MANNKIND CORP
Form 424B4
July 28, 2004

Table of Contents

Filed pursuant to Rule 424(b)(4)
Registration Nos. 333-115020 and 333-117702

PROSPECTUS

## 6,250,000 Shares

# MannKind Corporation

## Common Stock

This is the initial public offering of our common stock. No public market currently exists for our common stock. We are offering all of the 6,250,000 shares of our common stock offered by this prospectus.

Our common stock has been approved for quotation on The Nasdaq National Market under the symbol MNKD.

**Investing in our common stock involves a high degree of risk. Before buying any shares, you should carefully read the discussion of material risks of investing in our common stock in Risk factors beginning on page 9 of this prospectus.**

**Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.**

| | Per share | Total |
|---|---|---|
| Public offering price | $14.00 | $87,500,000 |
| Underwriting discounts and commissions | $ 0.98 | $ 6,125,000 |
| Proceeds, before expenses, to us | $13.02 | $81,375,000 |

The underwriters may also purchase up to an additional 937,500 shares of our common stock at the public offering price, less the underwriting discounts and commissions payable by us, to cover over-allotments, if any, within 30 days from the date of this prospectus. If the underwriters exercise this option in full, the total underwriting discounts and commissions will be $7,043,750 and our total proceeds, before expenses, will be $93,581,250.

The underwriters are offering the common stock as set forth under Underwriting. Delivery of the shares will be made on or about August 2, 2004.

## UBS Investment Bank

**Piper Jaffray**

**Wachovia Securities**

**Jefferies & Company, Inc.**

**Harris Nesbitt**

The date of this prospectus is July 28, 2004.

Table of Contents

The Technosphere Insulin System, including both the Technosphere dry-powder formulation of insulin and the MedTone inhaler, is restricted by United States law to investigational use only and is not approved for commercial sale.

---

You should rely only on the information provided in this prospectus. We have not, and the underwriters have not, authorized anyone to provide you with additional information or information different from that contained in this prospectus. We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The information contained in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or of any sale of shares of our common stock.

Through and including August 22, 2004 (the 25th day after the date of this prospectus), federal securities laws may require all dealers that effect transactions in our common stock, whether or not participating in this offering, to deliver a prospectus. This is in addition to the dealers obligation to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.

**TABLE OF CONTENTS**



---

Technosphere® is our registered trademark and we have applied to register MedTone™ with the US Patent and Trademark office. We have also applied for or registered company trademarks in other jurisdictions, including Europe and Japan. This prospectus also contains trademarks and service marks of other companies that are the property of their respective owners.

---

Table of Contents

# Prospectus summary

This summary highlights selected information appearing elsewhere in this prospectus and may not contain all of the information that is important to you. This prospectus includes information about the shares we are offering as well as information regarding our business and detailed financial data. You should read this prospectus in its entirety. Unless the context requires otherwise, the words MannKind, we, company, us and our refer to MannKind Corporation and its subsidiary.

**OVERVIEW**

We are a biopharmaceutical company focused on the discovery, development and commercialization of therapeutic products for diseases such as diabetes, cancer, inflammatory and autoimmune diseases. Our lead product, the Technosphere Insulin System, which is currently in late Phase II clinical trials for the treatment of diabetes, consists of our dry powder Technosphere formulation of insulin and our MedTone inhaler through which the powder is inhaled into the deep lung. On the basis of our clinical findings to date and our understanding of current diabetes therapy, we believe the performance characteristics, convenience and ease of use of our proprietary Technosphere Insulin System have the potential to change the way diabetes is treated.

We have discovered and developed the majority of our technology, including the technology associated with our Technosphere Insulin System and our cancer therapy. Currently, our operations encompass research, preclinical and clinical development as well as pharmaceutical manufacturing. We currently outsource the manufacture of our MedTone inhaler. As our products mature, we intend to either enter into sales and marketing collaborations with other companies, if available on commercially reasonable terms, or develop these capabilities ourselves.

According to the American Diabetes Association, 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. The United States Centers for Disease Control, or CDC, estimated that as of 2002 approximately 18.2 million people in the United States, or 6.3% of the population, suffered from type 1 or type 2 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. 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.

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 has not been an effective long-term solution for the vast majority of 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 injections of insulin each day. However, this treatment regimen is inadequate for many reasons, including the inconvenience and pain associated with injections that lead patients not to comply adequately with the prescribed treatment.

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 alternative to conventional insulin therapy being pursued by a number of 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, which, we believe, should increase patient compliance. We anticipate that the first pulmonary insulin product developed by another pharmaceutical company may be ready for commercial sale as early as 2005. However, we believe this product, as well as other pulmonary insulin products in development of which we are aware, will not address a significant shortcoming of conventional insulin therapy. In particular, based on several published reports,

including a 2004 review article published in *Diabetes Care*, it would appear that these pulmonary insulin products, if and when approved, may not deliver insulin to the bloodstream rapidly enough to approximate the so-called first-phase insulin release spike that is observed in healthy individuals.

The first-phase insulin release spike occurs when a healthy person begins to eat a meal. At the beginning of the meal, the body responds with a sharp spike of insulin release that acts as a signal to the liver to shut off its release of glucose into the bloodstream. This signal turns off the source of glucose that fuels the body between meals at a time when glucose is being supplied from food. Individuals with diabetes cannot produce a first-phase insulin release spike, so their liver continues to release glucose while they absorb additional glucose from the meal. As a result, these individuals develop abnormally high levels of blood glucose, which predisposes them to serious, adverse health consequences.

In contrast, we have observed in our clinical trials to date that our Technosphere Insulin System produces a profile of insulin levels in the bloodstream that does approximate the natural first-phase insulin release spike. In particular, inhalation of Technosphere Insulin generally produces a rapid increase in blood insulin levels that peaks within 10-14 minutes. As illustrated by the charts on page 52, the time-to-peak blood insulin levels produced by the Technosphere Insulin System approximates the rapid rise that has been demonstrated for first-phase insulin release in healthy individuals, which generally occurs within six minutes after food reaches the digestive system.

To date, we have conducted multiple Phase I and Phase II clinical trials of our Technosphere Insulin System involving more than 200 individuals in Europe and the United States. We are currently conducting late Phase II clinical trials to determine dosage tolerance and optimal dosing, which, when fully-enrolled, will involve approximately 325 individuals with type 2 diabetes in Europe and the United States. We expect results from some of these clinical trials to be available in the fourth quarter of 2004 with additional data to follow in early 2005. We intend to initiate Phase III clinical trials in the United States in the first half of 2005, subject to acceptance of our Phase III protocols by the United States Food and Drug Administration, or FDA. Because our studies involved a fairly small number of participants, we cannot be certain that we will be able to repeat and validate our results until we have completed larger studies of efficacy and longer-term safety.

**FEATURES OF OUR DIABETES THERAPY**

We believe that our Technosphere Insulin System has a number of attractive performance characteristics, including:

*Approximates natural first-phase insulin release spike.* Typically, regular insulin delivered by subcutaneous injection results in peak insulin levels in about 120 to 180 minutes. Insulin suppliers have developed rapid-acting insulin analogs, which are variations of insulin that reach peak blood levels in 30 to 90 minutes. Based on our analysis of published reports, including a 2004 review article in *Diabetes Care*, we believe that other pulmonary insulin products in development deliver peak insulin levels in 35 to 90 minutes. In contrast, our clinical trials have shown that our Technosphere Insulin System produces peak insulin levels in 10 to 14 minutes, which approximates the timing of the body s natural first-phase insulin release spike.

*Ease of use.* Our MedTone inhaler is light, is easy to use and fits in the palm of the patient s hand. To administer a dose, the patient opens the device, inserts a single-dose 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. Moreover, the optimal time for taking a dose of Technosphere Insulin appears to be at the start of a meal or shortly thereafter, so we believe there would be no need for a user to try to time an injection 15 to 45 minutes before the expected mealtime.

*More efficient delivery of pulmonary insulin.* Based on our clinical trials of Technosphere Insulin and on our analysis of publicly available information regarding the performance of other

Table of Contents

pulmonary insulin systems in development, we believe that the inhalation of a specified amount of insulin formulated as Technosphere Insulin produces blood insulin levels over a measured period of time that are approximately three times greater than that produced by the same amount of insulin administered via the pulmonary delivery systems being developed by other pharmaceutical companies.

*Safety.* Based on our clinical trials to date, Technosphere Insulin has not generated any serious, drug-related adverse events in our clinical trials to date, but these results are necessarily preliminary until we have completed long term safety studies.

Because of these advantages, we believe our Technosphere Insulin System will be beneficial in patients that have advanced to the point of requiring conventional insulin therapy, patients that are being treated with non-insulin oral medications as well as patients currently using diet and exercise therapy but who are having difficulty achieving proper blood glucose control. If further clinical trials confirm our observations to date, we believe that 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 alone. The use of insulin earlier in the progression of diabetes would represent a paradigm shift in the treatment of this disease.

**OUR STRATEGY FOR DIABETES THERAPY**

*Commercialize our Technosphere Insulin System for the insulin-using diabetes market.* We intend to advance our Technosphere Insulin System into and through Phase III clinical trials and then into commercialization, with the goal of establishing a significant presence for Technosphere Insulin in the 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, such as management by diet and exercise and by non-insulin oral medications. Given the potential advantages of our product, we believe our Technosphere Insulin System has the potential to become the preferred drug therapy for the broader type 2 diabetes population.

*Seek a strategic collaboration for the development, marketing and commercialization of our Technosphere Insulin System.* We are actively exploring collaborations with large pharmaceutical companies in the United States, Europe and Japan that would provide marketing, sales and financial resources to develop, commercialize and sell our Technosphere Insulin System. To date, 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.

We expect that our revenues from our Technosphere Insulin System will come from the sale of Technosphere Insulin cartridges and the MedTone inhaler. We expect that our costs will be the expenses to produce Technosphere Insulin cartridges and the inhalers, selling and marketing expenses if we elect to proceed without a collaborator, research expenses to expand our Technosphere platform technology and develop other potential products, as well as general and administrative expenses.

**OUR RESEARCH PROGRAMS**

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.

Table of Contents

We are also developing therapies for the treatment of solid-tumor cancers. We have conducted initial studies of our cancer therapy in Europe and the United States, including Phase I and II clinical trials in the United States that involved 42 patients who had progressed to late stages of skin cancer. We observed that the delivery of a prototype formulation was well tolerated by patients and produced an appropriate response by their immune system. Although we believe that our clinical data to date have been encouraging, 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 2005.

**RISKS ASSOCIATED WITH OUR BUSINESS**

We face a number of challenges in bringing the Technosphere Insulin System to market. We have not received regulatory approval for this product, nor do we expect to be the first company to bring a pulmonary insulin product to market. In order to complete the clinical trials for our Technosphere Insulin System and develop the sales and marketing capabilities necessary to commercialize the product, we will need to raise additional capital or enter into a collaborative agreement with a pharmaceutical company or both.

We are subject to a number of risks, which you should be aware of before you decide to buy our common stock. These risks are discussed more fully in Risk factors. We are a development stage company with no commercial products. We have not received commercial revenues from any of our product candidates. It is possible that we may never successfully commercialize any of our product candidates. As of March 31, 2004, we had an accumulated deficit of $383.4 million. We expect to continue to incur losses over at least the next several years, and we may never become profitable. Since our inception, we have funded our operations principally through the sale of equity securities, and we expect that we will need to secure additional funding or raise additional capital to enable us to continue to develop and commercialize our Technosphere Insulin System and other product candidates and for other reasons. We cannot assure you that we will be able to obtain additional financing on acceptable terms, or at all.

**CORPORATE INFORMATION**

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. The information contained in, and that can be accessed through, our website is not incorporated into and does not form a part of this prospectus.

**Table of Contents**

# The offering

| | |
|---|---|
| Common stock offered by us | 6,250,000 shares |
| Common stock to be outstanding after this offering | 32,391,461 shares |
| Use of proceeds | We estimate that the net proceeds from this offering will be approximately $79.6 million, or approximately $91.8 million if the underwriters exercise their over-allotment option in full. We intend to use the net proceeds from this offering to continue the development and prepare for the commercialization of our Technosphere Insulin System, to expand our Technosphere Insulin System manufacturing operations and quality systems, to expand our other product development programs, to fund operations, to provide working capital and for other general corporate purposes. See Use of proceeds. |
| Nasdaq National Market symbol | MNKD |

The number of shares of our common stock shown in the table above to be outstanding after the closing of this offering is based on approximately 26,141,461 shares of our common stock outstanding as of May 31, 2004 and excludes:

- 2,132,922 shares of our common stock issuable upon exercise of options outstanding as of May 31, 2004, with a weighted average exercise price of $10.18 per share, of which options to purchase 790,250 shares were exercisable as of that date at a weighted average exercise price of $11.09 per share;

- 175,227 shares of our common stock issuable upon exercise of warrants outstanding as of May 31, 2004, with a weighted average exercise price of $12.54 per share, all of which were exercisable as of that date;

- 3,659,926 shares of our common stock reserved for future issuance under our 2004 Equity Incentive Plan effective as of the completion of this offering; and

- 2,800,000 shares of our common stock reserved for future issuance under our 2004 Non-Employee Directors Stock Option Plan and 2004 Employee Stock Purchase Plan, which we have adopted effective upon the completion of this offering.

Unless otherwise indicated, all information in this prospectus assumes:

- a one-for-three reverse split of our common stock that occurred on July 22, 2004;

- the conversion, upon the closing of this offering, of all 267,212 shares of our Series A redeemable convertible preferred stock, all 192,618 shares of our Series B convertible preferred stock and all 980,392 shares of our Series C convertible preferred stock, each outstanding as of May 31, 2004, into an aggregate of 6,166,372 shares of our common stock; and

- that the underwriters do not exercise their option to purchase up to 937,500 shares of our common stock to cover over-allotments, if any.

Table of Contents

# Summary financial data

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 Corp., or AlleCure, and CTL ImmunoTherapies Corp., or 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. For periods prior to January 1, 2002, the results of operations have been presented on a combined basis. For periods subsequent to December 31, 2001, the financial statements of MannKind and its wholly-owned subsidiaries have been presented on a consolidated basis.

The following statements of operations data for the years ended December 31, 1999 and 2000 are unaudited. The following statement of operations data for the years ended December 31, 2001, 2002 and 2003 were derived from our financial statements, which have been audited by Deloitte & Touche LLP, an independent registered public accounting firm, and are included elsewhere in this prospectus. The balance sheet data as of March 31, 2004 and the statement of operation data for each of the three months ended March 31, 2003 and 2004 and for the period from inception (February 14, 1991) through March 31, 2004 have been derived from our unaudited financial statements, which include, in the opinion of management, all adjustments necessary to present fairly the data for such periods. The historical results are not necessarily indicative of results to be expected in any future period. See the notes to the audited financial statements included elsewhere in this prospectus for an explanation of the method used to determine the number of shares used in computing historical and pro forma basic and diluted net loss per share.

**Table of Contents**

The following financial data is only a summary and should be read in conjunction with our financial statements and the related notes included elsewhere in this prospectus and Management s discussion and analysis of financial condition and results of operations. The following selected financial data is not intended to replace our financial statements included elsewhere in this prospectus.

| Statement of operations data: | Year ended December 31, | | | | | Three months ended March 31, | | Cumulative period from February 14, 1991 (date of inception) to |
|---|---|---|---|---|---|---|---|---|
| | 1999 | 2000 | 2001 | 2002 | 2003 | 2003 | 2004 | March 31, 2004 |
| | (in thousands, except per share data) | | | | | | | |
| Revenue | $ 74 | $ 154 | $ 326 | $ | $ | $ | $ | $ 2,858 |
| Operating expenses: | | | | | | | | |
| Research and development | 3,994 | 20,542 | 19,763 | 42,724 | 45,613 | 11,564 | 12,799 | 156,446 |
| General and administrative | 1,654 | 4,854 | 10,629 | 13,215 | 20,699 | 8,807 | 3,769 | 61,226 |
| In-process research and development costs | | | 19,726 | | | | | 19,726 |
| Goodwill impairment | | | | 151,428 | | | | 151,428 |
| Total operating expenses | 5,648 | 25,396 | 50,118 | 207,367 | 66,312 | 20,371 | 16,568 | 388,826 |
| Loss from operations | (5,574) | (25,242) | (49,792) | (207,367) | (66,312) | (20,371) | (16,568) | (385,968) |
| Other income (expense) | 50 | 204 | 288 | 487 | (25) | (51) | 54 | (2,142) |
| Interest income (expense) | (155) | 379 | 1,261 | 617 | 459 | 86 | 105 | 4,744 |
| Loss before provision for income taxes | (5,679) | (24,659) | (48,243) | (206, 263) | (65,878) | (20,336) | (16,409) | (383,366) |
| Income taxes | | (2) | (2) | (2) | (1) | | | (14) |
| Net loss | (5,679) | (24,661) | (48,245) | (206,265) | (65,879) | (20,336) | (16,409) | (383,380) |
| Deemed dividend related to beneficial conversion feature of convertible preferred stock | | | | (1,421) | (1,017) | | (612) | (3,050) |
| Accretion on redeemable preferred stock | | (149) | (239) | (251) | (253) | (60) | (64) | (956) |
| Net loss applicable to common stockholders | $(5,679) | $(24,810) | $(48,484) | $ (207,937) | $(67,149) | $(20,396) | $(17,085) | $(387,386) |
| Basic and diluted net loss per share: | | | | | | | | |
| Historical | $ (1.38) | $ (3.95) | $ (4.60) | $ (15.43) | $ (3.63) | $ (1.24) | $ (0.86) | |
| Pro forma(1) | | | | | $ (3.34) | | $ (0.71) | |
| Shares used to compute basic and diluted net loss per share: | | | | | | | | |
| Historical | 4,125 | 6,278 | 10,534 | 13,472 | 18,488 | 16,466 | 19,975 | |
| Pro forma(1) | | | | | 20,107 | | 24,218 | |

*(1)*

*The pro forma basic and diluted net loss per share reflects the weighted effect of the pro forma conversion of convertible preferred stock at the conversion prices in effect during the periods presented. See Note 2 to our financial statements for information regarding computation of basic and diluted net loss per share and pro forma basic and diluted net loss per share.*

Table of Contents

| Balance sheet data: | As of March 31, 2004 | | |
|---|---|---|---|
| | Actual | Pro forma(1) | Pro forma as adjusted(2) |
| | | (in thousands) | |
| Cash, cash equivalents and marketable securities | $ 59,305 | $ 59,305 | $ 138,880 |
| Working capital | 52,586 | 52,586 | 132,161 |
| Total assets | 128,766 | 128,766 | 208,341 |
| Deferred compensation and other liabilities | 447 | 447 | 447 |
| Redeemable convertible preferred stock | 5,252 | | |
| Deficit accumulated during the development stage | (383,380) | (383,380) | (383,380) |
| Total stockholders equity | 114,431 | 119,683 | 199,258 |

*(1) Pro forma to give effect to the conversion, upon the closing of this offering, of all 267,212 shares of our Series A redeemable convertible preferred stock, all 192,618 shares of our Series B convertible preferred stock and all 980,392 shares of our Series C convertible preferred stock, each outstanding as of March 31, 2004, into 6,166,372 shares of our common stock.*

*(2) Pro forma as adjusted to give further effect to the sale of 6,250,000 shares we are offering pursuant to this prospectus and the receipt of the estimated net proceeds therefrom.*

Table of Contents

# Risk factors

*Investing in our common stock involves a high degree of risk. You should consider carefully the risks described below and the other information in this prospectus, including the financial statements and the related notes appearing at the end of this prospectus, before deciding to invest in our common stock. If any of the following risks actually occur, they may materially harm our business and our financial condition and results of operations. In this event, the market price of our common stock could decline, and you could lose part or all of your investment.*

**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, as of March 31, 2004, we had an accumulated deficit of $383.4 million and a net loss of $65.9 million for the year ended December 31, 2003 and $16.4 million for the three months ended March 31, 2004. The accumulated deficit has resulted principally from the write-off of goodwill, costs incurred in our research and development programs 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, including the proceeds of this offering, will enable us to continue planned operations into the second 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 a strategic business collaboration, the sale of equity and/or debt securities 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;
- 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 private placement of equity securities. We intend to raise additional capital through strategic business collaborations. In addition, 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 to Phase III clinical trials and demonstrate in these trials that our Technosphere Insulin System is safe and effective. We currently anticipate conducting several pivotal Phase III clinical trials as well as several special population studies involving, in total, several thousand 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 securing collaborations 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 collaborations 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 seeking to enter into a collaboration with respect to our Technosphere Insulin System. If we are not able to enter into a collaboration prior to the commencement of Phase III clinical trials, upon successful completion of our Phase II clinical trials we

intend to fund the initial Phase III clinical trials ourselves from the proceeds of this offering. We estimate that the cost of a Phase III program over the next 24 to 30 months would be approximately $70 to $80 million. Failure to enter into a collaboration with respect to our Technosphere Insulin System following initial Phase III clinical trials or for any other product candidate would 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.

**If testing of a particular product candidate does not yield successful results, we will 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 in our preclinical and initial clinical testing may be inconclusive or may not be predictive of results obtained in later-stage clinical trials or following long-term use and we may 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.

The long-term safety studies of our Technosphere Insulin system are 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 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.

Table of Contents



**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 are seeking to 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 at least 65 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. We are in the process of qualifying a third-party manufacturer to supply us with commercial quantities of the raw Technosphere material. We are currently negotiating a long-term supply agreement with a third party to manufacture our MedTone inhaler and the unfilled cartridges as well as the related molds.

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, which is currently our sole supplier for insulin. We are aware of at least five other suppliers of bulk insulin. We are currently negotiating a long-term supply agreement with 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 Good Manufacturing Practices, or cGMP. 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.

Table of Contents



**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 Aventis, in collaboration with Nektar Therapeutics, have been conducting Phase III clinical trials for the Exubera product and in March 2004 filed a submission seeking regulatory approval in Europe. Novo Nordisk A.S., in collaboration with Aradigm Corporation, has a pulmonary insulin product in Phase III clinical trials, and Eli Lilly and Company, in collaboration with Alkermes, Inc., is also developing a pulmonary insulin product, which is currently in Phase II clinical trials. In addition, a number of established pharmaceutical companies 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 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/$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 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. We estimate the cost to complete the soil cleanup plan is $500,000 to $1,500,000 over the next 18 to 24 months. 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 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 has entered into an agreement to be 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.

**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, 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.

**RISKS RELATED TO REGULATORY APPROVALS**

**Our product candidates must undergo rigorous preclinical and clinical testing and 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 interactions 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. We cannot be certain when or under what conditions we will undertake further clinical trials, including a Phase III program for our Technosphere Insulin System. The clinical trials of our product candidates may not be completed on schedule, and 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. The FDA likely 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). There have been some indications from the FDA that the review of a future 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.

**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 an entire system and that changes to either the MedTone inhaler, the Technosphere material or the insulin could result in FDA requirements to repeat clinical studies because the agency will not permit bridging studies. Bridging studies are traditionally performed on investigational medical products to demonstrate relevance of data obtained on older generation products to newer changed products. Our product candidates that are currently in development for the treatment of cancer and autoimmune and inflammatory diseases also face similar obstacles and costs.

**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.

Table of Contents



**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, we will be subject to stringent, ongoing government regulation.**

Even if regulatory authorities approve any of our product candidates, the manufacture, marketing and sale of these product candidates will be subject to stringent and ongoing government regulation. We also are required to register our establishments with the FDA and certain state agencies. We and any third-party manufacturers or suppliers must continually adhere to federal regulations setting forth requirements, known as cGMP (for drugs) and QSR (for medical devices), and their foreign equivalents, which are enforced by the FDA and other national regulatory bodies through their facilities inspection programs. If our facilities, or the facilities of our manufacturers or suppliers, cannot pass a preapproval plant inspection, the FDA will not approve the marketing of our product candidates. In complying with cGMP and foreign regulatory requirements, we and any of our potential third-party manufacturers or suppliers will be obligated to expend time, money and effort in production, record-keeping and quality control to ensure that our products meet applicable specifications and other requirements. QSR requirements also impose extensive testing, control and documentation requirements. State regulatory agencies and the regulatory agencies of other countries have similar requirements. In addition, we will be required to comply with regulatory requirements of the FDA, state regulatory agencies and the regulatory agencies of other countries concerning the reporting of adverse events and device malfunctions, corrections and removals (e.g., recalls), establishment registration, device listing, 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. We must rely on our MedTone inhaler and cartridge supplier to comply with relevant regulatory requirements including Quality System Regulations, or QSR, and other FDA requirements for medical device manufacturers. It also is likely that this supplier will be subject to an FDA preapproval inspection before the agency will approve a future marketing application for our Technosphere Insulin System. At the present time our supplier is certified to the ISO9001:2000

Table of Contents



Standard. There can be no assurance, however, that if the FDA were to conduct a preapproval inspection of our supplier, that the agency would find that the supplier substantially complies with the QSR. If we or any potential third-party manufacturer or supplier fail to comply with these cGMP or QSR requirements, 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 related technology fields or in other companies clinical trials could delay or prevent us from obtaining regulatory approval or negatively impact public perception of our product candidates.**

At present, there are a number of clinical trials being conducted by other pharmaceutical companies involving insulin delivery systems. The announcement of adverse results from these clinical trials, particularly trials involving the pulmonary delivery of insulin, as well as the FDA s response to these clinical trials, could negatively impact the timing of our clinical trials, our ability to obtain regulatory approval or the public perception of our products. For example, in 2001, Pfizer and Aventis announced that the planned filing for regulatory approval of their pulmonary insulin product would be delayed, citing two concerns. The first concern was that one patient out of more than 1,000 that had used the inhaled form of insulin had developed pulmonary fibrosis. The incidence of pulmonary fibrosis seen in their Phase III clinical trials was comparable to the general population incidence, so it was unclear that the pulmonary fibrosis was related to the use of inhaled insulin. However, the use of inhaled insulin could not be ruled out as a cause. The second concern was that four times as many patients inhaling their drug developed antibodies against insulin as those who injected insulin, although these antibodies did not appear to inhibit insulin activity. Because of these concerns, Pfizer and Aventis stated that the FDA would likely require more safety data. To date, they have filed for regulatory approval in Europe (in March 2004), but have not filed for regulatory approval in the United States. A review of this long-term safety data by the FDA may result in delays in approvals of any inhaled insulin product, including our Technosphere Insulin System. 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.

Table of Contents



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), be required to obtain a license from the other party in order to continue to commercialize the affected products, or 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 THIS OFFERING**

**Our stock price may be volatile and, as a result, you could lose some or all of your investment.**

Following this offering, the market price for our common stock is likely to be volatile, in part because our shares have not been traded publicly. In addition, there has been a history of significant volatility in the market prices of securities of biotechnology and biopharmaceutical companies. 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 and may result in a loss of some or all of your investment.

**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 May 31, 2004, Mr. Mann owned or controlled approximately 61.8% of our outstanding shares of capital stock and will own or control approximately 49.0% of our outstanding shares of common stock immediately following this offering. By virtue of his holdings, he is and will be able to effectively control the election of the members of our board of directors, control our management and 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 stockholders may view as unfavorable.

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 following the expiration of his lock-up agreement with the underwriters. 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.

Mr. Mann has agreed to certain provisions regarding the disposition of his shares, including a prohibition on the sale of his shares for a period of 180 days following the date of this prospectus. See Underwriting.

**You should not consider Mr. Mann s other businesses in deciding whether to purchase our stock.**

Mr. Mann has been and continues to be involved in the formation, financing and operation of many businesses unrelated to our business. These businesses have included, among others, Advanced Bionics Corporation, a company focused on the development of cochlear implants that was acquired by Boston Scientific Corporation; Second Sight LLC, a privately held company developing a visual prosthesis to restore a degree of sight to the blind; MiniMed, Inc., a company focused on diabetes

therapy and microinfusion drug delivery that was acquired by Medtronic, Inc. in 2001; Medical Research Group, Inc., a company involved in the development of an artificial pancreas that was also acquired by Medtronic, Inc. in 2001; and Pacesetter Systems and its successor, Siemens Pacesetter, a manufacturer of cardiac pacemakers that is now part of St. Jude Medical. Mr. Mann is also involved in numerous charitable organizations. You should not consider any of these businesses or activities and should only rely on the information provided in this prospectus in deciding whether or not to purchase our stock.

**The future sale of our common stock could negatively affect our stock price.**

After this offering, we will have approximately 32.4 million shares of common stock outstanding, or 33.3 million shares if the underwriters exercise their over-allotment option in full. The shares sold in this offering will be freely tradable without restriction under the federal securities laws unless purchased by our affiliates. The remaining shares of common stock outstanding after this offering will be available for public sale subject in some cases to volume and other limitations. See Shares eligible for future sale. Substantially all of our shares outstanding after this offering (excluding the shares sold in this offering) will be subject to the lock-up agreements with the underwriters described under Underwriting.

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. After this offering, the holders of approximately 913,015 shares of our common stock and the holders of warrants to purchase 135,328 shares of our common stock will 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.

**If an active, liquid trading market for our common stock does not develop, you may be unable to sell your shares quickly or at the market price.**

Prior to this offering, there was no public market for our common stock. An active trading market for our common stock may not develop following this offering. As a result, you may not be able to sell your shares quickly or at the market price if trading in our stock is not active. The initial public offering price may not be indicative of prices that will prevail in the trading market. See Underwriting for more information regarding the factors considered in determining the initial public offering price.

**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 in excess of 15% 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.

**If we do not effectively use our broad discretion in how we use the proceeds of this offering, our results of operations could suffer and the value of our stock could decline.**

Our management will have considerable discretion in the application of the net proceeds of this offering. We have not finalized how we will use these proceeds. We may use the net proceeds for corporate purposes that do not yield a significant return or any return at all for our stockholders. See Use of proceeds.

**As a new investor, you will incur substantial dilution as a result of this offering, and as a result, the market price of our common stock may decline.**

The historical net tangible book value of our common stock as of March 31, 2004 was approximately $119.7 million, or approximately $5.99 per share, based on 19,975,089 of shares outstanding as of March 31, 2004. Based upon the initial offering price of $14.00 per share, you will incur immediate and substantial dilution in net tangible book value of $7.85 per share, representing the difference between our pro forma net tangible book value per share after giving effect to this offering and the initial public offering price. You may incur additional dilution if the holders of outstanding options or warrants exercise those options or warrants. All purchasers of shares in this offering will contribute 21.0% of the total amount of the purchase price that has been paid by all stockholders but will own only 19.3% of shares outstanding after the offering. Additional information regarding the dilution to investors in this offering is included in this prospectus under the heading Dilution.

**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.

Table of Contents

## Special note regarding forward-looking statements

This prospectus contains forward-looking statements. The forward-looking statements are contained principally in, but not limited to, the sections entitled Risk factors, Management s discussion and analysis of financial condition and results of operations and Business. These statements involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance or achievements to be materially different from any future results, performances or achievements expressed or implied by the forward-looking statements. Forward-looking 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, ma potential, predicts, projects, should, will, would and similar expressions intended to identify forward-looking statements. Forward-lookin statements reflect our current views with respect to future events and are based on assumptions and subject to risks and uncertainties. We discuss many of these risks in this prospectus in greater detail under the heading Risk factors. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Also, forward-looking statements represent our estimates and assumptions only as of the date of this prospectus. You should read this prospectus and the documents that we reference in this prospectus and have filed as exhibits to the registration statement of which this prospectus forms a part completely and with the understanding that our actual future results may be materially different from what we expect.

Except as required by law, we do not undertake any obligation to update or revise any forward-looking statements contained in this prospectus or incorporated herein by reference, whether as a result of new information, future events or otherwise. Because of these risks and uncertainties, the forward-looking events and circumstances discussed in this prospectus may not transpire. Factors that could cause actual results or conditions to differ from those anticipated by these and other forward-looking statements include those described in the Risk factors section and elsewhere in this prospectus.

Table of Contents

## Use of proceeds

We estimate that we will receive net proceeds from the sale of shares of our common stock in this offering of approximately $79.6 million ($91.8 million if the underwriters exercise their over-allotment option in full) after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

We estimate that we will use approximately $58 million of the net proceeds of this offering to continue the development of our Technosphere Insulin System, including the continuation of our clinical trial program, and to develop additional applications for our proprietary Technosphere formulation technology. We expect, with these proceeds, to complete Phase II trials on Technosphere Insulin and initiate a Phase III clinical trial. Additionally, our efforts with respect to our Technosphere Insulin System will include expansion of our manufacturing operations and quality systems.

We estimate that we will use approximately $12 million of the net proceeds of this offering to expand our other product development programs, specifically developing therapies for the treatment of solid-tumor cancers and a variety of inflammatory and autoimmune diseases. We expect to begin preclinical safety tests for a cancer product candidate later this year, with the goal of commencing clinical trials in 2005.

We intend to use the balance of the net proceeds of this offering to fund operations, to provide working capital and for other 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.

As of the date of this prospectus, we cannot specify with certainty all of the particular uses for the net proceeds to be received upon the completion of this offering. 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 proceeds of this offering. 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. On December 12, 2003, our board of directors adopted our written investment policy. The investment policy imposes restrictions on our investments in order to ensure that we preserve our principal and maintain our liquidity. Any investment of the net proceeds from this offering will be made in accordance with the terms of our investment policy.

## 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.

Table of Contents

# Capitalization

The following table sets forth our capitalization as of March 31, 2004:

- on an actual basis;
- on a pro forma basis to give effect to the conversion, upon the closing of this offering, of all 267,212 shares of our Series A redeemable convertible preferred stock, all 192,618 shares of our Series B convertible preferred stock and all 980,392 shares of our Series C convertible preferred stock, each outstanding as of March 31, 2004, into an aggregate of 6,166,372 shares of our common stock; and
- on a pro forma as adjusted basis to give further effect to the sale in this offering of 6,250,000 shares of our common stock and the receipt of the estimated net proceeds therefrom, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

| | As of March 31, 2004 | | |
|---|---|---|---|
| | **Actual** | **Pro forma** | **Pro forma as adjusted** |
| | | **(in thousands, except share and per share data)** | |
| Cash, cash equivalents and marketable securities | $59,305 | $59,305 | $ 138,880 |
| Deferred compensation and other liabilities | 447 | 447 | 447 |
| Series A redeemable convertible preferred stock, $0.01 par value per share; 267,213 shares authorized; 267,212 issued and outstanding, actual; no shares issued and outstanding, pro forma or pro forma as adjusted | 5,252 | | |
| Stockholders equity: | | | |
| Series B convertible preferred stock, $0.01 par value per share; 192,618 shares authorized, issued and outstanding, actual; no shares issued and outstanding, pro forma or pro forma as adjusted | 15,000 | | |
| Series C convertible preferred stock, $0.01 par value per share; 980,393 authorized; 980,392 issued and outstanding, actual; no shares issued and outstanding, pro forma or pro forma adjusted | 50,000 | | |
| Common stock, $0.01 par value per share; 100,000,000 shares authorized and 19,975,089 shares issued and outstanding, actual; 100,000,000 and 90,000,000 shares authorized, pro forma and pro forma as adjusted, respectively; 26,141,461 and 32,391,461 shares issued and outstanding, pro forma and pro forma as adjusted, respectively | 200 | 261 | 324 |
| Additional paid-in capital | 434,202 | 504,393 | 583,905 |
| Notes receivable from stockholders | (1,438) | (1,438) | (1,438) |
| Notes receivable from officers | (153) | (153) | (153) |
| Deficit accumulated during the development stage | (383,380) | (383,380) | (383,380) |
| Total stockholders equity | 114,431 | 119,683 | 199,258 |
| Total capitalization | $120,130 | $120,130 | $ 199,705 |

Table of Contents

**Capitalization**

You should read the information in the table above in conjunction with Management s discussion and analysis of financial condition and results of operations and our financial statements and accompanying notes appearing elsewhere in this prospectus.

The number of shares in the table above excludes:

- 2,149,953 shares of our common stock issuable upon exercise of options outstanding as of March 31, 2004, with a weighted average exercise price of $10.20 per share, of which options to purchase 765,464 shares were exercisable as of that date, with a weighted average exercise price of $10.74 per share;

- 175,227 shares of our common stock issuable upon exercise of warrants outstanding as of March 31, 2004, with a weighted average exercise price of $12.54 per share, all of which were exercisable as of that date;

- 3,643,957 shares of our common stock reserved for future issuance under our 2004 Equity Incentive Plan effective as of the completion of this offering; and

- 2,800,000 shares of our common stock reserved for future issuance under our 2004 Non-Employee Directors Stock Option Plan and 2004 Employee Stock Purchase Plan, which we have adopted effective upon the completion of this offering.

We effected a one-for-three reverse split of our common stock on July 22, 2004. All share amounts set forth in the table above give effect to this stock split.

Table of Contents

# Dilution

Our historical net tangible book value as of March 31, 2004 was approximately $119.7 million, or $5.99 per share of common stock, based on 19,975,089 shares of common stock outstanding. Historical net tangible book value per share is equal to our total tangible assets minus total liabilities, all divided by the number of shares of our common stock outstanding as of March 31, 2004. Our pro forma net tangible book value as of March 31, 2004 was approximately $119.7 million, or $4.58 per share of our common stock. Pro forma net tangible book value per share gives effect to the conversion, upon the closing of this offering, of all then outstanding shares of our preferred stock into an aggregate of 6,166,372 shares of our common stock.

After giving further effect to the sale of the 6,250,000 shares of our common stock offered by this prospectus and after deducting underwriting discounts and commissions and our estimated offering expenses, our pro forma as adjusted net tangible book value as of March 31, 2004 would have been approximately $199.3 million, or $6.15 per share of our common stock. This represents an immediate increase in pro forma net tangible book value of $1.57 per share to existing stockholders and an immediate dilution of $7.85 per share to new investors. The following table illustrates this calculation on a per share basis:

| | | |
|---|---|---|
| Initial public offering price per share | | $14.00 |
| Net tangible book value per share as of March 31, 2004 | $ 5.99 | |
| Decrease per share attributable to the conversion of our convertible preferred stock and redeemable convertible preferred stock | (1.41) | |
| Pro forma net tangible book value as of March 31, 2004 | 4.58 | |
| Increase per share attributable to the offering | 1.57 | |
| Pro forma as adjusted net tangible book value per share after this offering | | |