaining amount of the $2,528,000, as adjusted for cancellations, related to unvested options and was being amortized to stock-based compensation expense over the remaining vesting period. During the years ended December 31, 2002, 2003, 2004 and the cumulative period from February 14, 1991 (date of inception) to December 31, 2004, $632,038, $274,532, $214,062 and $1,752,670, respectively, was recognized as stock-based compensation expense related to these options. As of December 31, 2004, there is no further expense to recognize.

The Company's Board of Directors approved certain option grants outside of the Company's 2001 Stock Awards Plan. During the year ended December 31, 2002, an employee who is also a majority stockholder was granted 240,972 options at an exercise price of $25.23 per share. The options vest annually over four years. These options were outstanding at December 31, 2004 and are included in the tables below.

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. The aggregate number of shares that may be sold under the plan is 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, 2005, the purchase plan share reserve was increased by 327,562 shares. On December 31, 2004, the Company sold 36,152 shares of its common stock to employees participating in the plan.

The following table summarizes information about stock options outstanding:

| | Year ended December 31, | | | | | |
|---|---|---|---|---|---|---|
| | 2002 | | 2003 | | 2004 | |
| | Options | Weighted average exercise price | Options | Weighted average exercise price | Options | Weighted average exercise price |
| Options outstanding at the beginning of the Period | 775,268 | $ 10.53 | 1,904,603 | $ 17.52 | 2,099,825 | $ 10.30 |
| Granted | 1,222,675 | 22.11 | 1,664,886 | 9.36 | 2,145,124 | 14.09 |
| Exercised | (17,771) | 5.49 | — | N/A | (86,066) | 12.54 |
| Canceled | (75,569) | 20.58 | (1,469,664) | 18.57 | (90,904) | 13.02 |
| Options outstanding at the end of the Period | 1,904,603 | 17.52 | 2,099,825 | 10.29 | 4,067,979 | 12.19 |
| Options exercisable at the end of the Period | 636,937 | 10.08 | 728,590 | 9.96 | 1,236,599 | 9.76 |

The weighted-average exercise prices and weighted-average fair values of options granted are as follows:

| | Year ended December 31, | | | | | |
|---|---|---|---|---|---|---|
| | 2002 | | 2003 | | 2004 | |
| | Weighted average exercise price | Weighted average fair value of option granted | Weighted average exercise price | Weighted average fair value of option granted | Weighted average exercise price | Weighted average fair value of option granted |
| Option price equal to the fair value of common stock on grant date | $ 25.23 | $ 21.41 | $ — | $ — | $ 14.63 | $ 10.29 |
| Option price greater than the fair value of common stock on grant date | — | — | — | — | — | — |
| Option price less than the fair value of common stock on grant date | 12.75 | 13.11 | 9.36 | 11.55 | 13.67 | 10.05 |

The following table summarizes information about stock options outstanding at December 31, 2004:

| Grant price range | Options outstanding | Weighted-average remaining contractual life (years) | Weighted-average exercise price | Options exercisable | Weighted-average exercise price |
|---|---|---|---|---|---|
| $0.33—$7.95 | 1,626,621 | 4.75 | $ 7.29 | 977,004 | $ 6.85 |
| $9.90—$12.75 | 90,141 | 6.65 | $ 10.29 | 57,623 | $ 10.56 |
| $12.99—$15.57 | 1,761,368 | 9.57 | $ 13.76 | 4,302 | $ 14.47 |
| $17.56—$25.23 | 589,849 | 8.05 | $ 21.28 | 197,670 | $ 23.80 |
| | 4,067,979 | 7.36 | $ 12.19 | 1,236,599 | $ 9.76 |

For employee options, the difference between the estimated fair value of the underlying stock and the option exercise price, if lower, is recognized as compensation expense over the vesting period in accordance with APB Opinion No. 25. For non-employee options, the Company recognizes stock-based compensation expense for the estimated fair value of the options, determined using the Black-Scholes option-pricing model, in accordance with EITF No. 96-18 and FIN 28. During the year ended December 31, 2002, previously recorded non-employee stock-based compensation expense of approximately $14,000 was reversed because of a decline in the estimated fair value of the Company's common stock underlying the non-employee options. During the year ended December 31, 2003, non-employee stock-based compensation expense of approximately $277,000 was recognized for outstanding non-employee options. During the year ended December 31, 2004, non-employee stock-based compensation expense of approximately $11,000 was recognized for outstanding non-employee options. As of December 31, 2004, non-employee options to purchase 43,239 shares of the Company's common stock at a weighted-average exercise price of $8.39 per share were outstanding and are reflected in the tables above. The in-substance stock options disclosed in Note 6, which resulted from the issuance of stock to certain individuals, are excluded from the tables above. 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. For the year ended December 31, 2004, the Company recorded approximately $1,105,000 in stock-based compensation expense relating to these agreements.

In January 2003, pursuant to a post-employment agreement with a former CTL executive, options to purchase 30,317 shares of common stock for $21.12 per share remain fully exercisable through January 2006. The change in option terms resulted in a new measurement date. Since the stock option was modified in connection with the former executive's post-employment activities to be provided through September 2003, stock-based compensation expense was recorded in 2003 in the amount of approximately $255,000, which was estimated using the Black-Scholes options pricing model.

In October 2003, pursuant to a settlement agreement with the Company's former Chief Executive Officer, options to purchase 83,333 shares of common stock were immediately vested and remain fully exercisable through April 2005. The change in option terms resulted in a new measurement date. On the date of the agreement, the outstanding options had an intrinsic value of approximately $153,000 that was recorded immediately as compensation expense. The options were exercised in October 2004.

In November 2003, pursuant to a settlement agreement with a former employee, options to purchase 5,000 shares of common stock were immediately vested and remain fully exercisable through May 2004. The change in option terms resulted in a new measurement date. On the date of the agreement, the outstanding options had an intrinsic value of approximately $25,000 that was recorded immediately as compensation expense.

During the year ended December 31, 2003, the Company extended the exercise period for certain employee options to purchase 174,855 shares of common stock at an exercise price of $6.24 per share. Also, in February 2003, pursuant to a settlement agreement with a former executive, the Company agreed that options to purchase 124,553 shares of common stock would remain exercisable at least until April 2006 (see Note 12). The Company recorded compensation expense of approximately $2,502,000 and $259,000 in the years ended December 31, 2003 and 2004, respectively, associated with all of these options.

On October 7, 2003, the Company's board of directors approved a re-pricing program for certain outstanding options to purchase shares of the Company's common stock granted under each of its stock plans. Under the re-pricing program, each holder of outstanding options granted under the stock plans who was an employee of the Company on November 5, 2003 could elect to exchange up to all of their outstanding options with an exercise price greater than $7.95 for re-priced stock options with an exercise price of $7.95 per share and a term of four years. The option re-pricing became effective on November 5, 2003. Vesting restarted immediately with 50% vesting in November 2004 and the remaining 50% vesting monthly until fully vested in November 2005. Employees who voluntarily resign in the 12-month period beginning November 5, 2003 will forfeit their re-priced options. Employees who are involuntarily terminated in the 12-month period beginning November 5, 2003 will vest 50% upon termination. In accordance with the terms of the re-pricing program, on November 5, 2003 the Company canceled 781,572 outstanding stock options with a weighted average exercise price of $19.83 per share and issued, in exchange for the canceled options, 781,572 new options with an

exercise price of $7.95 per share. Compensation cost for all options re-priced under the re-pricing program will be re-measured, using the intrinsic value method proscribed by APB No. 25, on a quarterly basis until the options are exercised or canceled or expire. Compensation cost for these options are recognized in accordance with the method prescribed by FIN 28. Since the amount of compensation cost attributable to the re-priced options is dependent on the fair value of the Company's common stock underlying the options on the future re-measurement dates, the amount of stock-based compensation recognized in any given future period cannot be predicted and may have a material impact on the Company's results of operations. For the year ended December 31, 2003, the Company recorded $595,000 in stock-based compensation expense related to the re-pricing program. For the year ended December 31, 2004, the Company recorded approximately $4,435,000 in stock based compensation expense relating to the re-pricing program.

Total stock-based compensation expense recognized in the accompanying statements of operations is as follows (in thousands):

| | Year ended December 31, | | |
|---|---|---|---|
| | 2002 | 2003 | 2004 |
| Employee related | $ 366 | $ 4,224 | $ 5,694 |
| Consultant related | (14) | 277 | 1,116 |
| Total | $ 352 | $ 4,501 | $ 6,810 |

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

| | Year ended December 31, | | |
|---|---|---|---|
| | 2002 | 2003 | 2004 |
| Research and development | $ 602 | $ 961 | $ 2,921 |
| General and administrative | (250) | 3,540 | 3,889 |
| Total | $ 352 | $ 4,501 | $ 6,810 |

**11. Warrants**

Warrants were issued during the years ended December 31, 1995 and 1996 to purchase shares of common stock. As of December 31, 2003 and 2004, warrants to purchase 175,227 and 131,628, respectively, shares of common stock were outstanding and exercisable at a weighted average exercise price of $12.54 per share. The outstanding warrants range in price from $12.53 to $12.70 per share and expire at various dates through 2007. Each warrant contains 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 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. On July 22, 2004, holders of warrants to purchase 39,899 shares of the Company's common stock exercised their right to convert the warrants into 22,309 shares of common stock. The Company may be in breach of certain notice provisions contained in the outstanding warrants. The Company believes the impact of any such breach would not be material to its financial position or results of operations.

On March 30, 2001, CTL issued a warrant to its majority stockholder in conjunction with the purchase of the Company's common stock. Pursuant to the plan of reorganization and agreement of merger between the Company and CTL, the Company assumed an obligation to issue 118,424 shares of its common stock upon the exercise of this warrant. The exercise price of the warrant, as adjusted by the merger, is $21.12 per share of common stock. The warrants remained outstanding as of December 31, 2002 and expired unexercised on March 31, 2003.

**12. Commitments and contingencies**

***Operating Leases***—The Company leases certain facilities and equipment under various operating leases, which expire at various dates through December 31, 2009. Future minimum rental payments, required under operating leases, are as follows at December 31, 2004 (in thousands):

| Year ending December 31, | |
|---|---|
| 2005 | $ 753 |
| 2006 | 502 |
| 2007 | 461 |
| After 2007 | 499 |
| Total minimum lease payments | $ 2,215 |

Rent expense under all operating leases for the years ended December 31, 2002, 2003 and 2004 was approximately, $851,000, $1,241,000 and $473,000, respectively.

***Capital Leases***—The Company's capital leases were not material for the years ended December 31, 2002, 2003 and 2004.

***Litigation***—The Company is subject to various claims and legal actions that arise in the ordinary course of business. In the opinion of management, the ultimate resolution of such matters will not have a material adverse impact on the Company's financial position or results of operations.

During the year ended December 31, 2000, the Company issued an aggregate 699,972 shares of common stock to three consultants in exchange for notes receivable aggregating approximately $10,891,000 (see Note 6). The notes are collateralized by the underlying common stock, bear interest at fixed rates, and are payable in October 2005. The notes-for-stock transactions are being accounted for as in-substance stock option grants to non-employees. On November 10, 2004, the borrowers notified the Company that they believed that they had entered into an agreement in October 2001 with the Company's majority stockholder under which the stockholder would purchase from the borrowers some of the common stock, with the proceeds to be paid to the Company to pay down the notes. The borrowers informed the Company that they believe both the Company and its majority stockholder are in breach of certain agreements related to the transaction and indicated they intend to seek alleged damages arising from any failure of the agreement to be performed. The Company has concluded that the matter does not have any financial statement impact as of December 31, 2004. The Company believes that the ultimate resolution of this matter will not have a material impact on the Company's financial position or results of operations.

***Guarantees and Indemnifications***—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 Company may terminate the indemnification agreements with its officers and directors upon 90 days written notice, but termination will not affect claims for indemnification relating to events occurring prior to the effective date of termination. 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. Accordingly, the Company has not recorded any liabilities for these agreements as of December 31, 2003 and 2004.

***Severance Agreements***—In February 2003, pursuant to a settlement agreement, the Company is obligated to pay a former executive approximately $1,049,000 over three years, comprised of approximately $775,000 in deferred compensation (see Note 8) from prior years and the remainder comprised of other severance-related items. As of December 31, 2004 the Company has paid approximately $765,000 of this amount. The remaining $284,000 is due in April 2005. The settlement agreement further provides that the options held by the former executive to purchase up to 46,585 shares of the Company's common stock remain fully exercisable through April 2007, and options to purchase up to 124,553 shares of the Company's common stock remain fully exercisable until at least April 2006. The change in option terms resulted in a new measurement date. On the date of the agreement, the outstanding options had an intrinsic value of approximately $1,091,000, which was immediately expensed as part of the $2,502,000 charge more fully described in Note 10.

In February 2003, pursuant to a settlement agreement, the Company became obligated to pay a former employee his base salary at the rate of approximately $22,000 per month through December 2003 and a lump sum payment of $67,000 in February 2005, which is included in accrued expenses in the accompanying balance sheet at December 31, 2003 and 2004.

In October 2003, under the terms of a severance agreement with its former Chief Executive Officer, the Company paid a severance payment of $165,000 and agreed to pay his base salary at the rate of approximately $28,000 per month through April 2005. Amounts owed under this agreement are included in accrued expenses in the accompanying balance sheet at December 31, 2003 and 2004. The

agreement also provides for accelerated vesting of an option held by the former executive permitting him to purchase up to 83,333 shares of the Company's common stock until April 7, 2005 (see Note 10). These options were exercised in October 2004.

***Other*—**In November 2004, the Company learned that the parent company of a vendor with whom the Company has equipment deposits in the amount of $2.9 million as of December 31, 2004 is experiencing financial difficulties. The vendor has indicated it intends to supply the equipment against which the deposits were made. The vendor and its parent company are located in France, and the Company has recently engaged counsel in France to assist it in evaluating the matter. The Company has assessed this matter in accordance with SFAS No. 5, *Accounting for Contingencies*, and concluded that, based on currently available information, a loss accrual is not warranted.

**13. Employee benefit plans**

As a result of the merger in December 2001, each respective 401(k) savings retirement plans of AlleCure, CTL and PDC were converted to the 401(k) Savings Retirement Plan (the "MannKind Retirement Plan") for the Company. For the years ended December 31, 2002, 2003 and 2004, the Company contributed $224,000, $235,000 and $249,000, respectively, to the MannKind Retirement Plan.

**14. 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 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, 2003 and 2004 are approximately as follows (in thousands):

| | 2003 | 2004 |
|---|---|---|
| Deferred Tax Assets: | | |
| Net operating loss carryforwards | $ 66,921 | $ 94,133 |
| Research and development credits | 3,494 | 6,095 |
| Accrued expenses | 7,592 | 7,959 |
| Non-qualified stock option expense | 2,442 | 5,273 |
| Depreciation | (416) | 663 |
| Total gross deferred tax assets | 80,033 | 114,123 |
| Valuation allowance | (80,033) | (114,123) |
| 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, 2002, 2003 and 2004:

| | December 31, | | |
|---|---|---|---|
| | 2002 | 2003 | 2004 |
| Federal tax benefit rate | 34.0% | 34.0% | 34.0% |
| State tax benefit, net of federal benefit | | — | — |
| Permanent items | (24.9) | (0.1) | — |
| Other | | 1.6 | — |
| Valuation allowance | (9.1) | (35.5) | (34.0) |
| 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 deferred tax assets have been fully reserved. Management reevaluates the positive and negative evidence on an annual basis. During the years ended December 31, 2002, 2003 and 2004, the change in the valuation allowance was $24,216,000, $29,336,000 and $34,090,000, respectively, for income taxes.

At December 31, 2004, the Company had federal and state net operating loss carryforwards of approximately $240,917,000 and $143,214,000 available, respectively, to reduce future taxable income and which will expire at various dates beginning in 2006 and 2008, respectively. At December 31, 2004, the Company had research and development credits of $6,095,000 that expire at various

dates through 2017. Ownership changes, as defined in Section 382 of the Internal Revenue Code, such as those resulting from the issuance of common stock in connection with the Company's initial public offering, may limit the amount of net operating loss and tax credit carryforwards that can be utilized to offset future taxable income or tax liability. The Company has not yet determined the amounts of such limitations, if any; however, they could be significant. Any such limitations that may have existed for any of the periods presented in the accompanying financial statements would not have impacted the amounts reported because the Company has provided a full valuation allowance against all of its deferred tax assets. To the extent the Company realizes taxable income in any future period, the amount of any such limitations could have a material impact on the reported financial statements.

**15. Related party transactions**

The Company issued 1,773,234 shares of its common stock to related parties during the year ended December 31, 2002 for proceeds of approximately $27,450,000. The Company issued 3,016,834 shares of its common stock to its majority stockholder during the year ended December 31, 2001 for proceeds of approximately $76,000,000. In connection with certain of these issuances, the board of directors approved the issuance of a warrant to purchase 118,424 shares of the Company's common stock at $21.12 per share, which expired unexercised on March 31, 2003.

During the years ended December 31, 2001, 2002, 2003 and 2004, the Company paid $426,000, $406,000, $497,000 and $218,000 respectively, to certain universities to conduct sponsored research programs, including clinical research. Certain stockholders of the Company are employees of these universities and oversee the sponsored research programs.

One stockholder was paid $48,000, $242,000, $6,000 and $48,000 for consulting services during the years ended December 31, 2001, 2002, 2003, and 2004 , respectively.

In December 2001, the Company's majority stockholder entered into an agreement with an executive of CTL that permitted the executive to require the majority stockholder to purchase shares of the Company's stock held by the executive, for a fixed price of approximately $2,949,000 (see Note 6).

From September 2001 to October 2003, the Company leased property located in Sylmar, California from Sylmar Biomedical Park LLC, a company controlled by the Company's majority stockholder. During the years ended December 31, 2002 and 2003 and for the period from February 14, 1991 (date of inception) to December 31, 2003, approximately $39,000, $20,000 and $59,000, respectively, was charged to general and administrative expenses in the accompanying statements of operations in connection with the property leased from Sylmar Biomedical Park LLC.

During the year ended December 31, 2002, while he was one of the Company's directors, the Company's former Chief Executive Officer provided the Company with consulting services relating to its research and development programs. The Company paid the executive approximately $124,000 for his services.

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 majority stockholder and other Company employees, the Company utilized the majority stockholder's private aircraft, and the Company paid the charter company that manages the aircraft on behalf of the Company's majority stockholder approximately $441,000, $321,000 and $145,000, respectively, for the years ended December 31, 2002, 2003 and 2004.

In 2004, the Company engaged one of its directors to provide consulting services related to seeking potential partners in the development and commercialization of the Company's technology. The Company paid approximately $47,000 for consulting services rendered for the year ended December 31, 2004.

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 12—Guarantees and indemnifications).

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

| | March 31 | June 30 | September 30 | December 31 |
|---|---|---|---|---|
| | (in thousands, except per share data) | | | |
| **2003** | | | | |
| Net loss | $ (20,336) | $ (13,109) | $ (13,870) | $ (18,564) |
| Net loss applicable to common stockholders | $ (20,396) | $ (14,046) | $ (14,078) | $ (18,629) |
| Basic and diluted net loss per share | $ (1.24) | $ (0.79) | $ (0.71) | $ (0.93) |
| Weighted average common shares used to compute net loss per share | 16,466 | 17,760 | 19,697 | 19,975 |

| | March 31 | June 30 | September 30 | December 31 |
|---|---|---|---|---|
| | (in thousands, except per share data) | | | |
| **2004** | | | | |
| Net loss | $ (16,409) | $ (18,245) | $ (20,188) | $ (21,150) |
| Net loss applicable to common stockholders | $ (17,085) | $ (18,241) | $ (39,398) | $ (21,150) |
| Basic and diluted net loss per share | $ (0.86) | $ (0.91) | $ (1.40) | $ (0.65) |
| Weighted average common shares used to compute net loss per share | 19,975 | 19,975 | 28,051 | 32,768 |

**Exhibit 21.1**

Subsidiaries of MannKind Corporation

| NAME: | JURISDICTION OF FORMATION: |
| --- | --- |
| Pharmaceutical Discovery Corp. | Connecticut |

**Exhibit 23.1**

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in Registration Statement No. 333-117811 of MannKind Corporation on Form S-8 of our report dated March 11, 2005, appearing in the Annual Report on Form 10-K of MannKind Corporation for the year ended December 31, 2004.

/s/ Deloitte & Touche LLP
Los Angeles, California
March 11, 2005

**Exhibit 31.1**

**CERTIFICATION**

I, Alfred E. Mann, certify that:

1. I have reviewed this annual report on Form 10-K of MannKind Corporation;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, 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;

c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 15, 2005

By: /s/ Alfred E. Mann
Alfred E. Mann
Chief Executive Officer

**Exhibit 31.2**

**CERTIFICATION**

I, Richard L. Anderson, certify that:

1. I have reviewed this annual report on Form 10-K of MannKind Corporation;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, 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;

c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 15, 2005

By: /s/ Richard L. Anderson
Richard L. Anderson
Corporate Vice President and
Chief Financial Officer

**Exhibit 32.1**

**CERTIFICATION**

Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 (18 U.S.C. § 1350, as adopted), Alfred E. Mann, Chief Executive Officer of MannKind Corporation (the "Company"), and Richard L. Anderson, the Corporate Vice President and Chief Financial Officer of the Company, each hereby certifies that, to the best of his knowledge:

**1.** The Company's Annual Report on Form 10-K for the period ended December 31, 2004, to which this Certification is attached as Exhibit 32.1 (the "Periodic Report"), fully complies with the requirements of Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934, as amended; and

**2.** The information contained in the Periodic Report fairly presents, in all material respects, the financial condition of the Company at the end of the period covered by the Periodic Report and results of operations of the Company for the period covered by the Periodic Report.

Dated: March 15, 2005

/s/ Alfred E. Mann
Alfred E. Mann
Chief Executive Officer

/s/ Richard L. Anderson
Richard L. Anderson
Corporate Vice President and
Chief Financial Officer

This certification accompanies the Form 10-K to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of MannKind Corporation under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Form 10-K), irrespective of any general incorporation language contained in such filing.