

MANNKIND CORP
Form S-3/A
September 16, 2005

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As filed with the Securities and Exchange Commission on September 16, 2005 Registration No. 333-128093

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

**Amendment No. 1
to
FORM S-3
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933**

MANNKIND CORPORATION
(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction of
incorporation or organization)

2834
(Primary standard industrial
Classification code number)

13-3607736
(I.R.S. Employer Identification
Number)

**28903 North Avenue Paine
Valencia, CA 91355
(661) 775-5300**
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

**Alfred E. Mann
Chief Executive Officer and Chairman
MannKind Corporation
28903 North Avenue Paine
Valencia, CA 91355
(661) 775-5300**
(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

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Approximate date of commencement of proposed sale to the public: As soon as practicable after the effective date of this registration statement.

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box: ☐

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest

reinvestment plans, check the following box: ☐

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering: ☐ _____

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering: ☐ _____

If delivery of the prospectus is expected to be made pursuant to Rule 434, please check the following box: ☐

CALCULATION OF REGISTRATION FEE

Title of each class of securities to be registered	Amount to be registered (1)	Proposed maximum offering price per share (2)	Proposed maximum aggregate offering price (2)	Amount of registration fee (3)
Common Stock, \$0.01 par value per share	17,131,682 shares	\$12.38	\$212,090,223	\$24,963
Common Stock, \$0.01 par value per share, issuable upon the exercise of warrants	3,426,340 shares	\$12.38	\$42,418,089	\$4,993
Total	20,558,022 shares		\$254,508,312	\$29,956

(1) Based upon the estimated maximum number of shares of common stock that may be sold by the selling stockholders. Pursuant to Rule 415 under the Securities Act of 1933, as amended, or the Securities Act, this registration statement also registers such additional shares of the Registrant's common stock as may hereafter be offered or issued to prevent dilution resulting from stock splits, stock dividends, recapitalizations or certain other capital adjustments.

(2) Estimated solely for the purpose of computing the amount of the registration fee pursuant to Rule 457(c) of the Securities Act. The price per share and aggregate offering price are based upon the average of the high and low sales prices of the Registrant's common stock on August 26, 2005, as reported on The Nasdaq National Market.

(3) Previously paid.

The registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the Registration Statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

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The information in this prospectus is not complete and may be changed. The selling stockholders may not sell the securities under this prospectus until the Registration Statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and the registrant is not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED SEPTEMBER 16, 2005

PROSPECTUS

20,558,022 Shares

Common Stock

The selling stockholders identified in this prospectus are offering for sale from time to time up to 20,558,022 shares of our common stock, \$0.01 par value per share, which includes 17,131,682 shares of our common stock held by the selling stockholders and 3,426,340 shares of our common stock issuable to the selling stockholders upon the exercise of warrants. The selling stockholders acquired their shares and the warrants from us in a private placement that closed on August 5, 2005 and is more fully described on page 23 of this prospectus under the heading Selling Stockholders. We will not receive any of the proceeds from the sale of the shares of our common stock by the selling stockholders.

The selling stockholders or their pledgees, donees, transferees or other successors-in-interest, may offer the shares from time to time through public or private transactions, at prevailing market prices or at privately negotiated prices, or through any other means described in this prospectus under Plan of Distribution.

Our common stock is quoted on the Nasdaq National Market under the symbol MNKD. On September 15, 2005, the last reported sale price for our common stock on the Nasdaq National Market was \$12.57 per share.

INVESTING IN OUR COMMON STOCK INVOLVES A HIGH DEGREE OF RISKS.

SEE RISK FACTORS BEGINNING ON PAGE 3 OF THIS PROSPECTUS TO READ ABOUT FACTORS YOU

SHOULD CONSIDER IN CONNECTION WITH PURCHASING OUR COMMON STOCK.

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

The date of this prospectus is _____, 2005.

You should rely only on the information contained or incorporated by reference in this prospectus and any applicable prospectus supplement. We have not, and the selling stockholders have not, authorized anyone to provide you with additional information or information different from that contained or incorporated by reference in this prospectus and any applicable prospectus supplement. The selling stockholders 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 and information appearing in any applicable prospectus supplement is accurate only as of the date of the applicable prospectus supplement. Additionally, information from other documents incorporated by reference in this prospectus or any applicable prospectus supplement is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of the prospectus or prospectus supplement or any sale of our common stock.

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PROSPECTUS SUMMARY

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

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PROSPECTUS SUMMARY

*The following summary provides an overview of selected information relating to this offering and does not contain all the information that you should consider before investing in our common stock. You should carefully read this prospectus, especially the risks of investing in our common stock discussed under the section **RISK FACTORS** below, all documents incorporated by reference, any prospectus supplement, and the additional information described under the caption **WHERE YOU CAN FIND MORE INFORMATION**, beginning on page 32, before buying securities in this offering. Reference to we, us, our, our company and MannKind refers to MannKind Corporation and its subsidiary, unless the context requires otherwise.*

We are a biopharmaceutical company focused on the discovery, development and commercialization of therapeutic products for diseases such as diabetes and cancer. We are currently in Phase 3 clinical trials in the United States and Europe of our lead product, the Technosphere Insulin System, to study its safety and efficacy in the treatment of diabetes. This therapy consists of a proprietary dry powder Technosphere formulation of insulin that is inhaled into the deep lung using our proprietary MedTone inhaler. We believe that the combination of unique performance characteristics, including the rapid transfer of the insulin into the blood and the significantly higher bioavailability, and the convenience and ease of use of the Technosphere Insulin System may have the potential to change the way diabetes is treated.

Our other products candidates are in research and pre-clinical development. We are developing additional applications for our proprietary Technosphere platform technology by formulating other drugs for pulmonary delivery, primarily for metabolic and immunological diseases. We are also developing therapies for the treatment of solid-tumor cancers.

We were incorporated in the State of Delaware on February 14, 1991. Our principal executive offices are located at 28903 North Avenue Paine, Valencia, California 91355, and our telephone number at that address is (661) 775-5300. Our website address is <http://www.mannkindcorp.com>. Our filings with the Securities and Exchange Commission, or SEC, including our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and any amendments to those reports are available free of charge through our website as soon as reasonably practicable after being filed with or furnished to the SEC. The information on our website and other information that can be accessed through our website are not part of this prospectus.

RISK FACTORS

An investment in our common stock involves a high degree of risk. Prior to making a decision about investing in our common stock, you should carefully consider the following risks factors and the risk factors described in any applicable prospectus supplement, together with all of the other information contained in this prospectus and any prospectus supplement or appearing or incorporated by reference in the registration statement of which this prospectus is a part. The risks described below are not the only risks we face. Additional risks that we do not currently think are material may also impair our business operations. If any of the events or circumstances described in the following risks actually occur, our business, financial condition or results of operations could suffer, the trading price of our common stock could decline and you might lose all or part of your investment in our common stock.

RISKS RELATED TO OUR BUSINESS

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

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

We have never been profitable, and, as of June 30, 2005, we had an accumulated deficit of \$492.3 million. The accumulated deficit has resulted principally from costs incurred in our research and development programs, the write-off of goodwill and general operating expenses. We expect to make substantial expenditures and to incur increasing operating losses in the future in order to further develop and commercialize our product candidates, including costs and expenses to complete clinical trials, seek regulatory approvals and market our product candidates.

This accumulated deficit may increase significantly as we expand development and clinical trial efforts.

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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 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 net proceeds from our private placement in August 2005, will enable us to continue planned operations into the third quarter of 2006. However, we cannot assure you that our plans will not change or that changed circumstances will not result in the depletion of our capital resources more rapidly than we currently anticipate. Accordingly, we expect that we will need to raise additional capital, either through the sale of equity and/or debt securities, a strategic business collaboration or the establishment of other funding facilities, in order to continue the development and commercialization of our Technosphere Insulin System and other product candidates and to support our other ongoing activities. The amount of additional funds we need will depend on a number of factors, including:

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

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

- our success in establishing strategic business collaborations;

- the timing and amount of milestone or other payments we might receive from potential third parties;

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

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

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

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

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

We have raised capital in the past primarily through the sale of equity securities. 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 and specific restrictions on the use of our assets, as well as prohibitions on our ability to create liens, pay dividends, redeem our stock or make investments.

We also may seek to raise additional capital by pursuing opportunities for the licensing, 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.

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

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

We have expended significant time, money and effort in the development of our lead product candidate, the Technosphere Insulin System, which has not yet received regulatory approval and which may never be commercialized. Before we can market and sell our Technosphere Insulin System, we will need to advance our Technosphere Insulin System through Phase 3 clinical trials and demonstrate in these trials that our Technosphere Insulin System is safe and effective. We currently anticipate conducting several pivotal Phase 3 clinical trials as well as several special population studies involving, in total, more than 3,000 patients, which will require the expenditure of additional time and resources. We must also receive the necessary approvals from the FDA and similar foreign regulatory agencies before this product can be marketed in the United States or elsewhere. Even if we were to receive regulatory approval, we ultimately may be unable to gain market acceptance of our Technosphere Insulin System for a variety of reasons, including the treatment and dosage regimen, potential adverse effects, the availability of alternative treatments and cost effectiveness. If we fail to commercialize our Technosphere Insulin System, our business, financial condition and results of operations will be materially and adversely affected.

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

A significant portion of the research that we are conducting involves new and unproven compounds and technologies, including our Technosphere Insulin System, Technosphere platform technology and immunotherapy product candidates. Research programs to identify new product candidates require substantial technical, financial and human resources. Even if our research programs identify candidates that initially show promise, these candidates may fail to progress to clinical development for any number of reasons, including discovery upon further research that these candidates have adverse effects or other characteristics that indicate they are unlikely to be effective 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 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 publicly announce the expected timing of some of these milestones. All of these milestones are based on a variety of assumptions. The actual timing of the achievement of these milestones can vary dramatically compared to our estimates in many cases for reasons beyond our control depending on numerous factors, including:

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

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product candidates, including insulin and other materials for our Technosphere Insulin System; and

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

In addition, if we do not obtain sufficient additional funds through sales of securities, strategic collaborations 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 would impact our ability to meet milestones. If we fail to commence or complete, or experience delays in or are forced to curtail, our proposed clinical programs or otherwise fail to adhere to our projected development goals in the timeframes we announce and expect, our business and results of operations will be harmed and the market price of our common stock may decline.

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

We initially are focusing on the development of the Technosphere Insulin System for the treatment of diabetes, and we face intense competition in this area. Pfizer, Inc. and Sanofi-Aventis, in collaboration with Nektar Therapeutics, have been conducting Phase 3 clinical trials for the Exubera product. In March 2004, these collaborators filed a submission seeking regulatory approval in Europe, and in March 2005, their new drug application, or NDA, was accepted by the FDA. Novo Nordisk A.S. has a pulmonary insulin product in development. In July 2005, Eli Lilly and Company, in collaboration with Alkermes, Inc., initiated a Phase 3 clinical trial required for registration of their inhaled insulin system and to define the safety and efficacy of the Lilly/Alkermes product. In addition, a number of established pharmaceutical companies have or are developing proprietary technologies or have entered into arrangements with, or acquired, companies with technologies for the treatment of diabetes. We also face substantial competition for the development of our other product candidates.

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 and cancer. These institutions are becoming increasingly aware of the commercial value of their findings and are more active in seeking patent and other proprietary rights as well as licensing revenues.

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

Our current strategy for developing, manufacturing and commercializing our product candidates includes evaluating the potential for collaborating with pharmaceutical and biotechnology companies at some point in the drug development process and for these collaborators to undertake the advanced clinical development and commercialization of our product candidates. It may be difficult for us to find third parties that are willing to enter into collaborations on economic terms that are favorable to us, or at all.

If we are not able to enter into a collaboration on terms that are favorable to us for our products, we could be required to undertake and fund product development, clinical trials, manufacturing and marketing activities solely at our own expense. For example, we are currently evaluating potential collaborations with respect to our Technosphere Insulin System. We currently estimate that the cost of a self-funded Phase 3 program over the next 12 months would be in the range of \$150 to \$175 million. However, this estimate may change based on how the program proceeds. Failure to enter into a collaboration with respect to our Technosphere Insulin System following initial Phase 3 clinical trials or

with respect to any other product candidate could substantially increase our
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requirements for capital, which might not be available on favorable terms, if at all. Alternatively, we would have to substantially reduce our development efforts, which would delay or otherwise impede the commercialization of our product candidates.

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

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

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

Our research and development programs are designed to test the safety and efficacy of our 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 as a result be forced to stop developing product candidates that we currently believe are important to our future;

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

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

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

We have initiated the second of our Phase 3 studies, a pivotal safety study of our Technosphere Insulin System, primarily to evaluate pulmonary function during long term use. Our Technosphere Insulin System is intended for multiple uses per day. Due to the size and time frame over which the clinical trials are conducted, the results of clinical trials may not be indicative of the effects of long-term use. If long-term use of our product results in adverse health effects or reduced efficacy or both, the FDA or other regulatory agencies may terminate our ability to market and sell our Technosphere Insulin System, may narrow the approved indications for use or otherwise require restrictive product labeling or marketing, or may require further clinical trials, which may be time-consuming and expensive, and may not produce favorable results.

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

If 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

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

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

We require a well-structured plan to make this transition. We are in the process of implementing the following measures, among others, to accommodate our transition and successfully implement our commercialization strategy for our Technosphere Insulin System:

- add a significant number of new personnel, particularly in clinical development, regulatory and manufacturing production, including personnel with significant Phase 3-to-commercialization experience;

- expand our manufacturing capabilities;

- develop comprehensive and detailed commercialization, clinical development and regulatory plans;

- implement standard operating procedures, including those for protocol development; and

- align our management structure to accommodate the increasing complexity of our operations.

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

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

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

We currently use our Danbury, Connecticut facility to manufacture raw Technosphere material, formulate Technosphere Insulin, fill plastic cartridges with Technosphere Insulin and blister package the cartridges for our clinical trials. We presently intend to increase our formulation, fill and finishing capabilities at Danbury in order to

accommodate our activities through initial commercialization. This expansion will involve a number of third-party
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suppliers of equipment and materials as well as engineering and construction services. Our suppliers may not deliver all of the required equipment, materials and services in a timely manner or at reasonable prices. If we encounter difficulties in our relationships with these suppliers, or if a supplier becomes unable to provide us with goods or services at the agreed-upon price, our facilities expansion could be delayed or its costs increased.

We have never manufactured any of our product candidates in commercial quantities. As our product candidates move through the regulatory process, we will need to either develop the capability of manufacturing on a commercial scale or engage third-party manufacturers with this capability, and we cannot assure you that we will be able to do either successfully. The manufacture of pharmaceutical products requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of pharmaceutical products often encounter difficulties in production, especially in scaling up initial production. These problems include difficulties with production costs and yields, quality control and assurance and shortages of qualified personnel, as well as compliance with strictly enforced federal, state and foreign regulations. In addition, before we would be able to produce commercial quantities of Technosphere Insulin at our Danbury facility, it will have to undergo a pre-approval inspection by the FDA. The expansion process and preparation for the FDA's pre-approval inspection for commercial production at the Danbury facility could take an additional six months or longer. If we use a third-party supplier to formulate Technosphere Insulin or produce its raw material, the transition could also require significant start-up time to qualify and implement the manufacturing process. If we engage a third-party manufacturer, our third-party manufacturer may not perform as agreed or may terminate its agreement with us.

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

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

For our Technosphere Insulin System to be commercially viable, we need access to sufficient, reliable and affordable supplies of insulin, our MedTone inhaler, the related cartridges and other materials. We currently have a long-term supply agreement with Diosynth B.V., an independent supplier of insulin and a subsidiary of Akzo Nobel, which is currently our sole supplier for insulin. We are aware of at least five other suppliers of bulk insulin but to date we have not entered into a commercial relationship with any of the five. Currently, we manufacture the raw Technosphere material, but we are in the process of qualifying a secondary manufacturer to supply us with commercial quantities of this raw material. We recently entered into a long-term supply agreement with Vaupell, Inc., the supplier of our MedTone inhaler and cartridges. We must rely on our suppliers to comply with relevant regulatory and other legal requirements, including the production of insulin in accordance with current drug Good Manufacturing Practices, or cGMP, and the production of MedTone inhaler and related cartridges in accordance with device Quality System Regulations, or QSR. The supply of all of these materials may be limited or the manufacturer may not meet relevant regulatory requirements, and if we are unable to obtain these materials in sufficient amounts, in a timely manner and at reasonable prices, or if we should encounter delays or difficulties in our relationships with manufacturers or suppliers, our development or manufacturing may be delayed. Any such events would delay the submission of our product candidates for regulatory approval or market introduction and subsequent sales and, if so, our business and results of operations will be harmed and the market price of our common stock may decline.

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

A broad base of physicians and specialists treat patients with diabetes. A large sales force will be required in order to educate and support these physicians and specialists. Therefore, we plan to enter into collaborations with one or more

pharmaceutical companies to sell, market and distribute our Technosphere Insulin System. If we fail to enter into collaborations, we will be required to establish our own direct sales, marketing and distribution capabilities. Establishing these capabilities can be time-consuming and expensive and we estimate that establishing a specialty sales force would cost more than \$20 million. Because of our size, we would be at a disadvantage to our potential competitors, all of which have collaborated with large pharmaceutical companies that have substantially more resources than we do. As a result, we would not initially be able to field a sales force as large as our competitors or

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

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

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

The degree of market acceptance of our product candidates will depend on many factors, including:

- the claims for which FDA approval can be obtained, including superiority claims;

- the perceived advantages and disadvantages of competitive products;

- 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 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, we may not be able to obtain insurance coverage that will be adequate to satisfy any liability that may arise, and because insurance coverage in our industry can be very expensive and difficult to obtain, we cannot assure you that we will be able to obtain sufficient coverage at an acceptable cost, if at all. If losses from such claims exceed our liability insurance coverage, we may ourselves incur substantial liabilities. If we are required to pay a product liability claim, we may not have sufficient financial resources to complete development or commercialization of any of our product candidates

and, if so, our business and results of operations will be harmed and the market price of our common stock may decline.

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

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

When we purchased the facilities located in Danbury, Connecticut, there was a soil cleanup plan in process. As part of the purchase, we obtained an indemnification from the seller related to the remediation of the soil for all known environmental conditions that existed at the time the seller acquired the property. The seller is, in turn, indemnified for these known environmental conditions by the previous owner. We estimate that the cost to complete the soil cleanup plan for industrial use is \$1.5 to \$3.0 million over the next 18 to 24 months. We also received an indemnification from the seller for environmental conditions created during its ownership of the property and for environmental problems unknown at the time that the seller acquired the property. These additional indemnities are limited to the purchase price that we paid for the Danbury facilities. In the event that any cleanup costs are imposed on us and we are unable to collect the full amount of these costs and expenses from the seller or the party responsible for the contamination, we may be required to pay these costs and our business and results of operations may be harmed.

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

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

The loss of the services of any principal member of our management and scientific staff could significantly delay or prevent the achievement of our scientific and business objectives. All of our employees are at will and we currently do not have employment agreements with any of the principal members of our management or scientific staff, and we do not have key person life insurance to cover the loss of any of these individuals. Replacing key employees may be difficult and time-consuming because of the limited number of individuals in our industry with the skills and experience required to develop, gain regulatory approval of and commercialize our product candidates successfully. In May 2005, we terminated the employment of Dr. Wendell Cheatham, our former Chief Medical Officer. Although Mr. Edstrom has assumed Dr. Cheatham's management responsibilities while we search for a senior executive to lead our development operations, there can be no assurance that we will be able to recruit such an individual with the appropriate skills and experience.

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.

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

Alfred Mann, our Chairman and Chief Executive Officer, is also serving as the Chairman and Co-Chief Executive Officer of Advanced Bionics Corporation, which was acquired by Boston Scientific Corporation. Mr. Mann is involved in many other business and charitable activities. As a result, the time and attention Mr. Mann devotes to the operation of our business varies and he may not expend the same time or focus on our activities as other, similarly situated chief executive officers. 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.

We have been sued by our former Chief Medical Officer. As a result of this litigation, we may incur material costs and suffer other consequences, which may adversely affect us.

In May 2005, Dr. Cheatham filed a complaint against us in the California Superior Court. The complaint alleges causes of action for wrongful termination in violation of public policy, breach of contract and retaliation in connection with the termination of Dr. Cheatham's employment. In the complaint, Dr. Cheatham seeks compensatory, punitive and exemplary damages in excess of \$2.0 million as well as reimbursement of attorneys' fees. In June 2005, we answered the complaint and also filed a cross-complaint against Dr. Cheatham, alleging claims for libel per se, trade libel, breach of contract, breach of the implied covenant of good faith and fair dealing and breach of the duty of loyalty. In July 2005, Dr. Cheatham filed a demurrer and motion to strike our cross-complaint under California's anti-SLAPP statute, the hearing for which is scheduled for September 28, 2005.

The litigation will result in costs and divert management's attention and resources, any of which could adversely affect our business, results of operations or financial position. We are also concerned that, despite the findings by an independent counsel following an investigation and despite the endorsement of the independent counsel's report by our board of directors, investors could give undue weight to Dr. Cheatham's allegations, resulting in damage to our reputation, or the FDA could begin an investigation, either of which could adversely affect the trading price of our common stock. If we are not successful in this litigation, we could be forced to make a significant settlement or judgment payment to Dr. Cheatham, which could adversely affect our business, results of operations or financial position.

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

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

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

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

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RISKS RELATED TO REGULATORY APPROVALS

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

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

product design, development, manufacture and testing;

product labeling;

product storage and shipping;

pre-market clearance or approval;

advertising and promotion; and

product sales and distribution.

Clinical testing can be costly and take many years, and the outcome is uncertain and susceptible to varying interpretations. We expect, based on our discussions with the FDA and on our understanding of the interactions between the FDA and other pharmaceutical companies developing pulmonary insulin delivery systems, that we will need safety data covering at least two years from patients treated with our Technosphere Insulin System and that we must complete a two-year carcinogenicity study of Technosphere Insulin in rodents to obtain approval, among other requirements. We cannot be certain when or under what conditions we will undertake further clinical trials. The clinical trials of our product candidates may not be completed on schedule, the FDA or foreign regulatory agencies may order us to stop or modify our research, or these agencies may not ultimately approve any of our product candidates for commercial sale. The data collected from our clinical trials may not be sufficient to support regulatory approval of our various product candidates, including our Technosphere Insulin System. Even if we believe the data collected from our clinical trials are sufficient, the FDA has substantial discretion in the approval process and may disagree with our interpretation of the data. Our failure to adequately demonstrate the safety and efficacy of any of our product candidates would delay or prevent regulatory approval of our product candidates, which could prevent us from achieving profitability.

The requirements governing the conduct of clinical trials and manufacturing and marketing of our product candidates, including our Technosphere Insulin System, outside the United States vary widely from country to country. Foreign approvals may take longer to obtain than FDA approvals and can require, among other things, additional testing and different clinical trial designs. Foreign regulatory approval processes include all of the risks associated with the FDA approval processes. Some of those agencies also must approve prices of the products. Approval of a product by the FDA does not ensure approval of the same product by the health authorities of other countries. In addition, changes in regulatory policy in the United States or in foreign countries for product approval during the period of product development and regulatory agency review of each submitted new application may cause delays or rejections. The process of obtaining FDA and other required regulatory approvals, including foreign approvals, is expensive, often takes many years and can vary substantially based upon the type, complexity and novelty of the products involved. To our knowledge, no pulmonary insulin product has yet been approved for marketing, and we are not aware of any precedent for the successful commercialization of products based on our technology or technologies similar to ours. However, an application for approval for another pulmonary insulin product candidate was recently filed in the United States, and we believe a decision could be made by the FDA in early 2006. The FDA has advised us that it will regulate our Technosphere Insulin System as a combination product because of the complex nature of the system that includes the combination of a new drug (Technosphere Insulin) and a new medical device (the

MedTone inhaler used to administer the insulin). The FDA indicated that the review of a future drug marketing application for our Technosphere Insulin System will involve three separate review groups of the FDA: (1) the Metabolic and Endocrine Drug Products Division; (2) the Pulmonary Drug Products Division; and (3) the Center for Devices and Radiological Health within the FDA that reviews medical devices. We currently understand that the Metabolic and Endocrine Drug Products Division will be the lead group and will obtain consulting reviews from the other two FDA groups. The FDA has not made an official final decision in this regard, however, and we can make no assurances at this time about what impact FDA review by multiple groups will have on the review and approval of our product or whether we are correct in our understanding of how the Technosphere Insulin System will be reviewed and approved.

Also, recent events regarding questions about the safety of marketed drugs, including pertaining to the lack of adequate labeling, may result in increased cautiousness by the FDA in reviewing new drugs based on safety, efficacy, or other regulatory considerations and may result in significant delays in obtaining regulatory approvals. Such regulatory considerations may also result in the imposition of more restrictive drug labeling or marketing

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requirements as conditions of approval, which may significantly affect the marketability of our drug products. FDA review of our Technosphere Insulin System as a combination product therapy may lengthen the product development and regulatory approval process, increase our development costs and delay or prevent the commercialization of our Technosphere Insulin System.

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

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

We have only limited experience in filing and pursuing applications necessary to gain regulatory approvals, which may impede our ability to obtain timely approvals from the FDA or foreign regulatory agencies, if at all. We will not be able to commercialize our Technosphere Insulin System and other product candidates until we have obtained regulatory approval. We have no experience as a company in late-stage regulatory filings, such as preparing and submitting NDAs, which may place us at risk of delays, overspending and human resources inefficiencies. Any delay in obtaining, or inability to obtain, regulatory approval could harm our business.

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

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

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

Even if regulatory authorities approve any of our product candidates, they could approve less than the full scope of uses or labeling that we seek or otherwise require special warnings or other restrictions on use or marketing.

Regulatory authorities may limit the segments of the diabetes population to which we or others may market our Technosphere Insulin System or limit the target population for our other product candidates. Based on currently available clinical studies, we believe that our Technosphere Insulin System may have certain advantages over currently approved insulin products or pulmonary insulin products in development, including its approximation of the natural first-phase insulin release spike. Nonetheless, there are no assurances that these and other advantages, if any, of the Technosphere Insulin System have clinical significance or can be confirmed in head-to-head clinical trials against appropriate approved comparator insulin drug products. Such comparative clinical trials are required to make these types of superiority claims in labeling or advertising. These aforementioned observations and others may therefore not be capable of substantiation in comparative clinical trials prior to our NDA submission, if at all, or otherwise may not be suitable for inclusion in product labeling or advertising and, as a result, our Technosphere Insulin System may not have competitive advantages when compared to other insulin products.

The manufacture, marketing and sale of these product candidates will be subject to stringent and ongoing government regulation. The FDA may also withdraw product approvals if problems concerning safety or efficacy of

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the product occur following approval. In response to recent events regarding questions about the safety of certain approved prescription products, including the lack of adequate warnings, the FDA and Congress are currently considering new regulatory and legislative approaches to advertising, monitoring and assessing the safety of marketed drugs, including legislation providing the FDA with authority to mandate labeling changes for approved pharmaceutical products, particularly those related to safety. We also cannot be sure that the current Congressional and FDA initiatives pertaining to ensuring the safety of marketed drugs or other developments pertaining to the pharmaceutical industry will not adversely affect our operations.

We also are required to register our establishments and list our products with the FDA and certain state agencies. We and any third-party manufacturers or suppliers must continually adhere to federal regulations setting forth requirements, known as cGMP (for drugs) and QSR (for medical devices), and their foreign equivalents, which are enforced by the FDA and other national regulatory bodies through their facilities inspection programs. If our facilities, or the facilities of our manufacturers or suppliers, cannot pass a preapproval plant inspection, the FDA will not approve the marketing of our product candidates. In complying with cGMP and foreign regulatory requirements, we and any of our potential third-party manufacturers or suppliers will be obligated to expend time, money and effort in production, record-keeping and quality control to ensure that our products meet applicable specifications and other requirements. QSR requirements also impose extensive testing, control and documentation requirements. State regulatory agencies and the regulatory agencies of other countries have similar requirements. In addition, we will be required to comply with regulatory requirements of the FDA, state regulatory agencies and the regulatory agencies of other countries concerning the reporting of adverse events and device malfunctions, corrections and removals (e.g., recalls), promotion and advertising and general prohibitions against the manufacture and distribution of adulterated and misbranded devices. Failure to comply with these regulatory requirements could result in civil fines, product seizures, injunctions and/or criminal prosecution of responsible individuals and us. Any such actions would have a material adverse effect on our business and results of operations.

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

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

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

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

At present, there are a number of clinical trials being conducted by us and other pharmaceutical companies involving insulin delivery systems. If we discover that our product is associated with a significantly increased frequency of adverse events, or if other pharmaceutical companies announce that they observed frequent adverse events in their

trials involving the pulmonary delivery of insulin, we could encounter delays in the timing of our clinical trials or difficulties in obtaining the approval of our Technosphere Insulin System. As well, the public perception of our products might be adversely affected, which could harm our business and results of operations and cause the market price of our common stock to decline, even if the concern relates to another company's product. For example, in August 2004, an analyst reported that the United Kingdom Committee on the Safety of Medicines had expressed concern that a European application for approval of a drug for the treatment of diabetes was not

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licensable at the time. Earlier in 2004, Sanofi-Aventis, on behalf of Pfizer and Nektar, filed for regulatory approval in Europe of Exubera. Although the identity of the drug was not disclosed in the analyst's report, the news nonetheless triggered temporary but sharp declines in the market prices of Nektar's common stock as well as our common stock. There are also a number of clinical trials being conducted by other pharmaceutical companies involving compounds similar to, or competitive with, our other product candidates. Adverse results reported by these other companies in their clinical trials could delay or prevent us from obtaining regulatory approval or negatively impact public perception of our product candidates, which could harm our business and results of operations and cause the market price of our common stock to decline.

RISKS RELATED TO INTELLECTUAL PROPERTY

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

Our commercial success depends, in large part, on our ability to obtain and maintain intellectual property protection for our technology. Our ability to do so will depend on, among other things, complex legal and factual questions, and it should be noted that the standards regarding intellectual property rights in our fields are still evolving. We attempt to protect our proprietary technology through a combination of patents, trade secrets, know-how and confidentiality agreements. We own a number of domestic and international patents, have a number of domestic and international patent applications pending and have licenses to additional patents. We cannot assure you that our patents and licenses will successfully preclude others from using our technologies, and we could incur substantial costs in seeking enforcement of our proprietary rights against infringement. Even if issued, the patents may not give us an advantage over competitors with similar technologies.

Moreover, the issuance of a patent is not conclusive as to its validity or enforceability and it is uncertain how much protection, if any, will be afforded by our patents if we attempt to enforce them and they are challenged in court or in other proceedings, such as oppositions, which may be brought in US or foreign jurisdictions to challenge the validity of a patent. A third party may challenge the validity or enforceability of a patent after its issuance by the US Patent and Trademark Office, or USPTO.

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

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

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

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

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

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

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

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

Although we own a number of domestic and foreign patents and patent applications relating to our Technosphere Insulin System and cancer vaccine products under development, we have identified certain third-party patents that a court may interpret to restrict our freedom to operate (that is, to cover our products) in the areas of Technosphere formulations, pulmonary insulin delivery and the treatment of cancer. Specifically, we have identified certain third-party patents having claims relating to chemical compositions of matter and pulmonary insulin delivery that may trigger an allegation of infringement upon the commercial manufacture and sale of our Technosphere Insulin System. We have also identified third-party patents disclosing methods of use and compositions of matter related to DNA-based vaccines that also may trigger an allegation of infringement upon the commercial manufacture and sale of our cancer therapy. If a court were to determine that our insulin products or cancer therapies were infringing any of these patent rights, we would have to establish with the court that these patents were invalid or unenforceable in order to avoid legal liability for infringement of these patents. However, proving patent invalidity or unenforceability can be difficult because issued patents are presumed valid. Therefore, in the event that we are unable to prevail in an infringement or invalidity action we will have to either acquire the third-party patents outright or seek a royalty-bearing license. Roy